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AN OFFICIAL PUBLICATION OF PHILIPPINE COLLEGE OF CHEST PHYSICIANS

PHILIPPINE JOURNAL OF CHEST DISEASES
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The PCCP Interhospital Conferences: The Ties That Bind

Evelyn Victoria E. Reside, MD, FPCCP
Editor-in-Chief

Every year, the PCCP family recognizes the efforts of its training institutions by handing out a "Best Interhospital Conference" award during its Annual Chest Convention. Largely a recognition of the creativity and tireless efforts of its training fellows, the Interhospital Conference never fails to highlight the most uncommon, the more difficult, the less understood, and the least expected among the numerous clinical cases encountered by these trainees and their mentors.

Of course, there are other more subtle reasons why we celebrate the tradition of the Interhospital Conference. We value camaraderie and learning from each other, as these Conferences allow us to come together as a College; and we strongly encourage research, which is, after all, the foundation of all our Interhospital Conferences.

For what is an Interhospital Conference than a Case Report or Case Series or a State-of-the-Art Manuscript magnified a hundredfold on a wide screen? Like a research paper, it starts with a question, sparked by curiosity, and it ends with a conclusion and several valuable learning points. In the middle, there is the usual patient case, a review of pertinent literature and a discussion of the facts.

Although the PCCP has long had its website as the sounding board off of which our training institutions share the proceedings of our Interhospital Conferences, it is through this issue of the PJCD where we finally recognize and fulfill their potential as scientific articles. The Conference proceedings highlighted here have been formatted to comply with that of a formal scientific manuscript; and with the circulation

and reach of the PJCD, we are now able to provide all PCCP members an opportunity to learn from the Interhospital Conference.

The PJCD envisions these proceedings to be regular features of succeeding issues; as such, we encourage all training institutions to contribute their Interhospital Conference proceedings to the journal. After all, the Conference is considered an integral part of any training program, and showcases the best and most up-to-date information available to us. Much like a rite of passage, no Fellow completes his or her training without participating in the Interhospital Conference. These Conferences, therefore, are one of the ties that bind us: it is a singular and common experience among all Fellows-in-Training that cuts through both year levels of training, and through generations of graduates.

Simply put, this issue features a collection of manuscripts which form an integral part of our Fellows' training, and is the product of effective collaboration between trainee and mentor. It is, in the end, a testament to our lifelong commitment to continuous education and growth. Let us enjoy as we read through these pages, and perhaps, in doing so, relive and reminisce our own personal experiences as trainees and mentors.

INTERHOSPITAL CASE PRESENTATION

"Rise of the Machines": A Case Series of Chronic Pulmonary Illnesses on Noninvasive Ventilation

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LEARNING OBJECTIVES, RELEVANCE AND SIGNIFICANCE

Medicine is a dynamic system. There have been major advances in the therapeutic approach, and we have developed better technologies. With the latest innovation, we may have in our hands an important tool for modernizing pulmonary medicine that will hasten our response to our patients' changing needs. In this case series, we present the use of noninvasive ventilation (NIV) modalities in three chronic respiratory illnesses as a bridge to improve the quality and quantity of life.

This case series aims to present non-pharmacologic therapy as an adjunct treatment to severe chronic obstructive pulmonary disease (COPD), ventilatory failure secondary to neuromuscular disease (myasthenia gravis), and congestive heart failure with Cheyne-Stokes respiration; present the latest modes of non-invasive ventilator support; and discuss the application of non-invasive ventilation on specific disease entities.

THE CASES

Case 1 is GPJ, an 85-year-old female diagnosed with severe COPD. She had been on oxygen (O2) support since 1999, i.e., O2 at 2 L/min during daytime and bilevel positive airway pressure (BiPAP) at nighttime. O2 saturation was 90%–97%. Patient was wheelchair borne and dependent on assistance for all activities. She presented with shortness of breath with a little effort. Patient was maintained on maximal medical treatment (salmeterol plus fluticasone, doxofylline, ipratropium plus salbutamol nebulization, tiotropium, n-acetylcysteine, methylprednisolone, azithromycin and roflumilast). Despite this, patient had recurrent hospital admissions. NIV was considered to decrease the effort of breathing, improve quality of life, and reduce morbidity. Table 1 shows the arterial blood gases (ABG) of the patient on admission.

Table 1. Arterial blood gas results of Case 1

pO_2	60 mmHg
pH	7.42
pCO_2	56 mmHg
HCO_3	37 mmHg
O_2 saturation at 1 L/min	89%

Case 2 is MTI, a 45-year-old female diagnosed with myasthenia gravis s/p thymectomy. She was on chronic steroids and immuno-suppressant. Patient was maintained on BiPAP. She was referred to assess the need to maintain on noninvasive positive pressure ventilation (NPPV). Upon assessment, she was noted to have episodes of difficulty in breathing, a weak voice, and a reduced ability to cough. She has no history of chronic carbon dioxide (CO2) retention. She presented with mild proptosis and upper extremity weakness. Nocturnal polysomnograph with assisted ventilation showed that sleep and respiration were adequately stable on inspiratory positive airway pressure (IPAP) 12, expiratory positive airway pressure (EPAP) 7. Spirometry

showed no obstructive lung defect. The forced expiratory volume in 1 second (FEV1)/forced vital capacity (FVC) ratio was within normal levels. FVC was reduced, probably due to a restrictive lung defect. Post-exercise study after 15 minutes on the treadmill showed an 18% and 8% improvement in FVC and FEV1 values, respectively, from baseline. Maximal voluntary ventilation (MVV) was low relative to FEV1, suggesting poor effort and/or neuromuscular disorder. Table 2 shows the ABGs of the patient on admission.

Table 2. Arterial blood gas results of Case 2

pO_2	91.6 mmHg
pH	7.37
pCO_2	50.3 mmHg
HCO_3	37 mmHg
O_2 saturation at room air	Normal

Case 3 is MS, a 73-year-old male diagnosed with COPD, class D; obstructive sleep apnea on BiPAP; and severe congestive heart failure with ejection fraction of less than 30%. He was referred due to a recent increase in shortness of breath and inability to sleep well at night. Polysomnography showed that he had obstructive and central sleep apnea-hypopnea (Cheyne-Stokes respiration). Sleep study showed apnea-hypopnea index (AHI) of 53 events per hour, central apneas/hypopneas of more than five per hour (patient had 15 central and 18 hypopneic episodes) and significantly disrupted sleep.

DISCUSSION AND COMMENTARY

The respiratory system consists of the lungs for gas exchange and a respiratory pump, which regulates mechanical movement, for ventilation.[1] The respiratory pump and lungs may be impaired through different mechanisms. Lung impairment involves pulmonary dysfunction, where there is hypoxemia and hypocapnia, leading to hypoxic respiratory failure. Respiratory pump impairment, on the other hand, involves failure of ventilation where there is hypoxemia and hypercarbia. This dysfunction is addressed by ventilator support, through invasive or noninvasive means.

NIV emerged in the 1980s and assumed an important role in patients with acute and chronic respiratory failure. It paved the way to fewer complications (e.g., ventilator-associated pneumonia, longer hospital stays, trauma, pneumothorax), decreased need for sedation, and intermittent use. It also allows feeding and preserves the natural airway defense.

Disadvantages include the possibility of aerophagia, air leak, mask discomfort, and facial ulcers; slower correction of arterial blood gas abnormalities; and delayed intubation.[2] Newer modes of NIV allow us to control one variable or the other based on a feedback loop: Has the desired or set tidal volume been delivered? Is the airway pressure exceeding the set pressure limit?[3]

Hence, machines have emerged with cutting edge advancement to keep at the forefront of pulmonary medicine: BiPAP, average volume assured pressure support (AVAPS), and adaptive servo ventilation (ASV).

In patients with COPD but without acute exacerbation, NIV may be considered to reduce the effort of breathing. Pressure support is delivered with or without back-up rate and O_2 supplementation. Case 1, a stage 4 COPD, can benefit from BiPAP through increased quality of life, improved mobility and stamina, and lower cost due to reduced hospitalization and shortened length of stay.[4]

A study by Duiverman et al. concluded that NIV and pulmonary rehabilitation in COPD patients improved health-related quality of life, functional status, and gas exchange. Significant p values were noted in the fatigue domain, the cognition domain, daytime arterial CO_2 pressure, daytime minute ventilation, and the results of the Maugeri Respiratory Failure questionnaire. A separate study in 2014 by Kohnlein et al. concluded that hospital admissions were signifi-

cantly reduced in severe, stable COPD patients given NIV. There is strong supporting evidence that the unloading of the ventilator muscles with higher NIV doses in terms of pressure support and usage times improves ventilation of the alveoli and decreases chronic elevation of CO_2.[6]

Windisch et al. identified indications of NIV in patients with COPD: chronic daytime $paCO_2$ ≥50 mmHg; nocturnal $paCO_2$ ≥55 mmHg; stable daytime $paCO_2$ 46–50 mmHg and a PT_2CO_2 rise to 10 mmHg during sleep; stable daytime $paCO_2$ 46–50 mmHg and at least two acute exacerbations; respiratory acidosis requiring hospitalization within the last 12 months; and following an acute exacerbation needing ventilator support.

Case 1 had a $paCO_2$ of 56 mmHg and at least two exacerbations requiring hospitalization. She was hooked on BiPAP at nighttime, felt well and had fewer COPD exacerbations. She had no hospital admissions in the past 6 months and was undergoing pulmonary rehabilitation once a week. Although wheelchair borne, she was able to travel out of town.

Emerson Kerr categorized patients who will benefit from AVAPS:

- Respiratory muscle weakness: amylotrophic lateral sclerosis, myasthenia gravis, Duchenne's dystrophy
- Restrictive disorders: scoliosis, obesity, hypoventilation
- Obstructive lung disease: COPD, and cystic fibrosis.[10]

Winsdisch et al. enumerated the indications of NIV in neuromuscular disease patients:

- with presumptive symptomatic respiratory muscle weakness of vital capacity <70% predicted,
- chronic daytime $paCO_2$ ≥45 mmHg,
- nocturnal paCO2 ≥50 mmHg,
- daytime normocapnia with a rise of PT_2CO_2 to ≥10mmHg during the night, and
- rapid, significant reduction in vital capacity.

Case 2 had a chronic daytime $paCO_2$ >45 mmHg and a rapid, significant reduction in vital capacity. However, BiPAP may have been inadequate for this patient because she had decreased inspiratory effort, as well as muscle weakness associated with impaired ventilatory function. Tidal volume could not be assured. In addition, neuromuscular disease patients have a dynamic ventilatory requirement that BiPAP might not have met fast enough.

The patient was started on AVAPS. Nocturnal NIV prevents hypoventilation during sleep.[7] Lisboa et al. reviewed several studies on this population and the effect of nocturnal NIV on pulmonary mechanics. Intermittent nocturnal ventilation allows muscles to rest and recover, with a consequent improvement in inspiratory muscle function, ventilation, and arterial blood gases (ABGs) during the day. Function is improved by recruiting atelectatic zones; increasing distensibility; improving ventilation-perfusion (V/Q); and resolving daytime sleepiness, fatigue, morning headache, cognitive dysfunction, and dyspnea.[8] Combs et al. identified diseases-related factors that create the need for advanced positive airway pressure modalities: bulbar involvement, diaphragm weakness, upper extremities weakness, and rapid disease progression. Progression in neuro-muscular disease can predicate the need for volume-assured advanced modality to guarantee adequate ventilator assistance despite worsening neuromuscular weakness over the 1–2 month period.[9]

In patients with neuromuscular disease, AVAPS automatically increases pressure support to maintain the target tidal volume. According to Emerson Kerr's AVAPS and AutoSV advanced lecture, the IPAP level will not rise above the maximum IPAP even if the target tidal volume is not reached. Conversely, AVAPS will reduce pressure support as the patient's effort increases, and the IPAP will not fall below the minimum IPAP even if the target tidal volume is exceeded. The bilevel pressure support device automatically provides constant tidal volume per breath, for

which the patient is not aware of breath-to-breath changes.[10]

In case 2, AVAPS automatically adapted to the progression of myasthenia gravis, adjusted to the patient's needs, provided comfort, and improved her ventilatory function. With the machine, the patient had less difficulty breathing although still with muscle weakness. She was maintained on AVAPS at daytime, with no desaturation, and post-rituximab infusion.

According to Morgenthaler et al, the driving forces in the pathophysiology of complex apnea include ventilator instability associated oscillation in $paCO_2$, the related increase in CO_2 elimination, and the activation of airway and pulmonary stretch receptors triggering the central apneas.[11]

Case 3's history, clinical assessment, and polysomnograph showed that the patient tolerated BiPAP but had central sleep apnea–Cheyne Stokes respiration persistence despite correction of obstructive events. BiPAP resolved obstructive events only, but central apneas emerged.

We noted that ASV had the least total arousal index in patients with central sleep apnea, as opposed to those receiving O_2, CPAP, and BiPAP.[12] The study of Yoshihisa et al noted that patients with chronic heart failure and Cheyne–Stokes respiration who were placed on ASV had significantly improved NYHA functional classes, BNP levels, and cardiac systolic and diastolic functions for 6 months. Patients on ASV had a significantly lower AHI and respiratory arousal index compared to those on CPAP due to elimination of residual hypopnea (0.2±2.4 p=0.002 and 2.4±4.5 p=0.012, respectively).[11]

Case 3 used the ASV at night with no desaturation. He had no recent hospitalization and played golf. Patient claimed that with the machine, he had no daytime fatigue, no morning headache, no excessive daytime somnolence, and no sleep disruption. The machine automatically adjusted ventilation by adjusting IPAP to achieve target tidal volume and peak flow on a breath-to-breath basis. During Cheyne-Stokes respiration, the crescendo pattern of peak flow rates, IPAP decreased to dampen the rise in inspiratory peak flow rate or tidal volume. During decrescendo pattern of peak flow rates, the IPAP increased to dampen the fall in inspiratory peak flow rate or tidal volume, and a set back-up rate fired when central apneas ensued.[14]

LEARNING POINTS

- NIV has established itself as an important ventilator modality.
- NIV can be considered the modality of choice and adjunct for therapy in several forms of chronic respiratory insufficiency (COPD, neuromuscular disease, severe congestive heart failure).
- NIV offers comfort, convenience, safety and cost advantages.

RECOMMENDATIONS FOR PRACTICE AND RESEARCH

We recommend further studies to establish the long-term effect of NIV on these chronic illnesses. Plan of management should be discussed and catered according to the patient's needs, with the primary goal of patient comfort and improved quality of life. Further training must be done to educate medical practitioners in the proper use and indication of these machines.

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INTERHOSPITAL CASE PRESENTATION

"The Fault in Our Stars": A Rare Case of Primary Endobronchial Hodgkin's Lymphoma

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LEARNING OBJECTIVES, RELEVANCE AND SIGNIFICANCE

The differential diagnoses of endobronchial mass lesions are varied and broadly categorized into malignant and non-malignant; about 98% of these lesions tend to be malignant. Bronchogenic carcinoma and carcinoid tumors are among the most common primary malignancies that cause endobronchial obstruction. Less common causes are lymphoma and tumors of salivary origin.

We report the case of a 56-year-old male, smoker, presenting with a history of cough, hemoptysis and fever that failed to respond to medical treatment with antibiotic therapy. Further work-up revealed an endobronchial mass obstructing the right upper lobe bronchus. A final diagnosis of primary endobronchial Hodgkin's lymphoma (HL) was made based on histologic and immunohistochemical examination of tissue samples.

Primary endobronchial HL is a rare disease entity which may present with symptoms that can mimic a more common yet more devastating diagnosis such as bronchogenic carcinoma. When limited to the lung, HL can offer a chance for a better prognosis for the affected individuals.

This paper aims to present a patient's case, discuss the pathophysiology and causes of atelectasis, and discuss HL and its pulmonary manifestations, particularly endobronchial HL staging and treatment.

THE CASE

DC was a 56-year-old male, married, Filipino, local politician, who was admitted due to cough and fever. He was a known hypertensive and diabetic but was non-asthmatic. He had no previous hospital admissions or any history of treatment for pulmonary tuberculosis. Heredo-familial diseases included hypertension, diabetes mellitus, and a significant family history of malignancy, with one brother with colonic carcinoma and another with a brain tumor. He was a cigarette smoker with a 50-pack-year smoking history. He was a non-alcoholic beverage drinker, and he denied illicit drug use.

The history of present illness started one month prior to admission, with the onset of productive cough with whitish to yellowish sputum that occasionally turned "rusty". This was associated with fever of an undocumented temperature and the unintentional loss of about 10% of the patient's usual body weight. He initially tolerated the condition and took over-the-counter medications for symptomatic relief. However, persistence of his symptoms prompted admission at their local hospital, where he was managed as a case of community-acquired pneumonia and was given a seven-day course of piperacillin-tazobactam. There was, however, no improvement of his symptoms, thus prompting transfer to our institution for further management 10 days after his previous admission.

The patient was seen in the emergency room awake and not in respiratory distress. Aside from a slightly elevated blood pressure of 140/90 mmHg, his vital signs were stable. His oxygen saturation at

room air was 95%. Upon physical examination, there was no peripheral lymphadenopathy noted. Chest and lung auscultation revealed decreased breath sounds in the right apex but no other adventitious sounds. Other physical examination findings were unremarkable. His initial complete blood count (white blood cells 9.4 x1012/L, neutrophils 74%, lymphocytes 15%; hemoglobin 141 g/L, hematocrit 0.436; platelet count 389 x 1012/L) and electrolytes were within normal limits. Sputum samples were sent for acid-fast bacilli (AFB) smears and routine microbiologic culture. Pending the results of these tests, the patient was started on imipenem-cilastatin.

A chest radiograph revealed a triangular homogenous density in the right upper lobe associated with upward displacement of the minor fissure; these findings were consistent with right upper lobe atelectasis. There was also a convex density in the right hilar region suspicious of a hilar mass (Figure 1). These findings were confirmed by chest computed tomography (CT), which showed atelectasis of the right upper lobe with subsequent elevation of the right hemidiaphragm and decrease in the right lung volume. There was also a note of a slightly enhancing heterogeneous mass in the right suprahilar region with suspicious encroachment into the right main bronchus (Figure 2). The chest CT scan further revealed enlarged right paratracheal and subcarinal lymph nodes (Figure 3). The rest of the lung parenchyma was unremarkable.

Flexible bronchoscopy was done to further evaluate the cause of the obstruction and to obtain tissue for a more definitive diagnosis. It showed nodular lesions on the posterior wall of the trachea about 5 centimeters from a blunted carina. There was also a fungating mass that was seen completely occluding the orifice of the right upper lobe (Figure 4). The rest of the bronchial segments were patent. Biopsy samples from both the tracheal lesions and the right upper lobe mass were taken and sent for routine histopathology.

Sputum AFB smears were negative. The final sputum culture grew *Candida albicans*, likely a

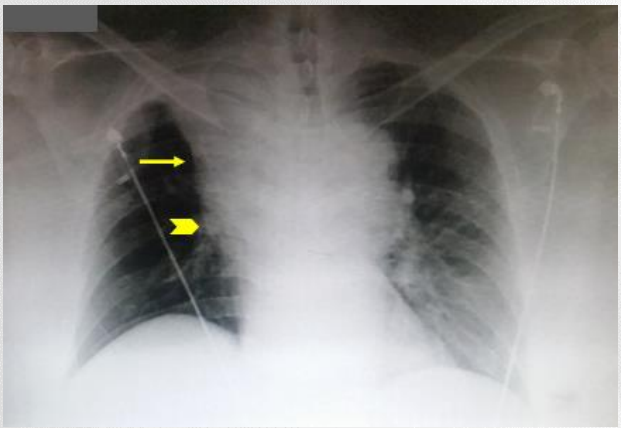

Figure 1. Postero-anterior chest radiograph showing right upper lobe atelectasis (yellow arrow) and a suspicious right hilar density (arrowhead)

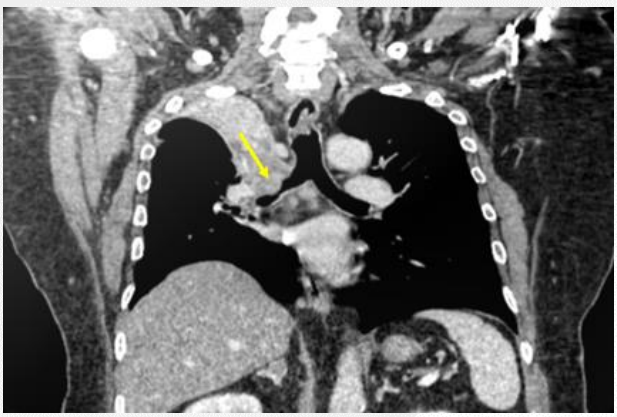

Figure 2. Coronal view of the chest showing right upper lobe atelectasis, elevated right hemidiaphragm and a suspicious right suprahilar mass (arrow) encroaching on the right main bronchus

contaminant. At that time, the primary consideration was bronchogenic carcinoma, particularly squamous cell carcinoma. Although the patient continued to have episodes of low-grade fever, he remained stable in all other ways. Thus, he was discharged while awaiting final biopsy results.

After 3 weeks, he was readmitted for diarrhea. During the course of his second admission, he was noted to have dyspnea and increasing oxygen requirement, from a baseline oxygen saturation of 96% at room air, to as low as 87% at 4 liters per minute via nasal cannula.

Physical examination revealed decreased breath sounds in the right lung field and decreased vocal fremitus.

Arterial blood gas showed metabolic alkalosis with uncorrected hypoxemia at 44% FiO_2 (pH 7.49, pCO_2 35.1 mmHg, HCO_3 26.4 mmHg, pO_2 78 mmHg, sO_2 96.2%).

Repeat chest radiograph showed complete opacification of the right hemithorax with rightward deviation of the tracheal air column and abrupt cut-off of the right main bronchus (Figure 5). This was suggestive of massive atelectasis of the right lung with a probable concomitant minimal right pleural effusion.

After initial stabilization of his oxygenation with supplemental oxygen, the patient was scheduled for a repeat bronchoscopy. This revealed interval disappearance of the previously noted tracheal lesions but an interval increase in the size of the endobronchial mass lesion in the right upper lobe, which now extended into the right main bronchus, causing about 90% stenosis (Figure 6). The lesion was observed to be very friable, oozing blood even prior to any intervention. Electrocautery was offered to the patient, but he refused the intervention, opting to await the final biopsy result for a more definitive treatment.

Histologic examination of the tracheal lesions showed respiratory epithelium-lined tissues with severe acute and chronic inflammation. Biopsy of the right upper lobe endobronchial mass was consistent with a poorly differentiated malignant neoplasm, to consider Hodgkin's lymphoma (HL) versus a neuroendocrine carcinoma. Immunohistochemical staining of the right upper lobe mass revealed a lesion that was negative for the following: cluster differentiation (CD) 20, CD3, cytokeratin, neuron-specific enolase (NSE) and vimentin. It was, however, positive for CD30, thus clinching the diagnosis of HL.

Initial staging was done by abdomino-pelvic CT scan, which revealed a normal-sized liver and spleen and no lymphadenopathy. Positron emission tomography (PET) was advised, but the patient refused the imaging test. He was also advised to have a bone marrow biopsy, but he again refused the procedure. Since his initial complete blood count was unremarkable, the patient was treated for stage II-B disease based on the involvement of two lymph node regions on one side of the diaphragm and the absence of

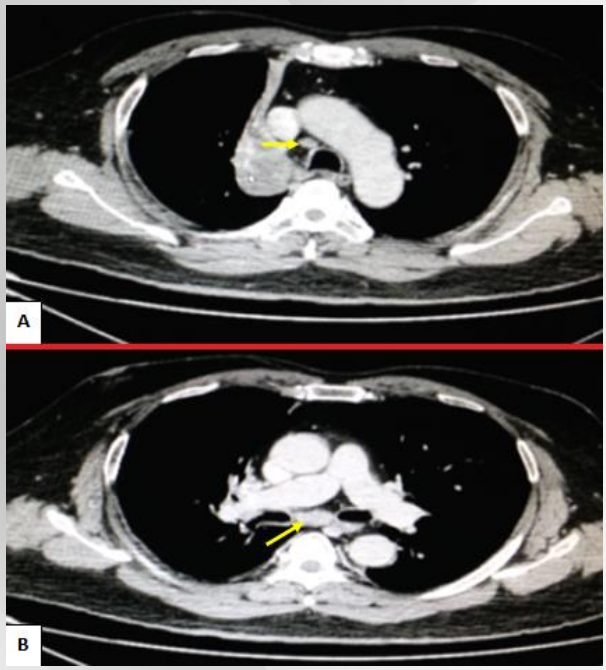

Figure 3. Axial views of the chest showing enlarged right paratracheal (A) and subcarinal lymph nodes (B)

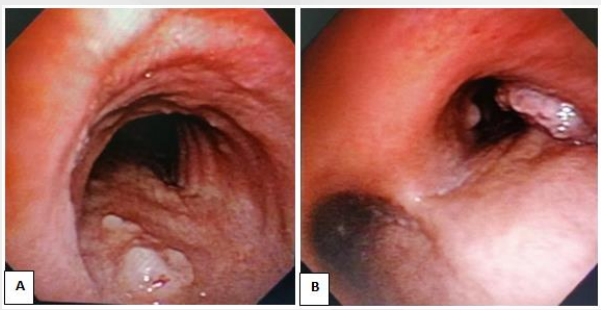

Figure 4. Nodular lesions on the posterior wall of the trachea (A) and a fungating mass completely occluding the right upper lobe bronchus (B)

extrathoracic extension.

The patient underwent six cycles of chemotherapy with a doxorubicin, bleomycin, vinblastine and dacarbazine (ABVD) regimen. He had significant improvement of his symptoms and a dramatic response radiographically. A repeat chest radiograph taken one month after he started chemotherapy showed resolution of the right upper lobe atelectasis, with only residual linear and hazy densities in the right upper lobe (Figure 7).

A repeat chest CT scan taken after the patient completed six cycles of chemotherapy revealed re-expansion of the atelectatic right apical segment, disappearance of the right suprahilar mass (Figure 8) and significant reduction in the size of the paratracheal and subcarinal nodes (Figure 9).

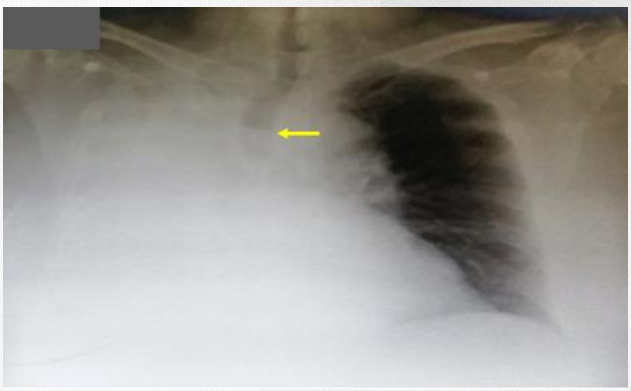

Figure 5. Antero-posterior chest radiograph showing a completely opacified right hemithorax and rightward deviation of the tracheal air column (arrow)

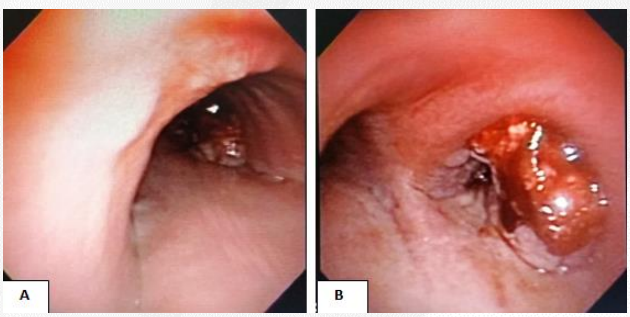

Figure 6. Interval disappearance of the tracheal lesions (A) but an increase in the size of the endobronchial mass lesion in the right upper lobe bronchus (B)

Although he remained in remission for almost 2 years, the patient eventually had recurrence of persistent low-grade fever and inguinal lymphadenopathy. Inguinal node biopsy and immunostaining confirmed the recurrence of HL. A repeat chest CT scan showed the presence of multiple pulmonary nodules. The patient was again advised to have a bone marrow biopsy, to which he consented. The bone marrow biopsy revealed no bone marrow involvement. He was given salvage chemotherapy with ifosfamide, carboplatin and etoposide, but he was unresponsive to this regimen and eventually succumbed to the disease.

DISCUSSION AND COMMENTARY

Atelectasis

Atelectasis, defined as a loss of lung volume due to collapse of lung tissue, is one of the most commonly encountered abnormalities on chest radiographs. It may be classified, based on its pathophysiologic mechanism, as obstructive or non-obstructive. Non-obstructive atelectasis may be due to (1) passive atelectasis, which results from loss of contact between the parietal and visceral pleura, such as in cases of

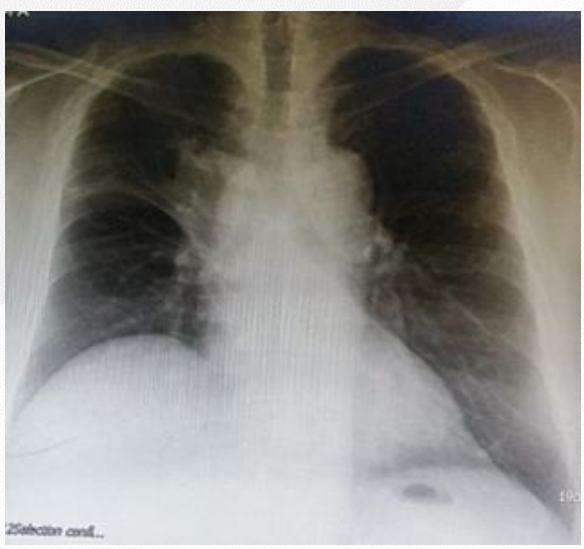

Figure 7. Postero-anterior chest radiograph after month 1 of chemotherapy

pneumothorax or pleural effusion; (2) compressive atelectasis, which results from parenchymal compression by a space-occupying lesion; (3) adhesive atelectasis, which results from surfactant loss or dysfunction, like in acute respiratory distress syndrome; and (3) cicatrization atelectasis, which is a consequence of scarring from chronic inflammatory processes. Pulmonary atelectasis may result from bronchial obstruction that eventually causes resorption of the air from the non-ventilated alveoli distal to the obstruction, resulting in the subsequent collapse of the affected regions.[1,2]

Our patient presented with cough, fever and weight loss and had atelectasis on his baseline chest radiograph. Although community-acquired pneumonia and pulmonary tuberculosis were among our primary considerations, a pulmonary malignancy could not be ruled out, given the patient's significant smoking history and age. This differential diagnosis became even more likely upon demonstration of a right suprahilar mass on his chest CT scan.

Further work-up with bronchoscopy showed a fungating endobronchial mass lesion, which on biopsy and immunohistochemistry was established to be HL.

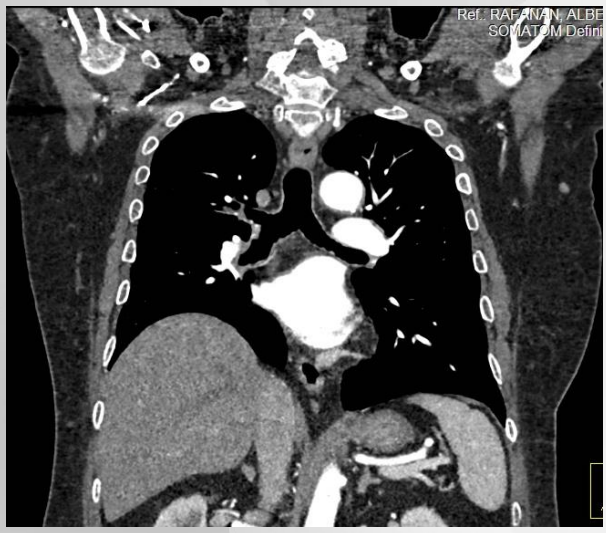

Figure 8. Coronal view of the chest showing re-expansion of the atelectatic right apical segment and disappearance of the right suprahilar mass

Endobronchial Hodgkin's Lymphoma

HL (formerly known as Hodgkin's disease) arises from the germinal center of B cells and has a unique cellular composition containing a minority of neoplastic cells, such as Reed-Sternberg cells or their variants, in an inflammatory background. It accounts for about 10% of all lymphomas and 0.6% of all cancers diagnosed in the developed world annually.[3] It has a bimodal distribution, peaking in young adults aged 15–34 years and again in adults over 55 years old.

HL presents as a painless mass in approximately 70% of cases, with the neck as the most commonly involved site. However, late in

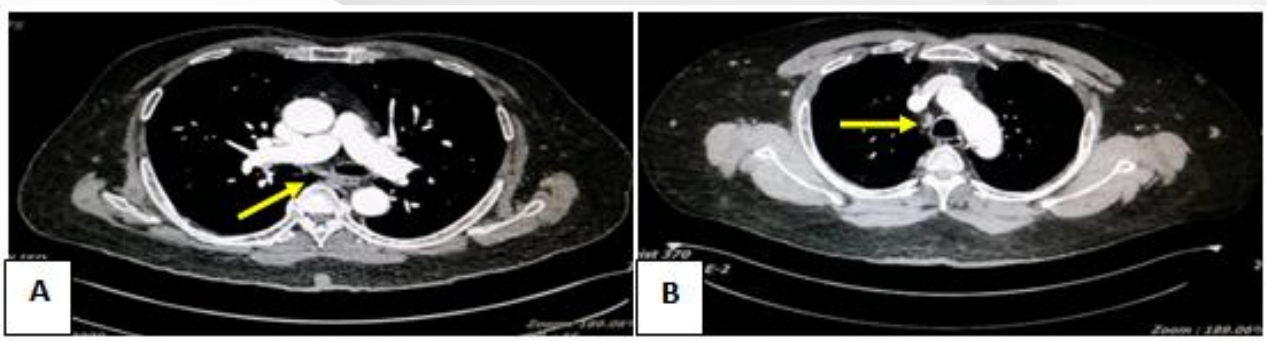

Figure 9. Axial views of the chest showing significant reduction in the size of the right paratracheal (A) and subcarinal lymph nodes (B)

the course of the disease, vascular invasion often leads to widespread hematogenous dissemination.[4] Although HL primarily affects the lymphatic tissues, it may present in extranodal organs, including the lungs.

Pulmonary involvement of HL is seen in 15%–40% of cases but most commonly in disseminated disease. Rarely, HL can primarily involve the lungs. Two criteria have been proposed for diagnosing primary pulmonary HL: (1) involvement of the lungs, whether lobar or primary bronchus, with or without mediastinal involvement; and (2) no other evidence of extrathoracic lymphoma at the time of diagnosis.[5] Our patient had endobronchial HL with mediastinal adenopathy but no extrathoracic involvement seen on preliminary staging.[6,7]

As a primary pulmonary pathology, HL is very uncommon, with fewer than 100 cases reported. Radiographically, primary pulmonary HL often appears as a solitary mass, a multinodular disease, or a cavitary lesion. Although the bronchi are frequently involved in disseminated disease, primary endobronchial lesions are rare. In a literature review by Tredaniel et al.,[8] only nine cases of HL primarily presenting

as an endobronchial tumor were observed over a 10-year period. To be recognized as endobronchial presentation of HL, the cases had to fulfill two criteria: (1) histological features of Hodgkin's disease and (2) bronchoscopic visualization of an endobronchial tumor at the time of the initial diagnosis of the disease in the absence of other parenchymal lung involvement. Our patient fulfilled both.

In a more recent literature review by Kiani et al.,[9] 26 patients presenting with endobronchial HL fulfilling the above criteria were identified. In the same literature review, the most frequent symptom was cough, seen in up to 80% of patients. It was followed by hemoptysis and dyspnea, seen in 35% and 30% of cases, respectively. About half of the patients were also reported to have B symptoms (i.e., fever, weight loss, night sweats). Our patient presented with cough and hemoptysis ("rusty" sputum) and had associated constitutional symptoms, including weight loss and fever.

The treatment of HL is primarily guided by the clinical stage of the disease as determined by the Ann Arbor Classification. Stage I refers to involvement of a single lymph node region; stage II, involvement of two or more lymph node regions on the same side of the diaphragm; stage III, involvement of lymph node regions or structures on both sides of the diaphragm; and stage IV, disseminated disease or involvement of one or more extranodal organs.

Stage I and II diseases are considered early-stage diseases and are further stratified into favorable- and unfavorable-prognosis diseases based on the presence or absence of certain clinical features. The European Organization for the Research and Treatment of Cancer (EORTC) defines the favorable prognostic group as patients aged 50 years or younger; without large mediastinal adenopathy; with an erythrocyte sedimentation rate of less than 50 mm/hr and no B symptoms; and disease limited to three or fewer regions of involvement.[10]

Most patients with HL will attain remission after induction chemotherapy, with or without radiation. However, relapse rates can range from 10%–20% in stage I and stage II diseases with favorable prognostic factors;11 they may reach up to 30%–40% in patients with unfavorable prognostic factors or more advanced diseases.12-16 Our patient, being 56 years old and presenting with B symptoms, had unfavorable stage II disease. Although he was highly responsive to induction chemotherapy, he eventually had a relapse of HL.

LEARNING POINTS

- HL presenting as pulmonary disease is rare.
- While HL often disseminates, its limitation to the lung may offer a chance for early treatment and a better prognosis as a result.
- Infrequently, the presence of unfavorable prognos-

tic factors increases the chances of relapse, dimming the prognosis of an otherwise treatable disease.

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INTERHOSPITAL CASE PRESENTATION

Thymic carcinoid tumor mimicking lung adenocarcinoma: a case report

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LEARNING OBJECTIVES, RELEVANCE AND SIGNIFICANCE

Carcinoid tumors arising primarily from the thymus are rare. Descriptions of their histologic variants are limited because of the scarcity of available literature, which mainly includes case reports and small case series. Cytologic features can even be confused with other tumor types, leading to misdiagnosis.

This paper presents the case of a previously diagnosed and managed lung adenocarcinoma that, upon further work-up, turned out to be a rare case of thymic carcinoid tumor. This report aims to increase knowledge on less common thoracic tumors that may mimic lung adenocarcinoma.

THE CASE

A 57-year-old male, retired soldier, married, Catholic, from Bacoor, Cavite, was admitted with a chief complaint of 2 months persistent cough and sputum production, with no consultation done and no medications taken.

One day prior to admission, the cough was accompanied by blood-streaked sputum and dyspnea even at rest. This condition prompted consultation at a local hospital in Cavite. Due to the hospital's lack of facilities, the patient was transferred to a medical center in Manila. Upon arrival at the said medical center, the patient was received in severe respiratory distress, tachypneic at 40 breaths per minute, and with an SpO2 of 50% at room air. He was eventually intubated. Then, due to his veteran status, he was transferred to the Veterans Memorial Medical Center for continuity of care.

Upon review of the patient's medical history, his doctor found that he was previously diagnosed with lung adenocarcinoma stage III-A (T3N2Mx) at a local hospital in Zamboanga City in May 2012, after he had undergone bronchoscopy and CT-guided biopsy for an incidental radiographic finding of an anterior mediastinal mass in an annual physical examination at the Western Mindanao Command. However, in the official histopathology report, the specimen was labelled as a right lung mass rather than an anterior mediastinal mass.

The patient moved to Manila in July 2012 and consulted at a local hospital there. He was started on chemotherapy using the paclitaxel/carboplatin protocol for 6 cycles and anti-tuberculosis (TB) therapy category I regimen for 6 months. He was advised to return for follow-up every three months thereafter, but he complied for two subsequent visits only.

Review of family history revealed that his sister had cervical cancer and his father was asthmatic. He was previously a 30-pack-year smoker and an occasional alcoholic-beverage drinker.

Upon arrival at the emergency room, he was noted to be conscious, coherent, and able follow commands. He was intubated with the following vital signs: blood pressure, 100/60 mmHg; cardiac rate, 112 beats per minute; respiratory rate, 32 cycles per minute; oxygen saturation, 98% at 40% FiO2; and temperature, 37.6°C. There was a note

of left supraclavicular lymphadenopathy. On auscultation, there was a note of crackles in both lung fields and dullness in the left lung base. There was a note of nail clubbing as well.

Chest radiograph revealed a non-homogenous opacity at the right parahilar area exhibiting the hilar overlay sign. The left lung showed patchy infiltrates from the second anterior intercostal space to the base, obscuring the hemidiaphragm and confirming the presence of pneumonia (Figure 1).

He was managed at the pulmonary intensive care unit as a case of acute respiratory failure type I from high-risk community-acquired pneumonia and obstructive pneumonia in the background of the history of lung adenocarcinoma stage III-B (T4N2Mx). He was put on mechanical ventilatory support, and intravenous piperacillin-tazobactam was administered. Concomitantly, the second sputum specimen revealed 3+ for acid-fast bacilli, while GeneXpert/ MDRTB screening had the result of "MTB not detected."

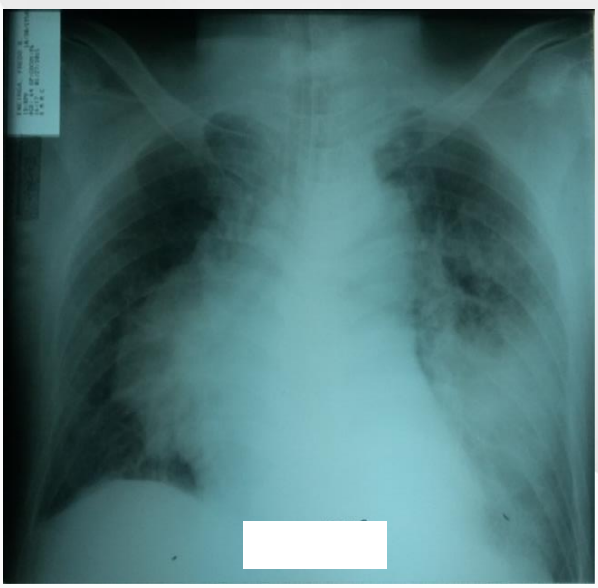

Figure 1. Chest radiograph, posteroanterior view showing a non-homogenous opacity at the right parahilar area, and left patchy infiltrates from the second anterior intercostal space to the base

He was started on category II anti-TB regimen. He clinically improved and was subsequently extubated and transferred to the regular ward.

A high index of suspicion on the incompatibility of the patient's disease course for lung adenocarcinoma prompted a review of the case. Repeat chest computed tomography (CT) was requested and done, revealing a large heterogeneously enhancing mass in the right paramediastinal, extending into the anterior mediastinum, measuring 11.4 x 8.7 x 5.0 cm (Figure 2). The mass was slightly compressing the left brachiocephalic vein and superior vena cava, as well as the right upper and middle lobes. Minimal pleural effusion in the left hemithorax, compressive atelectasis and multiple mediastinal lymph node were also noted.

He was referred to thoracocardiovascular surgery and underwent ultrasound-guided core needle biopsy. While waiting for the final histopathologic diagnosis, he was discharged

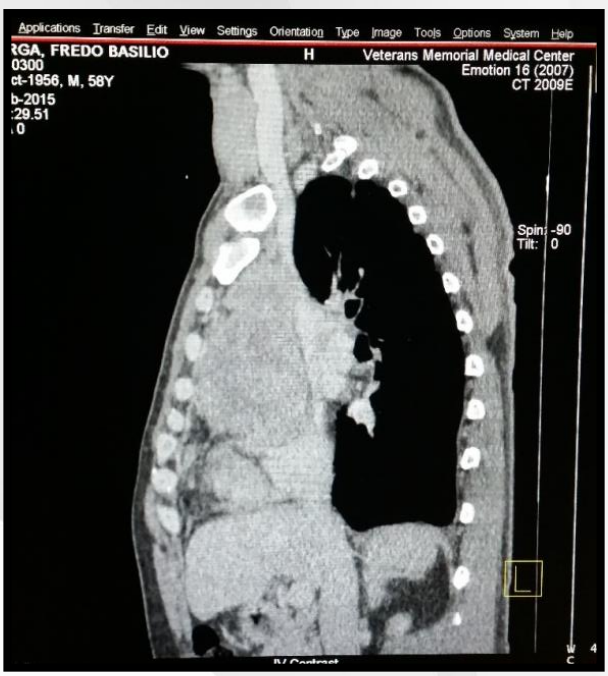

Figure 2. Contrast-enhanced CT scan of the chest showing large heterogeneously enhancing mass

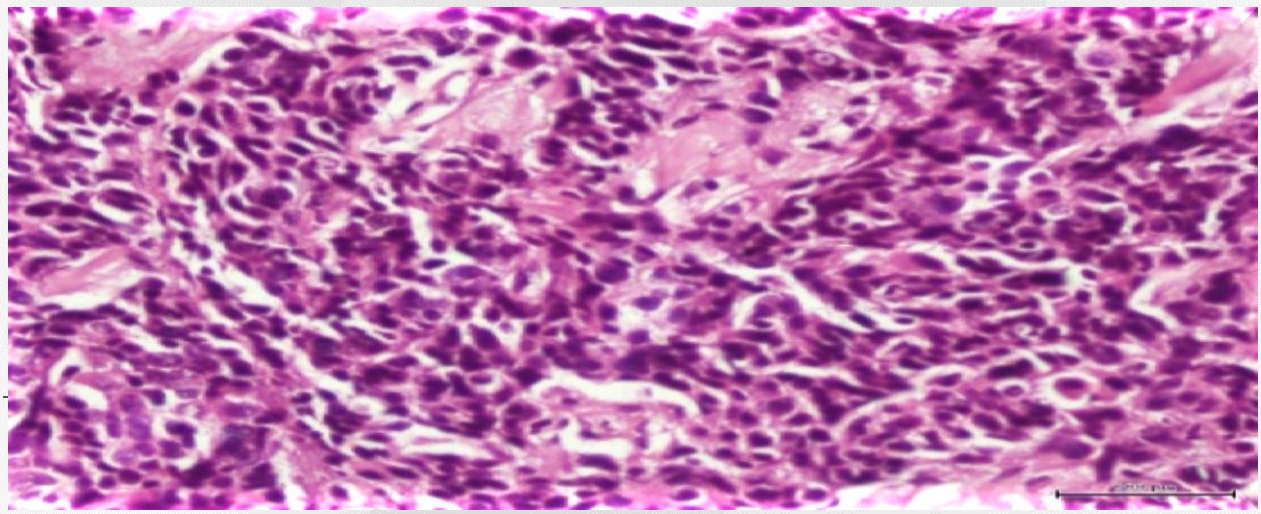

Figure 3. Pictomicrograph showing round to polygonal neoplastic epithelial cells with vesicular nuclei and prominent nucleoli with few lymphocytic cells infiltrating the fibrohyalinized stroma

improved while on pulmonary TB treatment.

Histopathologic report revealed "round to polygonal neoplastic epithelial cells with vesicular nuclei and prominent nucleoli with few lymphocytic cells infiltrating the fibrohyalinized stroma" (Figure 3). Immunohistochemical studies revealed TTF-1 negative and chromogranin A positive, leading to the final diagnosis of thymic carcinoid tumor.

Upon follow-up, disclosure was done and future management plans were discussed, but he was undecided of any intervention since he was asymptomatic and stable.

DISCUSSION AND COMMENTARY

Thymic carcinoid tumors were first identified as a separate entity from thymomas by Rosai and Higa in 1972.[1] Their overall age-adjusted incidence is 0.02/100,000 population per year, with a predilection for men at a 3:1 male-to-female ratio.[2]

A clinicopathologic study on 80 cases of carcinoid tumors of the thymus by Moran and Suster in 2000[3] concluded that thymic carcinoid tumors are histologically divided into low, or well-differentiated tumor type; intermediate, or moderately differentiated tumor type; and high, or poorly differentiated tumor type. The same study revealed that histologic grading has correlation with clinical behavior but not on tumor behavior. Well-differentiated tumors follow a relatively indolent course, like in this case. However, this study also observed that there were areas showing well-differentiated carcinoids in direct transition with areas of poorly differentiated carcinoids, which were indistinguishable from those of small-cell carcinoma of the lung. This supports the notion that these tumors represent part of a continuous spectrum of differentiation that ranges from well-differentiated through poorly differentiated neuroendocrine neoplasm.

Cytomorphologically, thymic carcinoid tumor cells can be confused with small-cell carcinoma, lymphoma, adenocarcinoma, plasmacytoma or neuroblastoma.[4] This is a plausible explanation for the misdiagnosis of adenocarcinoma in this case, apart from human error and mislabelling.

Duh et al.[5] stated that thymic carcinoids are clinically malignant in approximately 82% of cases, whereas bronchial carcinoids are malignant in only 26% of cases. Valli et al.,[6] in a study on thymic carcinoids, concluded that when such

tumors are located in the mediastinum, they essentially represent the equivalent of "atypical carcinoids" of the lung. They have the ability to invade adjacent structures in 30%–50% of cases, of which 88% spread to adjacent tissues, 40% to intrathoracic lymph nodes and 30% to either the lungs, bone or liver.[7]

Thymic carcinoid tumors manifest as incidental radiographic findings with no symptoms in one-third of cases,[7] such as this one.

Functionally active thymic carcinoid tumors present with endocrine abnormalities, either because of adrenocorticotrophic hormone secretion in Cushing's syndrome or because of their association with other endocrine neoplasms such as in multiple endocrine neoplasia types I and II.[7] They may produce acute symptoms of thoracic structure displacement or compression such as superior vena cava syndrome or cough and chest pain;[7] aside from pneumonia, superior vena cava syndrome was entertained in this patient because of the abutment of the mediastinal mass to the right brachiocephalic vein and superior vena cava. They may also present signs and symptoms of distant metastasis to the liver, lung, pancreas, pleura and bone.[7]

The European Society for Medical Oncology (ESMO)[2] clinical practice guidelines suggest chest X-ray followed by CT scan in the work-up of such patients. Specimens for histopathologic evaluation may be acquired from surgical excisions, CT-guided fine needle aspiration biopsy, or mediastinoscopy; sometimes thoracotomy may be required. In this case, ultrasound-guided core needle aspiration biopsy was done.

Immunohistochemical stains provide characteristic patterns for thymic neuroendocrine tumors. These have demonstrated reactivity for cytokeratins in virtually all cases. Seventy-five percent react positively with chromogranin A,[7] like in this case.

The primary treatment involves the complete resection of the tumor to the greatest extent possible. Existing literature has documented a recurrence rate as high as 67% after surgery. Recurrent local disease should be addressed surgically as well. Palliative surgical resection or debulking is indicated in patients with large compressive tumors, with tumor spread to the liver or other organs. Radiotherapy should be considered before and after operation, particularly in patients with capsular invasion.

The use of adjuvant radiation therapy and chemotherapy is controversial and has demonstrated variable levels of success. Drugs such as 5-fluorouracil, streptozocin, carmustine, VP-16 and cisplatin have been used but without significant effect on recurrence rates and overall survival.

Functional carcinoids rich with somatostatin receptors may be offered with somatostatin analogues such as octreotide and peptide receptor radiotherapy. However, the use of octreotide has been best studied in gut carcinoids, not in thymic carcinoids. To date, no randomized trials have been performed that could guide the treatment of thymic carcinoid tumors.[2]

The prognosis of patients with thymic carcinoid tumors is poor regardless of histopathologic features because of these tumors' tendency to local and distant metastases and their high incidence of recurrence after surgery.[7]

The 5-year and 10-year survival rates without intervention are 50% and 9%, respectively, in low-grade tumors; 20% and 0%, respectively, in moderate-grade tumors; and 0% in high-grade tumors. But even with extensive surgical excision, radiotherapy and chemo-therapy, the 5-year and 10-year survival rates are 29% and 9%, respectively, regardless of histopathologic type.[7]

LEARNING POINT

- The relatively indolent course of an anterior mediastinal mass despite adequate intervention should heighten the suspicion of an alternative disease entity apart from lung adenocarcinoma.
- The cytomorphology of thymic carcinoid

tumor cells can be confused as small-cell carcinoma, lymphoma, adenocarcinoma, plasmacytoma or neuroblastoma.

- The primary treatment for thymic carcinoid tumors include resection, although recurrence is high. Surgery also has a palliative role. Radiotherapy should be considered, particularly in patients with capsular invasion. Chemotherapy has failed to show significant benefit.

RECOMMENDATIONS FOR PRACTICE AND RESEARCH

The rarity and scarcity of available literature regarding anterior mediastinal tumors like the thymic carcinoid make diagnosis and management of the tumor challenging. More research is needed on the clinical course and early detection of this disease, as it is very often diagnosed only in its advanced stages. The presence of histologic variants and close mimickers (e.g., adenocarcinoma) make diagnosis even more difficult. Immunohistochemistry is a tool that could improve diagnostic yield, and should therefore be investigated.

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INTERHOSPITAL CASE PRESENTATION

"The road less travelled": an interhospital case presentation on TB patients with airway-esophageal fistula

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LEARNING OBJECTIVES, RELEVANCE AND SIGNIFICANCE

According to the HIV/AIDS and Antiretroviral Therapy Registry of the Philippines (HARP),[1] there was an increasing number of human immunodeficiency virus (HIV) cases reported in the Philippines in 2015. Majority of the infected demographic is male and aged 25–34 years old. Because of this, more people in this age group easily acquire respiratory diseases such as pneumonia and pulmonary tuberculosis (PTB).

This case presentation aims to discuss two cases of young immunocompromised patients presenting with cough, choking and dyspnea. It hopes to thereby increase awareness and raise the index of suspicion among healthcare individuals. It also intends to show the approach to diagnosis and management of recurrent choking in these patients.

THE CASES

Case 1 is VF, a 30-year-old male, single, who consulted due to difficulty of breathing.

Three months prior to admission, the patient started to have non-productive cough accompanied by night sweats and weight loss. This was associated with undocumented fever and generalized weakness.

One month prior to admission to our hospital, the patient was admitted for persistence of symptoms. He underwent work-up, which revealed normal results on chest radiograph and a positive acid-fast bacilli (AFB) smear result of 1+.

He was diagnosed with PTB category 1, bacteriologically confirmed, and was started on category 1 anti-TB regimen.

In the interim, the patient's symptoms improved. Two weeks prior to admission, the patient started to have difficulty swallowing both liquids and solids, with frequent choking episodes. Outpatient consultation was made with his attending physician.

A barium swallow was done. On oblique view, a slight protrusion of the esophageal wall was observed, adjacent to the trachea. On apico-posterior view, the contrast material could be seen outlining the tracheobronchial tree upon reaching the level of the T4 vertebra, confirming a direct communication between the esophagus and the trachea (Figure 1).

Further work-up with a chest computed tomography (CT) scan revealed erosions and ulcerations along the esophagus (Figure 2). The patient was advised admission. However, he refused.

On the night prior to admission, the patient started to have cough productive of whitish to yellowish phlegm, with occasional blood streaks, and dyspnea. He was then brought to our institution and was subsequently admitted.

Review of systems was unremarkable.

Medical history was positive for gastritis in 2014, for which he was given omeprazole. He had a family history of hypertension. He was a non-smoker and an occasional alcoholic beverage drinker. He was single and denied having had any

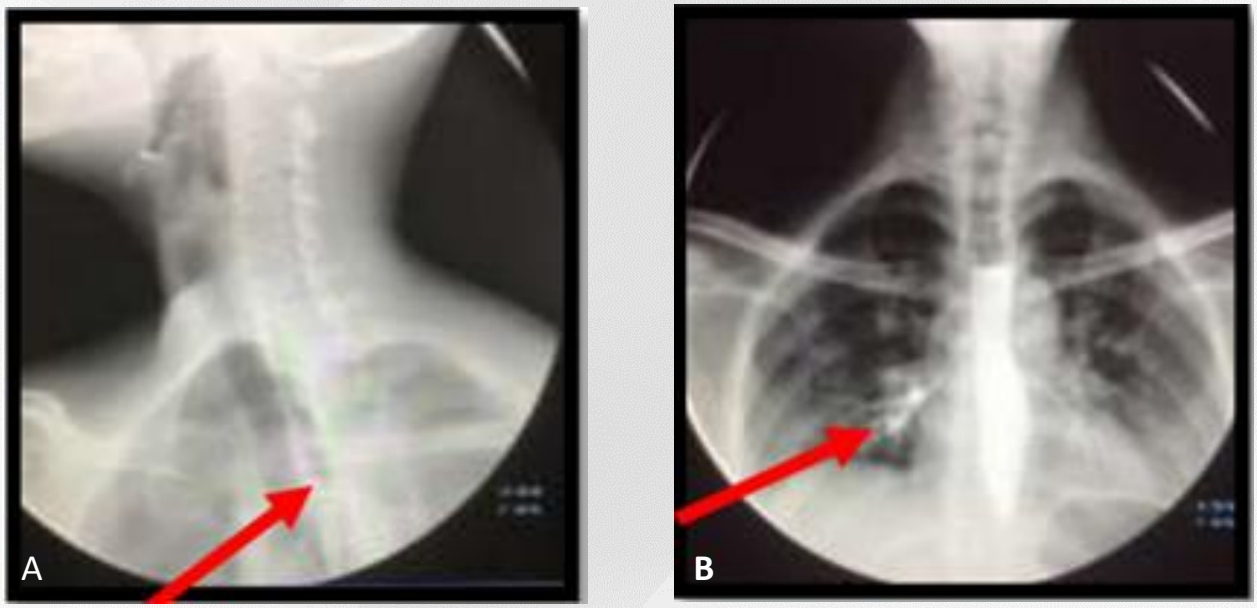

Figure 1. Case 1. A. Barium swallow oblique view (left) showing slight protrusion of the esophageal wall adjacent to the trachea (arrow). B. Apico-posterior view (right) showing contrast material outlining the tracheobronchial tree (arrow).

sexual contact.

On physical examination, he was found normotensive, tachycardic, tachypneic and febrile. He was hypoxemic at room air. Head and neck examination revealed a palpable left cervical lymph node. Chest and lung examination showed symmetric chest expansion, supraclavicular retractions and bilateral crackles. No wheezes or rhonchi were noted. Other physical examination findings were unremarkable.

On work-up, he was noted to have leukocytosis with neutrophilic predominance. Arterial blood gas taken at 44% FiO2 showed maximally compensated respiratory alkalosis with more than adequate oxygenation.

Sputum microscopy revealed a moderate growth of Candida albicans. Sputum AFB test showed negative conversion; during this time, the patient was already on his second month of intensive phase anti-TB treatment. Sputum TB GeneXpert was positive for Mycobacterium tuberculosis with no resistance to rifampicin.

Chest radiograph revealed hazy and ill-defined densities in the bilateral mid- to lower-lung fields (Figure 3).

The working diagnoses at that time were aspiration pneumonia; PTB category 1, bacteriologically confirmed; and tracheo-esophageal fistula (TEF).

For his aspiration pneumonia, he was given piperacillin-tazobactam. To address his PTB, category 1 anti-TB regimen was started. And for his TEF, he was put on *nil per os* (NPO) to prevent aspiration. Referrals to gastroenterology and thoracic and cardiovascular surgery (TCVS) services were done.

The thoracic surgeon made the following recommendations: treat the pneumonia, finish the intensive phase of his TB treatment, and achieve nutritional build-up as manifested by adequate weight gain and a target albumin level >3.0 mg/dl.

On his third hospital day, the patient underwent peg insertion. On endoscopy, there were whitish plaques along the entire length of the esophagus. There was also a fistulous tract located 25 cm from the incisors (Figure 4). The rest of the hospital stay was unremarkable, and

the patient was discharged on his eighth hospital stay with clinical and radiographic improvement of his infection.

Three months later, the patient was deemed well enough to undergo surgery. He successfully underwent right thoracotomy with TEF repair. A specimen was sent for histopathologic studies; it showed fibrous tissue with chronic inflammation.

Barium swallow was done 1 week after the surgery to determine the patency of the fistulous tract. Absence of the dye in the tracheobronchial tree signified successful closure of the fistula (Figure 5).

Case 2 is FD, a 33-year-old male who consulted due to body weakness.

His history started 1 month prior to admission, when he began to have non-productive cough accompanied by undocumented fever. Consultation was done with a physician who diagnosed him to have acute bronchitis and prescribed co-amoxiclav for 7 days, affording temporary relief. However, 2 weeks prior to admission, the patient's cough persisted, now productive of yellowish phlegm. He also had chills, anorexia, generalized body weakness and undocumented weight loss. He consulted at a nearby hospital, where he was diagnosed with pneumonia and oral candidiasis. He was given co-amoxiclav and fluconazole. However, the patient was lost to follow-up. In the interim, his symptoms persisted, now associated with frequent episodes of coughing out previously consumed food. He was then brought to our institution and was subsequently admitted.

Review of systems was unremarkable.

His medical history was unremarkable. He had a family history of type 2 diabetes mellitus. He was a 6-pack-year smoker and an occasional alcoholic beverage drinker. He had a history of having had multiple sexual partners of the same sex, one of whom was positive for HIV.

On physical examination, he was normotensive, tachycardic, tachypneic and febrile, with oxygen saturation of 93% at 28% FiO2. Head and neck

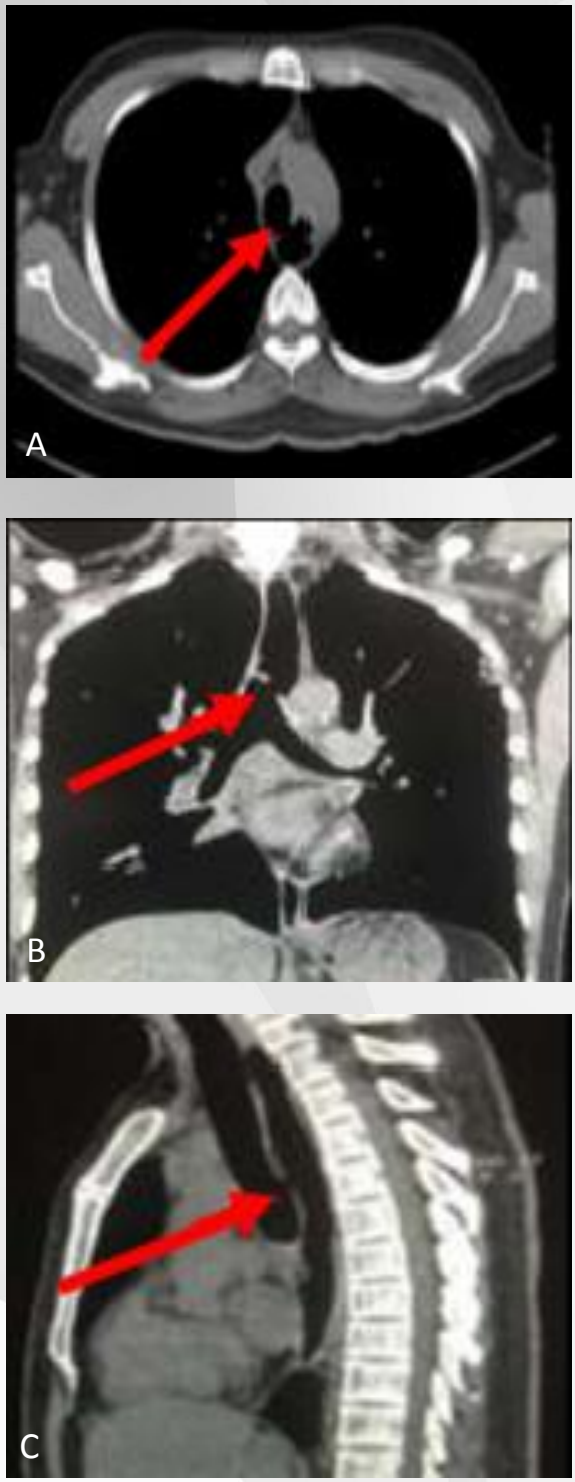

Figure 2. Case 1. Chest CT scan axial view (A), coronal view (B) and sagittal view (C) showing esophageal erosions and ulcerations (arrows).

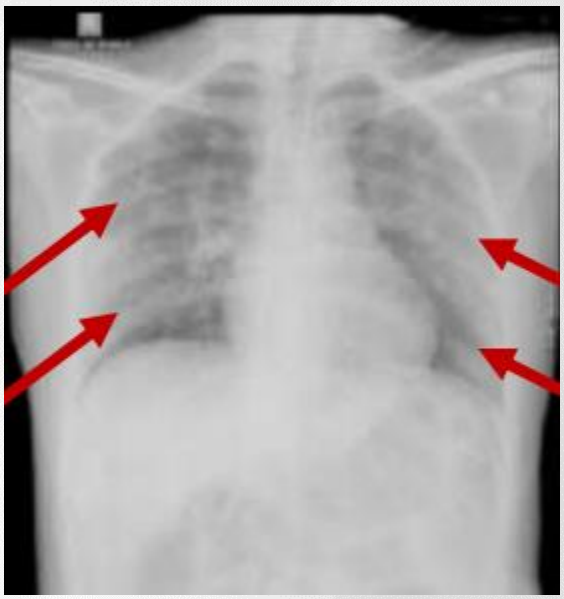

Figure 3. Case 1. Chest radiograph on admission, apico-posterior view showing bilateral hazy densities in the mid- and lower lung fields (arrows).

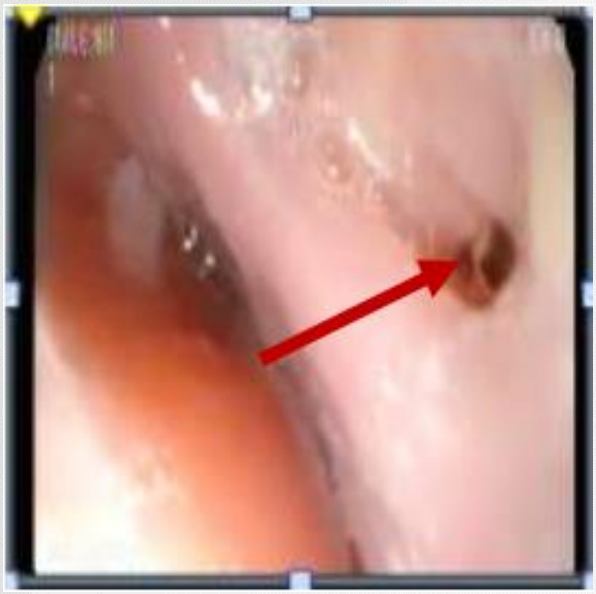

Figure 4. Case 1. Opening of the fistulous tract (arrow) located along the esophagus, 25 cm from the incisors.

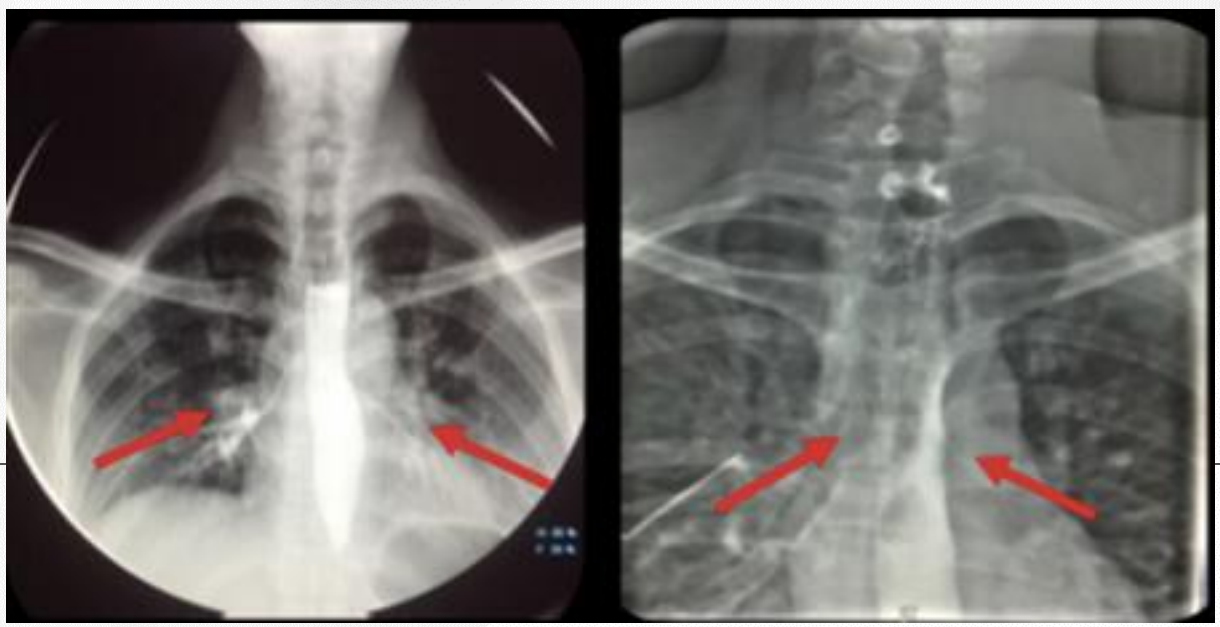

Figure 5. Barium swallow before surgery (left) and one week after surgery (right)

examination revealed oral thrush and palpable bilateral cervical lymph nodes. Chest and lung examinations showed symmetric chest expansion with no supraclavicular retractions.

He was noted to have bilateral rhonchi. The rest of the physical examination was unremarkable.

On work-up, his complete blood count,

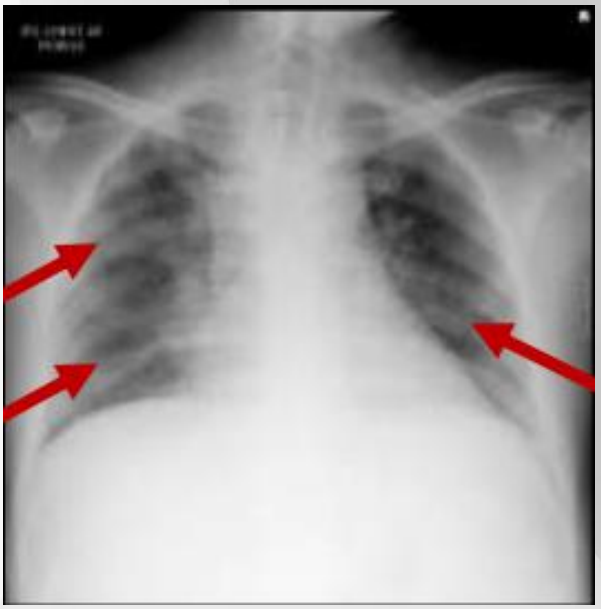

Figure 6. Case 2. Chest radiograph on admission, apico-posterior view showing confluent opacities in the right upper lobe and bilateral infrahilar regions (arrows).

electrolytes and liver enzymes were found to be within range. Arterial blood gas obtained at 28% FiO2 showed compensated respiratory alkalosis with adequate oxygenation.

Chest radiography revealed confluent patches of haziness at the right upper lobe and bilateral infrahilar regions (Figure 6).

Sputum microscopy was positive for AFB smear (1+). Sputum TB–polymerase chain reaction (PCR) and TB cultures were positive as well.

The working impression was aspiration pneumonia; oral candidiasis; PTB category 1, bacteriologically confirmed; to consider esophageal stricture. He was then started on intravenous antibiotics and was placed on NPO. To further investigate the consideration of an esophageal stricture, a neck and chest CT scan was ordered.

Chest CT scan showed irregular circumfer-

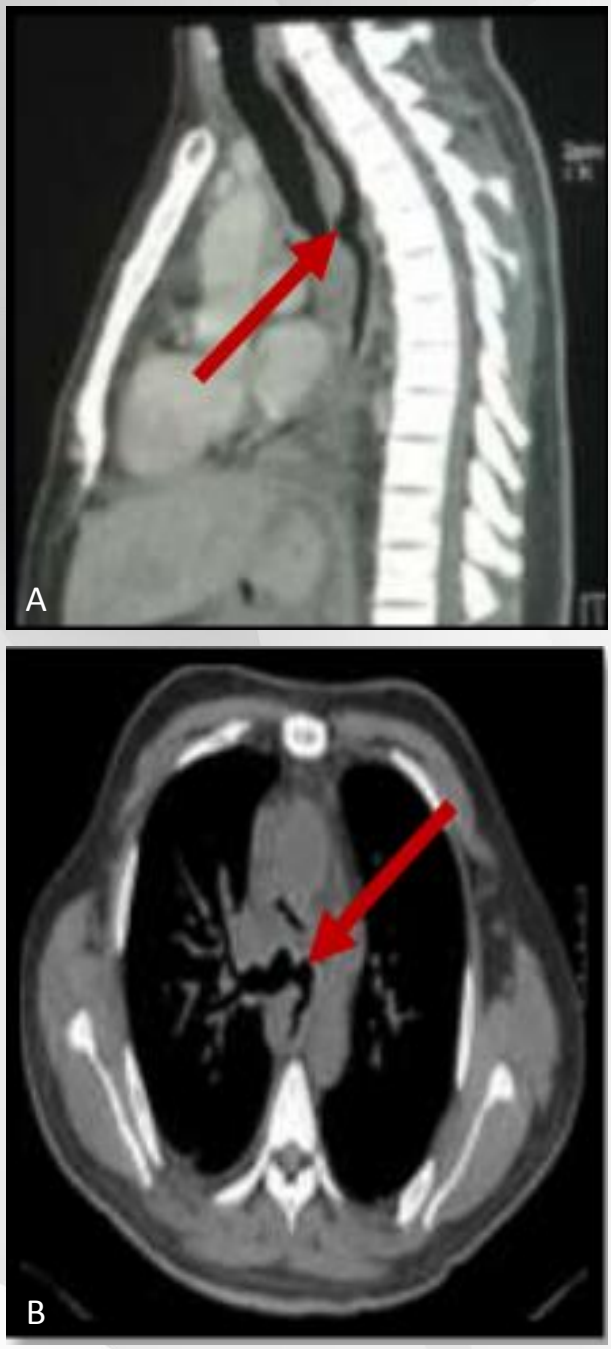

Figure 7. Chest CT scan on admission, sagittal view (A) and axial view (B) showing circumferential thickening of the esophagus and a fistulous tract (arrow) from the anterior aspect of the esophagus (T5 level) communicating into the posterior aspect of the left mainstem bronchus.

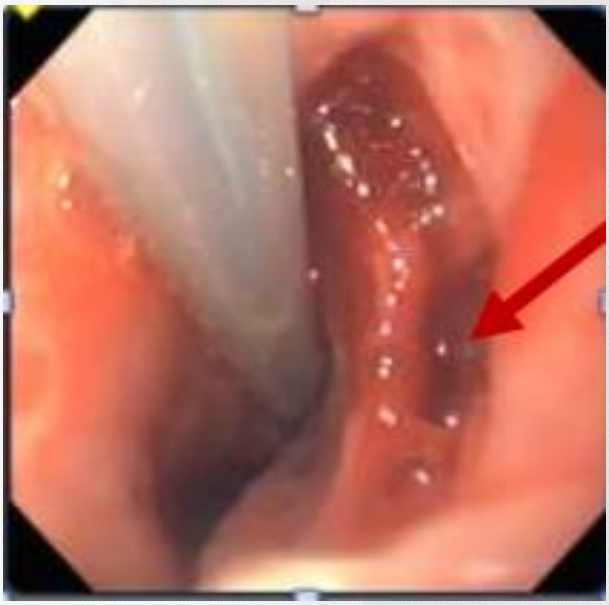

Figure 8. Sinus tract opening along the esophagus (arrow).

ential thickening of the entire length of the esophagus and a fistulous tract coming from the anterior aspect of the esophagus at the level of the T5 vertebral body, communicating into the posterior aspect of the left mainstem bronchus approximately 0.7 cm from the carina (Figure 7). Hence, the diagnosis of a broncho-esophageal fistula (BEF) was made.

To treat the patient's infections, co-amoxiclav was started for his pneumonia and fluconazole IV was given for his oral candidiasis. Category 1 anti-TB treatment was ordered. However, since the patient was on NPO, initiation of the medications was put on hold. For his BEF, the family agreed to a gastroenterology referral alone, because they had decided early on not to have any surgical intervention.

Gastroenterology service advised early peg insertion and bronchial stenting. However, the patient and his family opted for a more conservative approach. They consented only to nasogastric tube (NGT) insertion. Endoscopy-guided NGT insertion was done; it revealed signs of esophagitis and mucosal swelling throughout the entire length of the esophagus, with two sinus tract openings noted 23 cm (Figure 8) and 28 cm away from the incisors.

Esophageal biopsy was sent for examination. It was positive for TB-PCR with no rifampicin resistance. Histopathologic biopsy showed severe acute chronic inflammation with necrosis. Anti-TB medications were then started.

After 2 days, the patient was noted to have recurrence of coughing out milk-like substance similar to his feeding formula. The NGT was assessed to be displaced; hence, peg insertion was done. The patient gradually improved.

On his 23rd hospital day, the patient developed recurrence of fever and was treated for hospital-acquired pneumonia. However, despite adequate antibiotics and clinical and radiographic improvement of the pneumonia, his fever episodes persisted, now accompanied by yellowish peg-site drain. At this time, an intra-abdominal infection was entertained. Abdominal CT scan was ordered but was not done due to personal and financial reasons.

After staying in the hospital for 39 days, the patient was transferred to another institution where abdominal CT scan was done, showing a displaced peg tube, left psoas and splenic abscesses, and enlarged aortocaval and paraaortic lymph nodes. Aspirate of the psoas abscess showed positive for AFB smear (3+). Antibiotics were given, and category 1 anti-TB regimen was continued. He eventually improved and underwent esophagogastroduodenoscopy with stenting. He continued to recover and was eventually discharged improved and stable.

DISCUSSION AND COMMENTARY

We had two young patients, both with coughing and choking episodes. One was diagnosed with a TEF; the other, with a BEF.

An airway-esophageal fistula (AEF) is a general term describing the presence of a patent

tract from the airway to the upper gastrointestinal tract. It involves a complete interruption in the continuity of the esophageal lumen and most commonly occurs in the mid- to lower-third of the esophagus at the level of the carina. The patent tract may occur between the esophagus and the trachea; then it is called a TEF. If it occurs between the esophagus and the bronchi, it is called a BEF. Between BEFs and TEFs, the latter occurs more frequently.

Due to these anomalous connections, food particles travelling along the esophagus may be displaced and reach the airway. This event may cause characteristic signs and symptoms, one of which is uncontrolled coughing after swallowing or feeding, also known as Ono's sign. Other symptoms include chest pain, shortness of breath, hoarseness, dysphagia and a history of repeated respiratory tract infections.

According to Thomas,[2] the definite diagnostic criteria for AEF include (1) direct visualization of the fistula, (2) demonstrating contrast at the site of the fistula through radiologic means and (3) through an operative or surgical technique.

AEFs can be categorized into congenital and acquired conditions. Congenital AEF is the more common, showing predominance in the pediatric population. Table 1 lists the other types of AEFs. Congenital fistulas are caused by a defect in the lateral septation of the foregut into the esophagus and trachea. They are the most common cause of airway esophageal fistulas, detected early in life, usually associated with other congenital anomalies. They occur in approximately 1/3,500 live births. They are classified into five types based upon their anatomic variation and the presence or absence of esophageal atresia.

Acquired AEFs usually occur at the cervicothoracic junction. The anatomic site is the trachea in more than 50% of cases. Approximately 40% occur in the left and right mainstem bronchi, and a smaller number occur in the lung parenchyma.

Acquired fistulas can be further broken down into malignant or benign forms. According to Bartels et al.,[5] approximately 50% of all acquired TEFs are secondary to mediastinal malignancies. Of all cancers, esophageal tumors account for three-fourths of total cases. Fewer than 10% of all acquired cases are accounted for by lung, tracheal, laryngeal, and thyroid tumors, combined.

Table 1. Types of Airway-Esophageal Fistulaby etiology[3,4]

• Congenital
• Acquired
• Benign
• Mechanical ventilation
• Trauma
• Prior laryngectomy
• Prior esophagectomy
• Iatrogenic (esophageal stenting, endoscopy, transesophageal echocardiography)
• Caustic ingestion
• Granulomatous infection
• Malignant
• Mediastinal malignancy (esophageal 50%–75%; lung, tracheal, thyroid <10%)

Among the benign conditions, prolonged mechanical ventilation is the most common cause, followed by trauma and prior laryngectomy or esophagectomy.[4] Granulomatous infection and the ingestion of poisons or small batteries may also cause a benign TEF.

To diagnose an AEF, several procedures may be done. Plain radiography of the chest reveals whether the esophagus is dilated distal to the fistula, and whether the stomach is dilated as well. It could show pulmonary involvement manifested as infiltrates due to pneumonia or PTB. It also demonstrates the effects of repeated soiling and fleecy basal infiltrates. The extent of the white-out could reveal the severity of the disease.[6]

Barium swallow is for patients who are able to sit or stand. The ingested contrast demonstrates the fistulous tract that connects the esophagus and the airway through visualization of the leakage of contrast into the airway. Contrast demonstrates the defect in 70% of lesions.[5] The site, width, length and direction of the fistula can be also be identified.[7]

Chest CT scans can show thickening of the esophagus, signifying the inflammatory process occurring along the esophageal mucosa. Fistulous tracts can also be seen by the presence of gas- or contrast-filled tract between the esophagus and the airway. Chest CT scans could also reveal pulmonary or mediastinal lymph node involvement.[8]

Direct visualization is the gold standard for identifying AEFs. Endoscopy is valuable for visualizing the orifice of the fistula and for obtaining biopsy specimens for histopathology and organism isolation. Bronchoscopy also allows bronchoalveolar lavage, enabling targeted antibiotic therapy and airway clearance.

Both of our patients were young and had AEFs. Congenital fistulas generally manifest early in life. Both patients presented with symptoms in their 30s, so congenital causes are unlikely in their cases. Both patients underwent imaging studies. Malignancies are usually detected as enlarged masses seen on CT scans. No enlarged masses were detected in either patient. Therefore, although malignancy can only be confirmed through histopathology, is may be assumed that it is also an unlikely cause of these patients' diseases. Since neither patient had a history of mechanical ventilation, neck surgery, or other invasive procedures, nor ingestion of foreign substances, we can rule out these possible causes.

Granulomatous infection is a possible cause of AEFs. Granulomatous infections resulting to TEFs are uncommon, occurring in as few as 3%–10% of all cases of acquired tracheobronchial fistulas. A high index of suspicion should be present once the patient presents with immediate coughing while drinking or eating, plus radiographic evidence of pneumonia. Most of the reported cases of esophageal TB are secondary to TB elsewhere in the body, most commonly PTB. Esophageal TB can present as ulcers, strictures or fistulas.

The pathophysiology of tuberculous AEF starts with mycobacterial involvement of the submucosa of the esophagus. This is followed by the formation of tubercles. As the disease progresses, caseous necrosis occurs within the nodule. This is followed by ulceration. Usually it is a superficial ulcer with a pale gray, purulent base and rough, irregular edges, involving only the mucosa and submucosa.

The more serious ulcers occur rarely, often penetrating the muscle layer, breaking through the esophageal adventitia and resulting in esophageal perforation. Due to the contiguity of the esophagus to the airway, invasion of the airway can result in an AEF. Esophageal tuberculous ulcers often have a self-healing tendency due to the proliferation of fibrous tissue and scar formation. This leads to local esophageal stenosis.[8]

Esophageal TB could also begin through hematogenous spread of the tubercle bacilli to the esophagus, or the patient could have swallowed his infected sputum, causing translocation of the tubercle bacilli from the airways to the gastrointestinal tract.

Surgical repair is the definitive method for managing AEF. It is recommended for large fistulas that are complicated by recurrent respiratory infections. Rämö et al.[9] says that surgical closure of the fistulous tract is much safer and provides a more rapid recovery than medical management alone. The right thoracotomy approach provides the best exposure of AEF.

According to a study made by Shen et al.,[10] there are a number of postoperative complications associated with surgery (Table 2). Among these, respiratory failure and pneumonia are the most common. Shen et al. further state that the success rate of surgery is more than 90%,

with a median length of hospitalization of 14 days. The mortality rate associated with surgery is 3.2%–29.6%.

Numerous evidences show that medical management alone is sufficient to successfully manage fistulas. However, according to Rämö_et al.,[9] medical management can be done only if the disease is diagnosed early; if the fistula is short, narrow, and without abscess; or as preparation for major surgical procedures.

The principles of management of an acquired TEF are to minimize further aspiration through peg insertion; prevent and treat pulmonary infections; and provide adequate nutritional therapy until the patient is as fit as possible for surgery.

For TEF secondary to tuberculous infection, a standard drug regimen composed of isoniazid (H), rifampicin (R), ethambutol (E) and pyrazinamide (Z) for 2 months, followed by H and R for 4 months, is the mainstay of medical management of these patients. According to Rathinam et al.,[11] treatment with anti-TB drugs is effective. However, surgery may be required once TB complications such as a TEF occur.

Airway or esophageal stenting, on the other hand, is commonly done for fistulas secondary to malignant causes. Its primary aim is to improve the patient's quality of life. The principles of this approach are to reestablish the patency of compressed or strictured central airways; support weakened cartilages; and eventually seal off fistulas.

As mentioned, stenting is commonly performed in patients with malignant conditions, particularly esophageal, lung, tracheal, and thyroid. In cases where patients are ill enough to be at high risk for perioperative complications, stenting may be an option. Such a procedure can also be done on patients who have refused surgery. The success rate for such indications is 29%. The low success rate may be associated with the length and width of the fistula tract.

There are two types of stents: self-expanding plastic stents (SEPS) and self-expanding metallic stents (SEMS). In the management of acquired benign TEFs, there have been reports of spontaneous healing of fistulas with stent insertion; therefore, a retrievable stent should be used whenever possible. According to Sastry et al.,[12] SEPS are currently approved for the treatment of benign disease. On the other hand, SEMS that are placed for benign disease are associated with significant complications such as high migration rates, bleeding, fistulas and erosion.

Table 2. Complications of surgery

- Respiratory failure
- Pneumonia
- Esophageal leak
- Postoperative bleeding requiring reoperation
- Recurrent traceho-esophageal fistula
- Tracheal dehiscence
- Bacteremia
- Atrial fibrillation
- Prolonged air leak
- Wound dehiscence
- Acute respiratory distress syndrome
- Wound infection
- Chylothorax
- Empyema

However, stenting may have several complications (Table 3). According to Sharma et al.,[13] the most common side effect is stent migration, which has an incidence rate of 7%–75%. The risk of bleeding should also be emphasized, because there have been reports of such incidences leading to fatal outcomes. For our patients, bronchial stenting was preferred because of a higher risk of migration with esophageal stent, due to the peristaltic movement of the digestive tract.

As Aplasca et al.[15] states, it is important that patients with known or suspected HIV infection be screened for tuberculosis, because most of them present with atypical features. Conversely, people diagnosed with tuberculosis who have risk factors and have a high index of

Table 3. Complications of stenting[13,14]

- Migration
- Hemoptysis/bleeding
- Granuloma formation at stent ends
- Reobstruction by tumor, granuloma (uncovered stents)
- Halitosis and infection
- Perforation of airway walls
- Mucus impaction
- Pain
- Cough

suspicion for HIV should be worked-up as such.

Both patients were worked up for HIV. Both tested positive. Both had low cluster of differentiation 4 (CD4) counts.

According to Bartolome et al.,[16] AEFs are common among patients with AIDS who have extremely low CD4 cell counts, i.e., <50 cells/mL. Esophagitis is a common cause of morbidity, and complications in HIV include ulceration, perforation, fistula formation, hemorrhage, and stricture. Candida is the most common cause of esophagitis. Its presence increases the susceptibility of the mucosa to super-infection with swallowed Mycobacteria. However, fungi, viruses, and other bacteria may also produce esophagitis, either alone or in combination with each other or with *Mycobacteria*.

Few cases have been reported on the occurrence of AEFs in patients with AIDS and TB. However, it is not surprising that such instances can occur, because these patients tend to be severely immunocompromised and prone to numerous infections affecting the esophagus. TEF appears as one of the rare lesions in patients with PTB or as a complication of a TB-induced esophageal ulcer in patients with AIDS. It is important to consider the diagnosis of an AEF in the context of a persistent cough during swallowing in patients with AIDS and TB.

LEARNING POINTS

- Most patients with HIV or AIDS develop PTB, leading to complications such as AEF.
- Once confronted with a young immunocompromised patient with history of recurrent respiratory tract infection, cough, choking and dyspnea, one should highly suspect AEF immediately.
- Timely diagnosis and management will make a big difference in the prognosis of these patients.

RECOMMENDATIONS FOR PRACTICE AND RESEARCH

Limited studies on benign AEF are available locally and internationally. With the increasing incidence of PTB in HIV/AIDS patients, it is likely that there will also be increasing incidence of AEF worldwide. Therefore, we highly recommend further investigation on the management outcomes of the different approaches to AEF (i.e., medical, stenting, and surgical repair) to determine which patients will benefit from each of these treatment approaches.

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INTERHOSPITAL CASE PRESENTATION

"Serendipity": An interhospital case symposium on a rare cause of hemoptysis

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LEARNING OBJECTIVES, RELEVANCE AND SIGNIFICANCE

Bronchiectasis is a common but poorly defined cause of respiratory morbidity.[1] Its precise prevalence has not been determined; its causes vary across different eras and geographical areas.[2] Up to 92% of cases have either an idiopathic or post-infection etiology,[2-4] which means the possibilities for differential diagnosis are numerous, and rare etiologies can be easily missed.

This paper aims to present a case of bronchiectasis with a rare etiology; identify the different diagnostic tests that were used in the evaluation of a patient with bronchiectasis; and describe how the case was managed and treated.

THE CASE

DA, a 58-year-old female, first presented with hemoptysis 24 years prior to admission with approximately less than 50 ml each episode and no other associated symptoms. She sought consult; however, no work-ups were done. She was given multivitamins, and symptoms resolved spontaneously.

The patient remained asymptomatic until 11 years prior to admission, when she had another episode of hemoptysis with approximately 120 ml each bout. There was no associated fever, dyspnea, night sweats, weight loss, or abdominal pain. Chest radiography showed pneumonitis, while a chest CT scan showed a tree-in-bud appearance. She was given co-amoxiclav.

Symptoms persisted, so she sought consult at St. Luke's Medical Center (SLMC) and was subsequently admitted. Complete blood count (CBC) and bleeding parameters were unremarkable. Assessment was to consider bronchiectasis and rule out pulmonary tuberculosis (PTB). She was then started on tranexamic acid and cefuroxime.

High-resolution computed tomography (HRCT) scan of the chest showed bronchiectatic changes in the right middle lobe and left lingula, with tree-in-bud opacities in the left upper lobe, left lingula and the superior segment of the left lower lobe. Fiberoptic bronchoscopy revealed generalized endobronchitis with 30% stenosis of the right middle lobe bronchus secondary to edema, erythematous mucosa with bloody secretions, and no active mass lesions. Active bleeding was noted from the lingula and inferior portion. Bronchial washings yielded negative results for acid-fast bacilli (AFB). There was no growth in *Mycobacterium* cultures, and no growth of microorganisms on routine cultures. After 2 days, there was no recurrence of hemoptysis. The patient was discharged with cefuroxime and tranexamic acid. During the interim, she was asymptomatic.

Four years prior to admission, the patient again presented with hemoptysis at approximately 1 tablespoon per episode occurring five to seven times a day, prompting admission. Chest radiogra-

phy now showed thickened bronchopulmonary vascular markings in the right middle lobe and the inferior lingular segment of the left upper lobe, representing bronchiectatic changes with possible concomitant pneumonia. Faint ill-defined shadows that could have been due to a granulomatous infection were seen in the superior segment of the left lower lobe. CBC and bleeding parameters were unremarkable. All three sputum smears were negative for AFB.

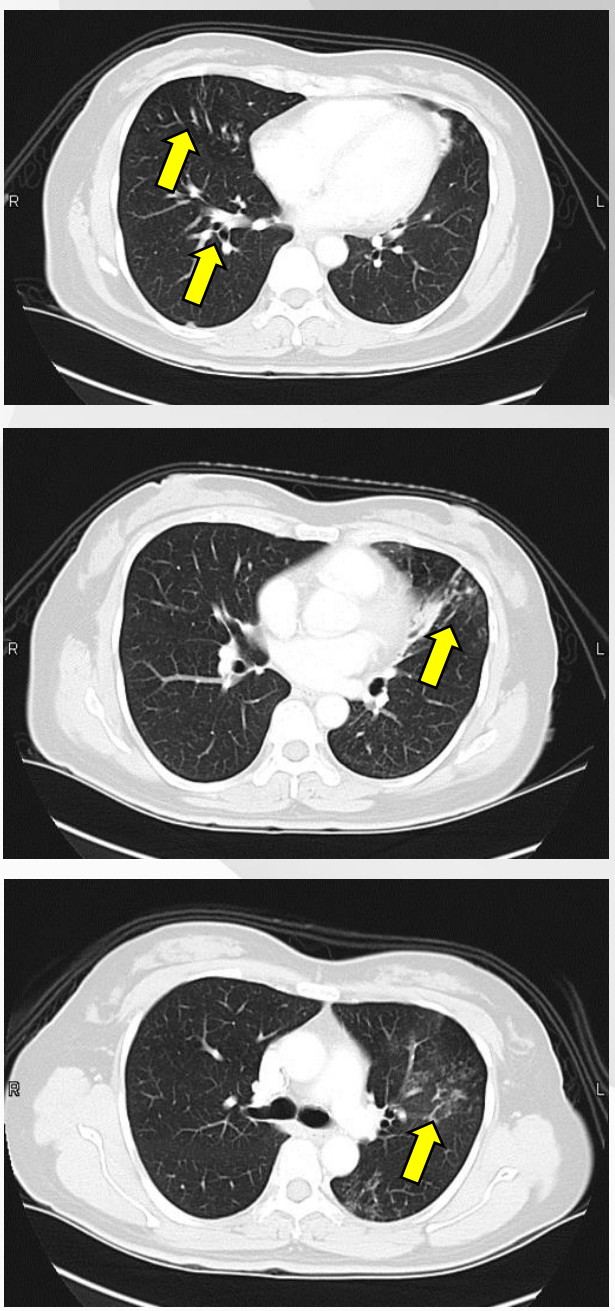

Figure 1. A chest CT scan (2004) showing tree-in-bud sign (arrows)

Assessment at this time was hemoptysis secondary to bronchiectasis versus PTB; community acquired pneumonia, moderate risk. She was initially started on cefuroxime, azithromycin and tranexamic acid.

Repeat HRCT of the chest revealed the progression of bronchiectatic changes, now with interval appearances of abnormal densities within the right middle and lower lobe bronchi, which may represent blood or mucus plugs (Figure 2). There was also a progression of reticulonodular densities, which now involved both lungs, and interval appearance of ground glass opacities and nodule in the right lung.

Sputum culture isolated a little growth of *Moraxella atlantae*, which was sensitive to cefuroxime. The patient was then managed as a case of PTB and was started on anti-Koch's medications. Other medications included levofloxacin, clindamycin, and tranexamic acid.

Symptoms resolved until one day prior to admission, when the patient had episodes of

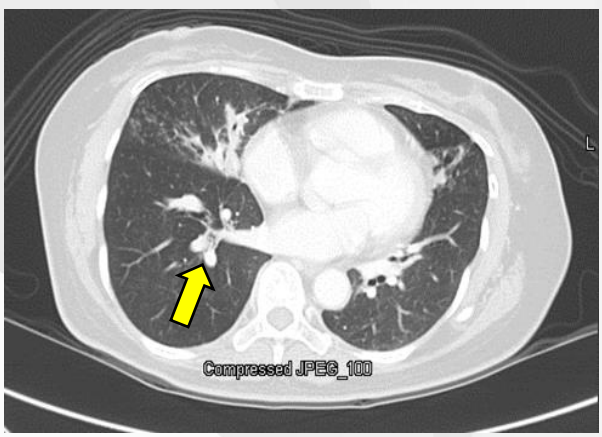

Figure 2. High-resolution CT (2011) showing bronchiectatic changes and tree-in-bud opacities (arrow) in the right middle lobe.

hemoptysis approximately 50 ml four to five times a day. She denied dyspnea, chest pain, shortness of breath, fever, and abdominal pain. This prompted emergency room (ER) consult and subsequent admission.

Review of symptoms was unremarkable. The patient denied hypertension, diabetes, bronchial asthma, and connective tissue diseases. She was a nonsmoker but had been exposed to secondhand smoke for 16 years. She and her husband kept a lot of animals, which included dogs, cats, and birds. Her husband collected tarantula and scorpions and bred imported cockroaches to feed them.

On physical examination, she was conscious, coherent and not in respiratory distress, with the following vital signs: blood pressure (BP) 110/70 mmHg, heart rate (HR) 72 bpm, respiratory rate (RR) 20 cpm, temperature (T) 36.8°C, and oxygen (O2) saturation 98% at room air. Eyes, ears, nose and throat were unremarkable.

She had symmetric chest expansion, no retractions, resonant on percussion, with rhonchi at the right base. She had unremarkable heart findings. Abdomen, extremities and neurologic exam were also unremarkable.

Upon admission, laboratory tests showed CBC and bleeding parameters within normal limits.

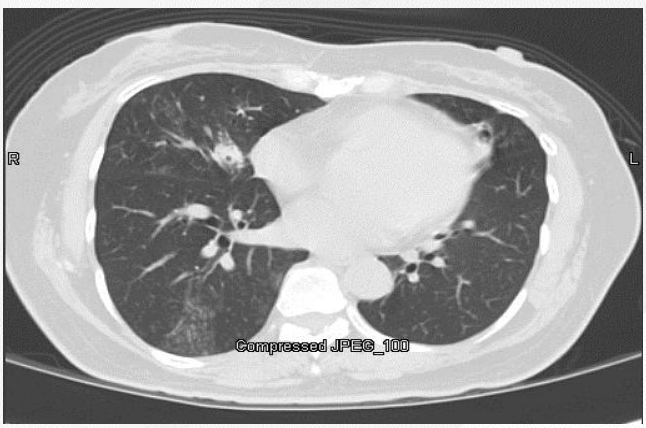

Figure 3. Repeat HRCT of the chest revealing centrilobular nodules/ ground glass densities in the right lower lobe and posterior right upper lobe (arrows) suggestive of endobronchial spread of infection and/or bronchiolitis.

Results of electrolyte and liver function tests were also normal.

Chest radiography showed well-aerated lungs with no acute infiltrates or consolidation. Repeat HRCT of the chest revealed tiny centrilobular nodules and ground glass densities in the right lower lobe, right middle lobe and posterior right upper lobe (Figure 3), suggestive of endobronchial spread of infection or bronchiolitis. There was also progression of right lower lobe bronchiectatic changes, as well as subsegmental atelectasis and parenchymal fibrosis. The patient was then started on cefepime, azithromycin and tranexamic acid.

On the patient's third hospital day, she underwent fiberoptic bronchoscopy, which revealed pooling of blood at the pyriform sinus, endobronchitis of the left bronchial segments, and fibrin clots completely obstructing the right middle lobe (Figure 4). Bronchial washing was done with the following results: negative for AFB, negative for fungal elements, no microorganism seen on routine gram stain, negative for galactomannan, and negative for GeneXpert. A *Mycobacterium tuberculosis* (MTB) culture test was requested and came out negative. The wet smear, however, revealed a moving flagellated organism. A Giemsa stain demonstrated the flagella. The organism was later identified as the protozoan *Lophomonas blattarum* (Figure 5).

The patient was given metronidazole and was scheduled for repeat chest CT scan and bronchoscopy; however, she was lost to follow-up. Her final diagnosis was recurrent non-massive hemoptysis secondary to generalized endobronchitis secondary to *L. blattarum* infection and bronchiectasis of the right middle lobe and bilateral lower lobes.

DISCUSSION AND COMMENTARY

Bronchiectasis is caused by damage to airway walls, usually secondary to infection from acquired or congenital causes. Once bronchiecta-

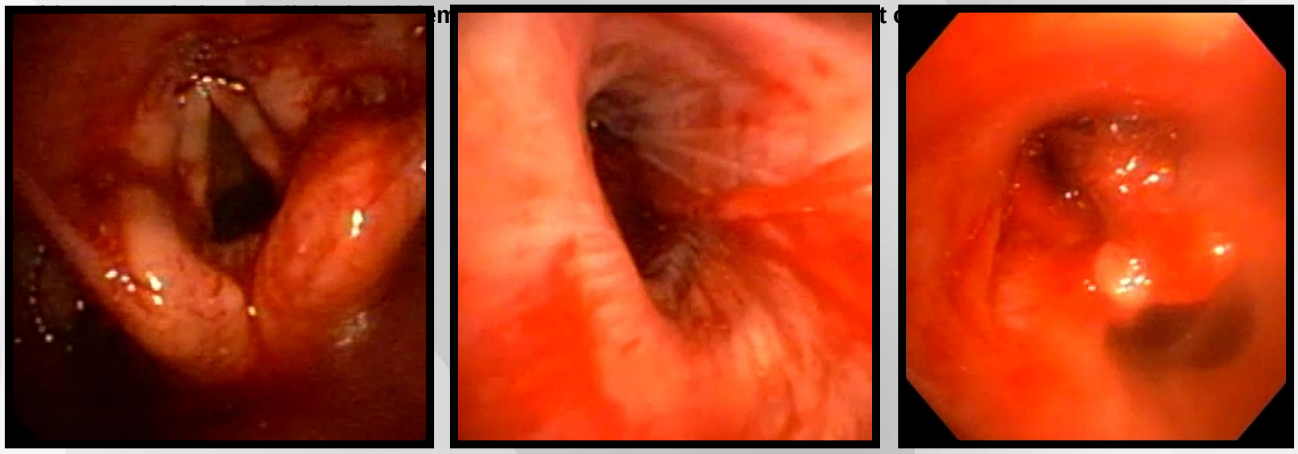

Figure 4. Fiberoptic bronchoscopy showing pooling of blood at the area of the pyriform sinus (A), endobronchitis of the left bronchial segments (B), and fibrin clots completely obstructing the right middle lobe (C).

sis sets in, organisms such as bacteria, fungi, or atypical *Mycobacterial* infection are able to colonize the bronchi more easily, thus causing ongoing damage and episodic infectious exacerbation, as in the case of this patient.

PTB is an important cause of bronchiectasis in developing countries. The most common pattern of TB bronchiectasis is traction bronchiectasis, where the tracheobronchial tree bends towards the apices or the area of the abnormality due to volume loss. TB bronchiectasis features fibrosis, scarring and tissue granulation. In this patient's case, fibrosis and traction bronchiectasis in the upper lobe were not observed. Also, the patient had repeated sputum cultures that came back negative. Therefore, PTB as a cause was largely ruled out.

In 2004, a CT scan was done on the patient, and the radiologist reported a tree-in-bud appearance. *Mycobacterium avium* complex (MAC) infection has been described as tree-in-bud. MAC findings include cylindrical bronchiectasis, along with multiple small peripheral bronchiocentric pulmonary nodules with branching configurations. However, MAC rarely occurs among immunocompetent individuals like this patient.

A congenital cause of bronchiectasis may predispose individuals to recurrent infection. Cystic fibrosis (CF), for instance, manifests in recurrent bacterial infections leading to symptoms of bronchiectasis and hemoptysis. CF presents with a tree-in-bud appearance, centrilobular nodular opacities or branching opacities, which were present in our patient. However, the median survival age of cystic fibrosis is around 39 years old, and our patient was already 58.

Nontuberculous mycobacterial (NTM) bronchiectasis features dominant bronchiectatic changes with little or no cavitation. The distrib-

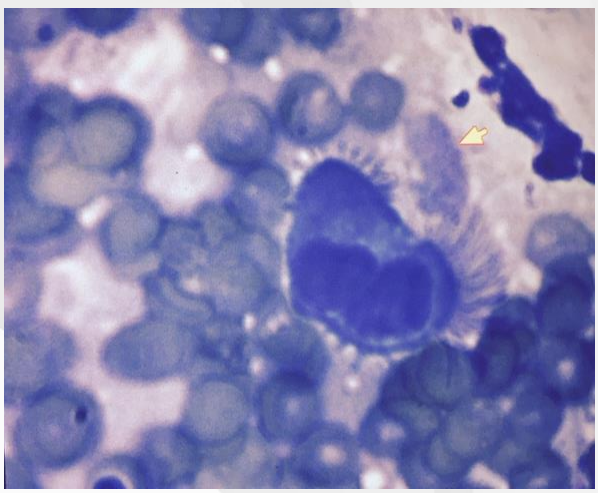

Figure 5. Microscopy of endobronchial washings showed the flagellated protozoan, *Lophomonas blattarum*.

ution of the tree-in-bud opacity is usually in the middle lobe/lingula and superior segment of the left lower lobe. In this patient's case, cavitation was not identified. There were tree-in-bud opacities and bronchiectatic changes in the right middle lobe/lingula and superior segment of the left lower lobe. Therefore, the radiographic images suggested NTM; however, they did not ineluctably establish it.

L. blattarum infection is a rare cause of bronchopulmonary infection. From the time Chen and Meng[5] described the first case of pulmonary *L. blattarum* infection in 1993, until 20 years later, only 136 cases have been reported. The organism has been reported in adult patients with bronchopneumonia and bronchial asthma. Sixty-nine percent of the cases involved males. The ages of patients ranged from 9 days to 95 years. The reason for the infections' male predisposition is unclear. Among the 136 reported cases, more than three-quarters were identified from the southern area of China.[6]

The clinical manifestations and signs of *L. blattarum* infection are nonspecific. This infection is difficult to differentiate from other common infections with similar symptoms such as pneumonia and bronchitis. In almost all the case reports, cough was always present. Varying degrees of expectoration were reported, including small quantities of white sputum, yellowish purulent sputum and bloodstained sputum. Fever, shortness of breath, chest tightness and wheezing were also reported.

Radiographic findings were also nonspecific. According to Yao et al.,[7] the chest radiograph of patients with bronchopulmonary *Lophomonas* infections may show nonspecific findings of patchy nodular or linear opacities that are scattered throughout both lungs. Lung abscess and pleural effusion were also reported, as well as central bronchiectasis with infection and bronchitis with pneumonia, which was documented in one of the chest radiographs of our patient. CT imaging may show ground glass opacity and patchy consolidation distributed in both lung fields, which were also seen in our patient. Bronchoscopy showed that affected airways were narrowed, with obstruction of the bronchial orifices. Bronchial mucosa appeared congested and edematous. The carina is noted to be sharp, with the right and left main bronchi appearing congested. Small bronchioles are edematous, with obstructions of blood clots and necrotic materials.

Bronchopulmonary ciliated epithelium can be confused with protozoa in sputum samples. Morphological differences between the two are minimal, and thorough evaluation is required for differentiation. *L. blattarum* is oval in shape, has a granular cytoplasm and usually has phagocytosed particles and a tuft of flagella that is responsible for the organism's locomotion and food ingestion. Ciliated bronchial epithelial cells on the other hand are columnar in shape and have a nucleus at basal end with a visibly marked terminal bar where cilia are inserted. The cilia should be straight, uniform in length and located at the apex of the cell, while *L. blattarum* organisms have flagella of variable length. It is presumed that *L. blattarum* is present in the gut of cockroaches and is subsequently eliminated from the hindgut thru their feces. The parasite enters the human respiratory tract via inhalation of dust with trophozoites and cysts. These forms can survive even in adverse external conditions and given suitable humidity, temperature, and oxygen concentration could undergo excystation. This produces free trophozoites in the respiratory airway epithelium, thus inducing its pathogenic mechanism.[8]

L. blattarum enters the bronchial lumen and adheres to the bronchial mucosa in a process known as cytoadherence, so it is not easy for patients to cough it out. These adhesions break down epithelial barriers via protein-activated receptors. The parasite's secretions can also induce allergic reaction of the bronchial mucosa, causing eosinophilia, and elevated IgE and IgA antibodies. Consequently, this parasitic infection can produce bronchial and parenchymal lesions and continuously induce hypersensitivity and airway inflammation.

Lophomoniasis diagnosis is generally based on the observation of the flagellated protozoan in either fresh wet mount or stained sputum smears. Samples from bronchoalveolar lavage, bronchial washings and tracheal aspirates can also be used. However, if the organism is fixed and stained, there can be deformation, which increases the difficulty of identification; hence, normal saline smear is preferred for microbiological diagnosis. In our patient's case, *L. blattarum* was detected in the wet mount and identified via the Giemsa stained smear. Treatment of *L. blattarum* infection is generally done with metronidazole, with tinidazole or albendazole as alternatives.[8]

LEARNING POINTS

- Lophomoniasis is a rare cause of bronchiectasis.
- The clinical manifestations and signs of *L. blattarum* infection are nonspecific.
- Lophomoniasis diagnosis is based on the observation of *L. blattarum* in fresh wet mount or stained smears.
- Fresh specimens should be examined before staining so that potentially crucial pathogens are not destroyed and missed.
- *L. blattarum* infection is treated with metronidazole.

RECOMMENDATIONS FOR PRACTICE AND RESEARCH

We have presented the case of a patient with recurrent non-massive hemoptysis of unusual etiology. She was previously treated for PTB, but pertinent laboratory work-up showed worsening bronchiectasis on chest CT scan and generalized endobronchitis on bronchoscopy.

Various differential diagnoses were presented and discussed, but none were correct until unexpected options were explored. *L. blattarum* is such a rare pathogen, hardly anyone ever suspects it.

In this case, the *L. blattarum* infection was only discovered because a doctor thought out of the box: the request was only for an MTB culture, but the pathologist examined the concentrated wet smear as well. If this "extraneous" step had not been taken, the diagnosis could have been completely missed.

We therefore recommend that whenever body fluids are examined, the wet smear should always be looked at first because one never knows what one might find. Once staining is applied, all other cells and organisms will be destroyed. We also recommend concentrating body fluids to reduce the risk that organisms will be missed.

One important question about *L. blattarum* infection is why it is so rare. The pathogen is borne by cockroaches, an insect that billions of people all over the world are regularly exposed to. And yet, over 90% of recorded infections happened only in China. In the case presented above, both the patient and her husband were exposed to the suspected carrier of the protozoan, but only the patient got sick. Further research on predisposing factors for this infection is thus needed.

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INTERHOSPITAL CASE PRESENTATION

"The Theory of Everything": An Interhospital Case Presentation on ALS

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LEARNING OBJECTIVES, RELEVANCE AND SIGNIFICANCE

Amyotrophic lateral sclerosis (ALS) is a rare progressive neurodegenerative disease with an international prevalence of 2/100,000 per year.[1-16] In its latter stages, it presents with symptoms in the bulbar and limb regions that are not easy to overlook.[17] Diagnosis of ALS is generally confirmed within 14±4 months from the onset of symptoms.[18,19] Early diagnosis is important, however, because although 85%–90% of victims die within 2–4 years after the onset of symptoms,[16] death can come even sooner, within a matter of weeks, if proper management is not provided.[20]

The objectives of this paper are to present the case of a 73-year-old male with neuromuscular disease; to discuss the approach in the diagnosis of the patient; and to identify the modalities in the patient's pulmonary management.

THE CASE

The patient is a 73-year-old male from Laguna who came in with the chief complaint of choking.

The present illness started nine months prior to admission, when the patient experienced a disturbance in phonation, described as nasality of voice, associated with a weight loss of approximately 20% within six months. There were no other associated signs or symptoms. No medications were taken. No consultation was done.

Seven months prior to admission, the patient's disturbance in phonation persisted, and it was now associated with anorexia, progression of weight loss, and generalized body weakness. He was, however, still able to do his daily routine. He consulted a physician, who requested laboratory examinations that revealed unremarkable results. The patient then consulted a neurologist, and an electromyogram (EMG)/nerve conduction study (NCV) was done to rule out the possibility of neuromuscular diseases. However, results of these studies were undisclosed.

Six months prior to admission, the disturbance in phonation and generalized body weakness progressed. They were now accompanied by productive cough and difficulty in swallowing liquids and solids. The patient was then brought to a private clinic, where he was treated for pneumonia with unrecalled antibiotics. After 1 week of treatment, the cough resolved. The patient did not return for follow-up.

Three months prior to admission, the patient had a recurrence of productive cough. Again, he was treated for recurrence of pneumonia, with improvement of cough after 1 week of antibiotic treatment.

Two weeks prior to admission, the disturbance in phonation, weight loss and dysphagia worsened. There was also a recurrence of productive cough and a development of shortness of breath in supine position. The patient also complained of fragmented sleep and difficulty

in ambulation. However, he still refused to seek treatment.

A few hours prior to admission, there was a worsening of dysphagia, now accompanied by choking. This prompted immediate consultation at the Philippine Heart Center.

At the emergency room, the patient was noted to be drowsy and in severe cardiorespiratory distress. Immediate intubation was done. Analysis of arterial blood gas (ABG) prior to intubation revealed acute-on-top-of-chronic respiratory acidosis with adequate oxygenation.

Past medical history showed that the patient had hypertension maintained on losartan, which he took regularly. Family medical history was unremarkable except for hypertension. The patient was a previous 36-pack-year smoker who stopped 10 years ago. He was also a previous alcoholic beverage drinker. He worked as a farmer and was a former barangay captain.

Pertinent in the review of systems were constipation, urinary frequency and incontinence.

On physical examination, the patient was intubated, malnourished, tachycardic, and in cardiorespiratory distress. His skin was dry and wrinkled and his lips were dry. Physical examination of chest and lungs revealed symmetrical chest expansion, shallow breathing with intercostal retractions, expiratory wheezes on both lung fields, and bibasal crackles. His abdomen was scaphoid. His upper and lower extremities were atrophied, with a baseline mid-arm circumference of 22 cm and a mid-calf circumference of 30 cm; and there were fasciculations in both upper extremities.

After intubation, repeat ABG showed metabolic alkalosis with adequate oxygenation. Chest radiography revealed pneumonia with minimal bilateral pleural effusion. Complete blood count (CBC) revealed leukocytosis with neutrophil predominance. Based on the patient's history and the presence of dysphagia with choking, aspiration pneumonia was considered and antibiotics were started.

Once the patient was stabilized, complete neurological examination was done with the following pertinent findings: awake, follows commands; with tongue fasciculations; motor strength 3/5 on upper extremities and 4/5 on lower extremities; hyporeflexia on upper extremities and hyperreflexia on lower extremities; no meningeal signs nor pathologic reflexes.

Based on the combined presence of dysphonia, dysphagia, choking, generalized body weakness, hyperreflexia, fasciculations, hyporeflexia, muscular atrophy, and hypotonia, the diagnosis of amyotrophic lateral sclerosis (ALS) was made.

On the second hospital day, patient was referred to a neurologist, who concurred with the diagnosis. Riluzole was prescribed but was not available, so gabapentin was given instead.

On the sixth hospital day, assessment for weaning was done. The patient was conscious, with stable vital signs, minimal endotracheal secretions, resolving pneumonia, normal serum electrolytes and adequate oxygenation at 40% FiO2. The dynamic and static compliances and rapid shallow breathing index (RSBI) were all within acceptable levels (Figure 1 and 2). Though the maximal inspiratory pressure (MIP) remained less negative, weaning was initiated by pressure support ventilation (PSV) starting at 14 cm H_2O.

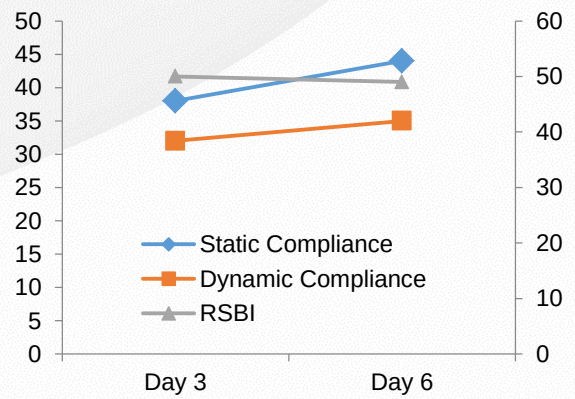

Figure 1. Pulmonary compliance (cmH2O) and Rapid Shallow Breathing Index (RSBI) (cpm/mL)

There being no specific weaning protocol for patients with neuromuscular diseases, we modified the weaning strategy. On the 12th hospital day, once a pressure support of 8 cm H2O was reached, weaning through T-piece alternating with PSV mode was done. However, due to tachypnea, fatigue and desaturation, weaning failed.

On the 15th hospital day, due to prolonged intubation and persistent weaning failure, tracheostomy and percutaneous endoscopic gastrostomy (PEG) tube insertion were done to facilitate adequate nutrition.

On the 16th hospital day, with the patient maintaining normal lung compliances and RSBI but with less negative MIP, a trial of tracheal mask alternating with PSV mode was resumed; but this again led to weaning failure.

On the 18th hospital day, the patient was referred to pulmonary rehabilitation with stretching, cycle ergometer, and arm and leg exercises for 15 minutes daily. Forward and lateral arm raising with 1-pound weights were started.

On the 28th hospital day, the patient was able to tolerate at least 6 hours of tracheal mask and then PSV for the rest of the day, especially at night, due to sleep-related hypoventilation.

On the 39th hospital day, the patient was able to sit at bedside with assistance and was discharged at 1-liter tracheal mask for at least 6 hours alternating with PSV during the day and placed on PSV during the night. His final diagnoses were ALS; respiratory failure, type 2; aspiration pneumonia; hypertension, stage 1; malnutrition; status/post tracheostomy and PEG insertion.

DISCUSSION AND COMMENTARY

Diagnosis

The approach to diagnosis for patients presenting with dysphonia includes good clinical history and direct visualization through a flexible or rigid laryngoscope. However, the latter was not done on our patient because he had been immediately intubated upon admission. To narrow the differential diagnoses, we identified the causes of dysphonia: infection, anatomic/structural, trauma, autoimmune, malignancy, and neuromuscular. Although infection, anatomic or structural abnormalities, laryngeal cancer, and trauma of the vocal organs present with many of the symptoms found in the patient, these cannot explain the abnormal neurological findings. Autoimmune causes such as dermatomyositis present was also unlikely due to the presence of overt abnormal neurological findings, and the absence of distinct features, such as rash and joint pains.

Neuromuscular diseases can damage the nerve cells that send messages controlling voluntary muscles. They can affect the central nervous system, brainstem, motor neurons, spine, neuromuscular junction and muscle. To easily differentiate the causes of neuromuscular diseases, we classified them based on predominating symptoms. Our patient presented with bulbar symptoms, i.e., dysphonia, dysphagia and choking; upper motor neuron (UMN) lesion symptoms, i.e., muscle weakness and hyperreflexia; and lower motor neuron (LMN) lesion symptoms, i.e., fasciculations, hyporeflexia, muscle atrophy and hypotonia (Table 1). Neuromuscular diseases manifest with either bulbar, UMN or LMN lesion symptoms. However, the constellation of all these three manifestations or the combination of UMN and LMN lesion symptoms can only be seen in patients with ALS (Table 2).

To establish our diagnosis, we utilized the revised EL Escorial Criteria,[21] which were developed by the World Federation of Neurology in 1980, revised in 1999, and has a 62% sensitivity and 98% specificity. Based on these criteria, our patient is a clinically definite ALS (Table 3).

Furthermore, an electromyogram was done prior to admission. Findings of acute denervation (e.g., fibrillations and sharp waves)

Table 1. Symptoms of neuromuscular disease, by presentation

Bulbar	Upper motor neuron	Lower motor neuron
• Dysphonia • Dysphagia • Choking • Nasal regurgitation • Difficulty chewing	• Muscle weakness • Hyperreflexia • Spasticity • Hypertonia	• Fasciculations • Hyporeflexia • Muscle atrophy • Hypotonia • Fibrillation • Muscle paresis

Table 2. Types of neuromuscular disease, by presentation

Bulbar	Upper motor neuron	Lower motor neuron
• Myesthenia gravis • Oculapharyngeal muscular dystrophy • Brainstem lesion	• Spondylopathic myelopathy • Hereditary spastic paraplegia • Multiple sclerosis	• Spinal muscular atropy • Bulbospinal neuropathy • Inclusion body myositis
Amyotrophic lateral sclerosis		

Table 3. EL Escorial Criteria for the diagnosis of amyotrophic lateral sclerosis

Definite ALS	Probable ALS: laboratory supported	Possible ALS
• UMN signs and LMN signs in three regions • UMN signs and LMN signs in two regions with at least some UMN signs rostral to the LMN signs	• UMN signs in 1 or more regions and LMN signs defined by EMG in at least two regions	• UMN and LMN signs in one region (together), or • UMN signs alone in two or more regions • UMN and LMN signs in two regions with no UMN signs rostral to LMN signs

UMN signs: clonus, Babinski sign, absent abdominal skin reflex, hypertonia, loss of dexterity
LMN signs: atrophy, weakness. If only fasciculations, search with EMG for active denervation
Regions reflect neuronal pools: bulbar, cervical, thoracic and lumbosacral

and chronic denervation (e.g., fasciculations, large amplitude and prolonged duration) were all present in our patient and were consistent with ALS. Moreover, a nerve conduction study was done which showed less than 20% difference in the proximal compound muscle action potential (CMAP) at the elbow from the distal CMAP at the wrist. This was also consistent with ALS.

Clinical Features

In ALS, there is a loss of UMNs and LMNs involving the motor cortex, the brain stem and the central spinal cord. Several genetic mutations are associated with ALS, the most common of which is the mutation of superoxide dismutase 1 (SOD1), which normally converts superoxide radicals to hydrogen peroxide and oxygen, while a mutant SOD1 leads to the production of free radicals, mitochondrial damage and intracellular aggregates. Though there are other proposed mechanisms, all these lead to motor neuron death and muscle atrophy.

The muscle atrophy in ALS can be further explained by the change in fiber composition of the skeletal muscles, leading to muscle weakness and fatigue.[22] Skeletal muscles are composed of three fiber types: Type 1, or slow-twitch fibers, have low contractile force and slow response, but they are more resistant to fatigue because they function through aerobic oxidation, which produces adenosine triphosphate (ATP) with carbon dioxide and water. This is quite enough for these fibers, which consume only little ATP. Type 2a and 2b are fast fibers with high contractile force and fast response, owing to their larger motor neuron size. However, they are more prone to fatigue because they operate by anaerobic glycolysis, especially type 2b. Anaerobic glycolysis causes lactate accumulation and cytosol acidification, leading to reduce contractile force and muscle fatigue.

In the diaphragm, type 1 and type 2 fibers are in equal proportion. Features such as small fiber size, abundance of capillaries, and a high aerobic oxidation give them the resistance to fatigue that is required by their continuous activity. On the other hand, intercostal muscles contain a higher proportion of type 2 fibers, which are used as accessory during respiratory distress but are more prone to fatigue.

In the early stage of ALS, there is a preferential loss of the largest units: the type 2b fibers. Thus, the decline in contractile force is greater than the decrease in motor unit numbers.[22] This manifests as muscle atrophy, which was observed in our patient as weight loss and weakness. In a chronic state, there is an increase in type 2 fibers, compared to type 1, to compensate for the decreased contractile force. This leads to type 2 muscle fiber predominance, increasing the risk for fatigue. This occurs with a persistent reduced contractile force due to the progressive loss of type 2 fibers.

The condition of the patient was aggravated by acute respiratory failure caused by severe pneumonia, as what occurred in our patient. Hypoxemia promotes anaerobic oxidation, and hypercapnea leads to low mitochondrial ATP due to increased degradation by adenosine monophosphate (AMP) deaminase. These events lead to a further decrease in contractile force and greater fatigue, as previously described.

These changes, due to motor neuron death, lead to muscle denervation, significant muscle atrophy and a change in fiber composition that is seen in all skeletal muscles, including the diaphragm and accessory respiratory muscles. These form the basis for the clinical features of ALS.

In the bulbar type of ALS, dysphonia – the initial symptom of our patient – is due to the loss of voluntary control of the laryngeal muscles, which leads to involuntary spasms of the vocal cords, which in turn leads to the closing of the vocal folds and cutting off of the voice.[23] Furthermore, due to the degeneration of the corticobulbar pyramidal fibers in ALS, there is a loss of control of the cricopharyngeal muscles of the upper esophageal sphincter, leading to their delayed opening and premature closure, which manifests as dysphagia to solids and liquids, as seen in our patient.

ALS affects the respiratory system in terms of the control of breathing, sleep-related disturbances, respiratory muscle function and fatigue. In neuromuscular diseases, there is an impaired ventilatory response to hypoxia and hypercapnia due to severe muscle weakness and disordered afferent and efferent output from motor neurons. This leads to a low tidal volume and a high respiratory rate characterized by rapid shallow breathing, as was seen in our patient despite changes in his oxygenation.

Breathing during sleep is abnormal in chronic neuromuscular disease. Patients have significant episodes of nocturnal desaturation and hypoventilation prevalent during REM sleep. Some hypotheses have been proposed: Rapid and shallow breathing during REM sleep leads to increased dead-space ventilation, promoting hyp-

ercapnia and worsened oxygenation. Also, accessory respiratory muscle activity during REM sleep is depressed, requiring a greater contribution of the diaphragm for maintenance of eucapnia and oxygenation. This aggravates the already weak diaphragm in ALS and leads to frequently impaired sleep quality, hypercapnia and hypopnea. This was why the patient was placed on PSV during sleep.

Respiratory muscle weakness in ALS may demonstrate as fatigue, dyspnea, recurrent pneumonia, impaired control of secretions, and acute or chronic respiratory failure, all of which were observed in our patient. A decrease in inspiratory muscle tone leads to diminished respiratory muscle force generation and unopposed lung elastic recoil, which reduces lung volume, leading to a rapid and shallow breathing pattern. Even just a 30% decrease in inspiratory muscle strength leads to hypercapnia, as seen in our patient upon admission. As expiratory muscle weakness progresses, the pleural pressure generated during coughing efforts are reduced, causing impaired airway clearance and leading to recurrent pneumonia, for which our patient was treated before his subsequent admission.

The progression of respiratory muscle weakness can be evaluated using the pulmonary function test. According to Baumann et al., forced vital capacity (FVC) falls with disease progression.[24] An abnormally low FVC predicts a shorter survival time than with normal FVC. It further shows that an FVC <50% of the normal levels is a predictor of poor prognosis in ALS patients. Other parameters that decrease with the disease are MIP and maximal expiratory pressure (MEP), which also predict survival.

The most common symptom of neuromuscular disease is muscle fatigue. However, the type of respiratory muscle fatigue seen in other diseases is different from what is seen in neuromuscular disease. In other diseases, there is high-frequency fatigue due to continuous maximal contraction of respiratory muscles. In this type of muscle fatigue, there is accumulation of potassium ions in the T-tubules during distress, and there is a rapid release of these ions during recovery. This enables calcium release, leading to faster muscle recovery and facilitating faster weaning. But in chronic neuromuscular disease, there is low-frequency fatigue due to continuous low-frequency stimulation of the respiratory muscles in order to increase the minute ventilation. With potassium ions having no role to play, there is repeated entry to and exit from the sarcoplasmic reticulum of calcium ions. This leads to muscle damage; thus, recovery is prolonged, reaching up to 1–2 hours. This leads to difficulty in weaning ALS patients from mechanical ventilation. Therefore, an individualized weaning strategy is useful for this condition.

Respiratory Management

ALS affects all three main functions of the neuromuscular system: ventilation, swallowing, and airway protection and coughing. Ventilatory dysfunction and bulbar muscle weakness, which were present in our patient, cause diurnal ventilation failure and sleep disordered breathing, which are evidenced by alveolar hypoventilation with increased pCO2. These mechanisms are responsible for the respiratory failure in ALS and are addressed with mechanical ventilation.

Ventilation

The choice of mechanical ventilation depends on presenting symptoms, bronchial secretions, availability, cost, patient preference and care. This algorithm (Figure 2) shows the respiratory management in ALS.[21] For patients presenting with respiratory symptoms at the time of diagnosis, ventilation treatment options should be discussed with the patient and the family members. Noninvasive positive-pressure ventilation (NPPV) is recommended as the initial method of treatment in patients with ALS who

present with respiratory symptoms, patients who have functional respiratory dysfunction, and those with symptoms of hypoventilation.

NPPV alleviates the aforementioned symptoms, stabilizes vital capacity and improves gas exchange. Radunovic et al.[25] suggested that NPPV in ALS significantly improves quality of life and prolongs survival in the absence of a severe bulbar involvement. In bulbar-type ALS, however, the European Federation of Neurological Societies (EFNS) recommends long-term mechanical ventilation through a tracheostomy, as it prolongs survival and is the procedure of choice for those who want to continue living.[21] Tracheostomy, in general, is associated with a decline in risks and complications such as barotrauma, pneumonia and oxygen toxicity. Consequently, invasive ventilation with tracheostomy was the option we chose for our patient.

Assist-control ventilation (ACV) allows complete respiratory rest to unload the inspiratory muscles and improve gas exchange. ACV can be shifted to pressure support ventilation (PSV) once recovery is clinically evident. PSV reduces the effort of breathing, offers acceptable synchrony and prepares the patient for weaning. For those who have chosen to be tracheotomized for long-term ventilation, like our patient, the aim should be to wean them into the minimum ventilator support compatible with symptomatic relief and comfort.

Conventionally, weaning covers the entire process of liberating the patient from mechanical support. Success in weaning occurs when a balance is observed between the neurorespiratory capacity and the ventilatory needs. In ALS, because of chronic low-frequency muscle fatigue, an imbalance favoring the latter causes weaning failure. Hence, the conventional way of weaning is both arduous and unsuitable for patients with ALS.

ALS patients who are difficult to wean may benefit from a gradual withdrawal of ventilator support such as the use of a once-daily trial of spontaneous breathing using T-piece or PSV. The pressure support is decreased in gradation until the minimum of 8 cm H2O is reached.[26] Synchronized intermittent mandatory ventilation (SIMV) seems to be the least effective method for weaning difficult patients, even when combined with PSV. Tracheostomy has expedited the weaning process of our patient, and the use of a tracheal collar in alternation with PSV facilitated it further until the desired minimum was reached at the time of discharge. Our main reiteration is that specialized cases like ALS warrant personalized protocols for weaning.

Airway Protection and Coughing

Cough insufficiency in ALS is considered when there is difficulty in expectoration and a history of recurrent respiratory infections, as were manifested by our patient. This problem can be mitigated by cough augmentation procedures, which we were not done for our patient as he was intubated at the outset. These procedures include manually-assisted cough (e.g., butterfly technique and forearm technique), high-frequency chest-wall oscillation, and mechanical insufflator-exsufflator.

Recurrent pneumonia is a life-threatening menace in patients with ALS. Aggressive treatment with broad-spectrum antibiotics is merited, tailored to the culture and sensitivity results. Although we are unaware of any controlled studies that pinpoint a specific preferred antibiotic for this purpose, we know that there are antibiotics we should be wary of. Most of the antibiotics we use for pneumonia have been found to have serious neurotoxic effects. Therefore, these should be used with caution for those who are critically ill and with neurologic disorders.

Swallowing

Notable in our patient is the swallowing dysfunction. Andersen et al.[21] recommend the placement of a percutaneous endoscopic gastro-

stomy tube. This procedure was performed in our patient. The timing is mainly based on the degree of bulbar symptoms, malnutrition and respiratory function.

Pharmacologic Treatment

Riluzole has been used as the only approved treatment for ALS since 1995, but its mechanisms of action in slowing the progression of this disease remain obscure. It has been found to inhibit glutamic acid release, block amino acid receptors, inhibit sodium and calcium channels, and activate intracellular-buffering processes. All these lead to the inhibition of glutamatergic excitotoxicity, translating to inhibition of programmed cell death of motor neurons, thus improving muscle function and survival.[27]

Riluzole has been shown to improve 1-year survival by 15%. However, this drug is not available in the Philippines commercially. In lieu of riluzole, gabapentin was given to our patient. Gabapentin has been found to modulate the glutamatergic system. Mazzini et al.[28] reported that it prolonged survival in patients with ALS. However, a phase III study by Miller et al.[29] found no significant difference in the decline of arm muscle strength. Moreover, there was no beneficial effect on the decline of the secondary measures.

Pulmonary rehabilitation

Though there are no specific trials evaluating the effect of pulmonary rehabilitation in ALS, we still started our patient on pulmonary rehabilitation in the hope of improving his present physical and psychological condition.

In general, these are the five components of pulmonary rehabilitation: education, psychological support, breath retraining, general exercise training, and outcome assessment. The aim of education is to promote collaborative self-management and self-efficacy; this forms the foundation of pulmonary rehabilitation. Psychological support is important because there is a high incidence of depression and anxiety in ALS. Programs must be initiated for the early identification and treatment of these two conditions, and referral to a psychiatrist should be done if needed. Family support was encouraged for our patient, as it has been shown to decrease depression and anxiety and improve exercise outcome.

Exercise training is the cornerstone of pulmonary rehabilitation. In our patient, this includes stretching exercises; upper extremity exercises such as endurance training through cycle ergometer and resistance training using 350 ml water as weights to accommodate the patient's grip; and lower extremity endurance training, also with a cycle ergometer. Stretching exercises, in general, improve flexibility by maintaining muscle length and joint mobility. According to Moreno et al.,[30] respiratory muscle stretching significantly improves the MIP and MEP, as well as enhances thoracic expansion and abdominal mobility in the general population. Upper extremity exercise through endurance and resistance training aims to improve cardiorespiratory fitness and increase muscle strength. It has also been shown to significantly increase FVC after a 6-week program. Calik-Kutukcu et al.[31] also mentioned that endurance training through arm ergometer reduces dyspnea perception levels. Lastly, a 4-week upper extremity resistance-training program[32] has been shown to significantly improve MIP and MEP, which reflects increase in respiratory muscle strength. Our patient's MIP, though not significant, improved to –5 cm H2O, which one may surmise is a trend towards benefit.

The fourth component of pulmonary rehabilitation is breath retraining, which aims to maintain pulmonary compliance and chest wall mobility, maintain normal alveolar ventilation, facilitate airway clearance and increase respiratory muscle strength and endurance. It includes breathing techniques such as pursed-lip breathing and diaphragmatic breathing to reduce

the work of breathing. It also uses various ventilatory devices to aid in inspiratory and expiratory muscle training. The breath training measures we could apply to our patient were limited by the severity of the disease and the presence of a tracheostomy. These measures could have been applied in the early stage of ALS or with the use of a one-way valve for tracheostomized patients.

The last component of pulmonary rehabilitation is outcome assessment. The ALS Severity Scale[33] provides a rapid and accurate assessment of the patient's disease status, while the Modified Borg Scale assesses exercise performance in patients with ALS.

With this comprehensive management comprised of pharmacologic treatment, respiratory management, and pulmonary rehabilitation, our patient was able to sit at bedside with assistance. We were able to wean him off to at least 6 hours on tracheal collar, with only ventilatory support at night.

LEARNING POINTS

- A combination of UMN and LMN symptoms in three regions is a definite indicator of ALS.
- Respiratory muscle weakness in ALS may demonstrate as fatigue, dyspnea, recurrent pneumonia, impaired control of secretions, or acute or chronic respiratory failure.
- Tracheostomy prolongs survival in late-stage bulbar ALS.
- PSV and daily spontaneous breathing trial is advised for cases that are difficult to wean.
- Education, psychological support, exercise training (especially upper extremity training), breath retraining and outcome assessment work together to facilitate weaning.
- The aim of ALS management is to achieve a minimum number of hours per day on ventilatory support.

RECOMMENDATIONS FOR PRACTICE AND RESEARCH

At present, ALS is a disease that cannot be adequately treated with any known pharmacologic agent. Riluzole has marginal benefit and is not readily available; the outcomes for gabapentin are inconclusive. Further research on efficacious medication for ALS is needed.

Another challenge is public education. The breadth and spectrum of ALS clinical presentations may lead patients to believe that their illness has a supernatural cause. This prevents them from seeking medical help until late in the disease where interventions becomes less beneficial. Publicity from social media stunts and the voice of prominent people with ALS has jumpstarted awareness of this disease. However, it is the medical practitioner's challenge to ensure that this momentum will be sustained.

When treating ALS, it is important to remember that a multidisciplinary approach is required. Adequate management of this disease requires, at the very least, a neurologist, a pulmonologist, and a physiatrist in the team. Emotional support is also very important because patients know that although their disease is treatable, it is incurable. Keeping in mind that this disease invariably ends in demise that is often preceded by a period of intubation or tracheostomy, patients and their families should be advised about advance directives to ensure that the wishes of the patient can be made known and respected.

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