Case Report

Thermal Ablation and Intralesional Cisplatin Injection as Adjunct to Systemic Chemotherapy in Managing Malignant Central Airway Obstruction: A Case Report

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ABSTRACT

Endobronchial ultrasound (EBUS)-guided intralesional chemotherapy and thermal ablation using cryotherapy and electrocautery can be used for the management of malignant central airway obstruction (CAO). This is a case of a 62-year-old male presenting with cough, hoarseness, and shortness of breath. He was diagnosed with squamous cell carcinoma stage IVA (T4N2M1a), causing malignant CAO that progressed to impending respiratory failure (ECOG performance status 4). Chest CT scan findings included a left main bronchus mass measuring 3.7 x 5.8 x 5.9 cm causing complete atelectasis, a right pleural-based mass, and osteolytic destruction of the 3rd lateral ribs. Bronchoscopy showed a fungating, friable mass in the carina extending to the orifice of the right and left mainstem bronchus with 70% and 100% occlusion, respectively. A multimodality treatment approach was taken with tumor debulking by thermal ablation with cryotherapy and electrocautery, EBUS-guided intralesional cisplatin, and systemic chemotherapy. Subsequently, there was an interval decrease in the size of the tumor in multiple areas, with left lung re-expansion. The clinical symptoms of the patient significantly improved and ECOG status increased to 1. No adverse effects were noted post procedure. Intralesional cisplatin can be an effective and safe adjunct treatment in malignant CAO, alongside thermal ablation and systemic chemotherapy.

Keywords: malignant airway obstruction, intralesional chemotherapy, cisplatin, cryotherapy, non-small cell lung cancer

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INTRODUCTION

Non-small cell lung carcinoma (NSCLC) is the most common cause of malignant central airway obstruction (CAO). In unresectable cases, systemic chemotherapy is the standard of care that offers survival benefits. This can also be given with concomitant radiation therapy. However, in cases of CAO, intravenous chemotherapy alone is often inadequate in terms of disease control, and small gains are obtained at the cost of significant toxicity.[1]

Endobronchial ultrasound (EBUS)-guided intratumoral chemotherapy can be considered a new life-saving palliative method in patients with life-threatening airway obstruction. In the study of *Mehta et al*, it was demonstrated that transbronchial injection of cisplatin can be used in improving the patency of central airways that are largely or completely occluded by endobronchial malignant tumors.[2,3]

In this case report, we summarized our experience with using EBUS-guided intralesional injection of cisplatin, thermal ablation, and systemic chemotherapy as a treatment option for patients with advanced inoperable NSCLC with life-threatening CAO.

CASE PRESENTATION

A 62-year-old male with impending respiratory failure due to malignant CAO was transferred to our center for further management.

One month prior to admission, the patient experienced non-productive cough, hoarseness, and shortness of breath, with ECOG performance status 2. He was a non-smoker with a family history of esophageal and laryngeal cancer. Computed tomography (CT) scan of the chest revealed a left main bronchus mass measuring 3.7 x 5.8 x 5.9 cm causing complete atelectasis, a right pleural-based mass in the right upper hemithorax, multiple osteolytic lesions, with subcarinal and hilar involvement. The patient underwent *ultrasound-guided transthoracic needle aspiration biopsy* of the right pleural-based mass, and was advised close monitoring pending the biopsy result. The patient was eventually diagnosed as a case of squamous cell carcinoma stage IVA (T4N2M1a), causing malignant CAO. Immunohistochemistry was as follows: P40 positive, TTF1 equivocal, no mutation on EGFR, low PDL-1 (1-49%), ALK negative, and ROS1 negative. Six days prior to transfer, the patient developed progressive dyspnea at home with severe desaturations. He was admitted to another hospital where he received five sessions of radiotherapy to alleviate the symptoms of malignant CAO. Bronchoscopy for airway evaluation was advised, however, the patient opted to transfer to our center for further management.

Upon transfer, the patient was in severe respiratory distress, ECOG status 4. He was hooked to high-flow nasal cannula with fraction of inspired oxygen of 60% which partially improved the dyspnea and addressed the desaturation. He underwent fiberoptic bronchoscopy, revealing the carina infiltrated with a fungating friable mass which extended to the orifice of the right mainstem bronchus (RMB) causing 70% occlusion, and complete occlusion of the left mainstem bronchus (LMB) (Figures 1a, 1b). The patient underwent tumor debulking by thermal ablation using cryotherapy and electrocautery, resulting in visualization of the RMB. Post-procedure, oxygen support was shifted to low-flow nasal cannula, and after 24 hours, the patient was able to tolerate room air. He was discharged and later readmitted for chemotherapy.

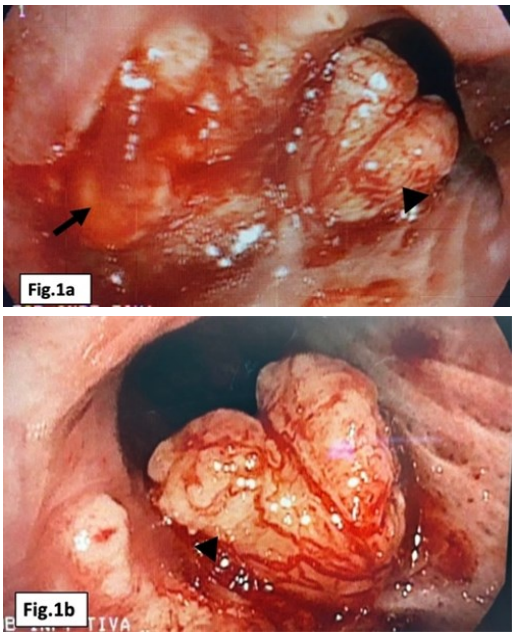

Figure 1a. Bronchoscopy showing carina infiltrated with fungating friable mass extending to the orifice of the RMB (arrow head), causing 70% occlusion. LMB (arrow) is completely occluded. **Figure 1b.** Magnified view of the mass occluding the RMB. RMB, right mainstem bronchus; LMB: left mainstem bronchus.

Table 1. Treatment timeline

Days since first biopsy confirmation of malignancy	Procedure
D30 -	Radiotherapy for 5 sessions
Transfer to our center/1st admission	
Day 36	FOB with thermal ablation using cryotherapy and electrocautery
2nd admission	
D60	Cycle 1 EBUS-guided intralesional cisplatin (10 ml: right subcarinal area, 30 ml: main mass, left)
D62	Cycle 1 gemcitabine-carboplatin
3rd admission	
D70	Cycle 2 gemcitabine
D71	Cycle 2 EBUS-guided intralesional cisplatin (10 ml: right subcarinal area, 30 ml: main mass, left)
D82	Cycle 3 EBUS-guided intralesional cisplatin (40 ml: subcarinal area)
D84	Cycle 3 gemcitabine-carboplatin
D97	Cycle 4 EBUS-guided intralesional cisplatin (40 ml: subcarinal area)
D103	Cycle 4 gemcitabine-carboplatin
5th admission	
D112	FOB surveillance with cryoablation of endobronchial mass
D114	Cycle 5 gemcitabine; subsequent chemotherapy was done as outpatient

FOB: fiberoptic bronchoscopy; EBUS: endobronchial ultrasound

Bronchoscopy was again done and EBUS-guided intralesional cisplatin was given at a dose of 40 mg (40 ml of 50 mg/50 ml cisplatin: 10 ml at right subcarinal area, 30 ml at main mass, left). Following cisplatin administration, magnesium and potassium-supplemented hydration was given. Systemic chemotherapy with gemcitabine and carboplatin was initiated three days after. The patient tolerated the procedures well and was discharged.

The patient was readmitted for subsequent cycles of chemotherapy, with delays caused by limitations in healthcare resources, among other factors. In relation to systemic chemotherapy, corresponding cycles of intralesional cisplatin were given anytime from 6 days prior to 1 day after. By the 3rd cycle, owing to prior restoration of patency of the RMB, the full dose of cisplatin was injected at the subcarinal area. The patient underwent a total of four cycles of intralesional cisplatin and five cycles of systemic chemotherapy as inpatient (gemcitabine 1200 mg/m^2 and carboplatin area under the curve 5 mg/ml min). Prior to the 5th cycle of systemic chemotherapy, the patient underwent repeat cryoablation of the bronchial mass.

Table 1 summarizes the treatment timeline. Treatment response was assessed based on ECOG, repeat chest X-ray and CT scan, and bronchoscopy (Figures 2 to 4) . The patient's performance status improved significantly from ECOG 4 to 1. Repeat chest X-ray revealed re-expansion of the atelectatic left lung (Figure 2h), and chest CT scan findings showed a decrease in the size of the left hilar/perihilar and subcarinal mass, and diminution of the endobronchial mass extension (Figure 3b). Bronchoscopy finding of more than 50% increase in the diameter of the airway lumen denoted good response to treatment (Figure 4f).

Bronchoscopic surveillance was done at three and six months post-treatment, with findings of a tumor-eroded carina with necrotic tissues; and a blunted carina, stenotic LMB, and a patent RMB, respectively. Positron emission tomography/CT scan at 10 months revealed no evidence of local tumor recurrence in the left lung, no evidence of hypermetabolic lymphadenopathies, and interval resolution of previously reported mediastinal lymph node. However, repeat chest CT scan at 12 months showed progression of bone metastases. Currently, the patient is on second-line chemotherapy with docetaxel and is alive 14 months after diagnosis. He is capable of self-care and ambulates without assistance. He has limitations in doing strenuous activities but is not dyspneic with activities of daily living and not on oxygen support.

DISCUSSION

Intralesional chemotherapy with cisplatin can improve the patency of airways occluded by endobronchial malignant tumor. It directly targets the tumor microenvironment and offers several advantages over systemic treatment for centrally -located NSCLC.[2,4,5] Cisplatin is widely used to treat lung cancer because of its ability to interfere with cell replication.[7] There are several studies on the therapeutic potential of directly injecting cisplatin (40 mg/40 mL) into lung tumors that are adjacent to the airways through an EBUS-guided intratumoral needle injection, with a survival benefit of 8 months among responders to treatment.[2,5,6,8] An effective dose of cisplatin would be possible if the drug was apportioned between five appropriately selected sites throughout the tumor rather than being delivered in its entirety at a single central site.[9] In our case, an effective dose of cisplatin was given in two sites rather than being concentrated in one site.

Based on previous publications in the field of intralesional chemotherapy, it is not merely considered an ablation technique for treatment of endobronchial tumor but also has a significant specific chemotherapeutic effect on malignant cells

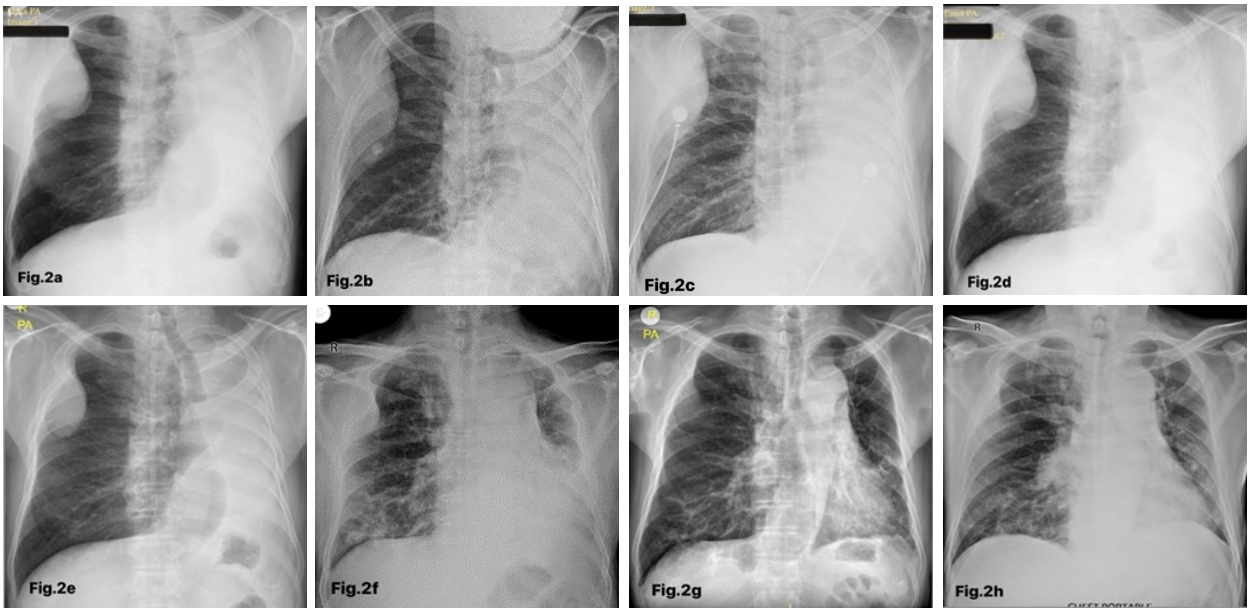

Figure 2. Serial chest X-rays during treatment course. **2a:** Baseline chest X-ray at the time of biopsy of the right upper lobe mass showing left lung atelectasis with ipsilateral mediastinal deviation, mass-like lesion in the right upper lung with lytic changes of the 3rd rib, and compensatory hyperaeration of the right lung. **2b:** Upon transfer as a case of CAO, in impending respiratory failure; no significant change noted. **2c:** Post-FOB with cryotherapy; no significant change noted. **2d to 2g:** During chemotherapy (four cycles of intralesional cisplatin as adjunct to systemic chemotherapy); with significant improvement in the opacity in the left lung with eventual re-expansion and an apparent decrease in the size of the right upper lobe pleural-based mass. **2h:** After four cycles of intralesional cisplatin with systemic chemotherapy; re-expansion of the atelectatic left lung noted. CAO, central airway obstruction; FOB, fiberoptic bronchoscopy

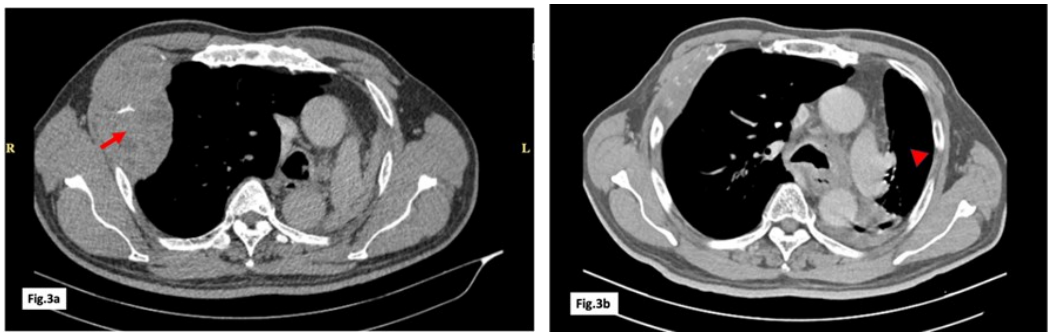

Figure 3. Chest CT scan with contrast (mediastinal view), pre- and post-treatment with thermal ablation and four cycles of intralesional cisplatin as adjunct to systemic chemotherapy. **3a:** Pre-treatment scan shows a collapsed left lung with compensatory hyperaeration of the right lung, and a solid heterogeneously-enhancing pleural-based mass (arrow) in the right upper hemithorax associated osteolytic destruction of the 3rd lateral ribs. 3b: Post-treatment scan shows an interval partial re-expansion of the left lung (arrow head) with interval decrease in the size of the pleural-based mass with lytic expansile lesion along the right 3rd rib, 6.9 x 2.8 cm in maximal axial diameter (previously 10.6 x 6.4 cm). RMB: right mainstem bronchus; LMB: left mainstem bronchus

through the localized action of cytotoxic drug.[1,3,10,11] The advantages include: precise delivery within the tumor; local concentration of drug can be 10- to 30-fold higher than could be achieved with systemic delivery to kill a greater proportion of neoplastic cells; toxic side effects which normally occur with conventional systemic chemotherapy may be avoided; and local injection of the drug can target draining lymph nodes, and disrupt the structural integrity and vascular supply of the tumor.[6,16] The procedure is contraindicated in patients with renal impairment, electrolyte imbalance, myelosuppression, and pregnancy.[12,13,14] There are reported cases of rare adverse events to intralesional chemotherapy such as mediastinitis, fistula formation, bleeding, pneumothorax, and extravasation into the airway.[15] In our case, none of these were encountered. There was also no nausea, vomiting, fever, and arrhythmia. Response to treatment is evaluated based on the patient's performance status, bronchoscopy findings, and imaging.

CONCLUSION

Intralesional injection with cisplatin can be an effective and safe therapeutic option in conjunction with tumor debulking by thermal ablation, cryotherapy, electrocautery, and systemic chemotherapy in malignant CAO. The combined local and systemic treatment improves patient's symptoms with an improvement in quality of life, especially alleviating dyspnea in end-stage lung cancer patients with malignant CAO.

Ethical Consideration

The authors declared that appropriate written informed consent was obtained for the publication of this manuscript and accompanying images.

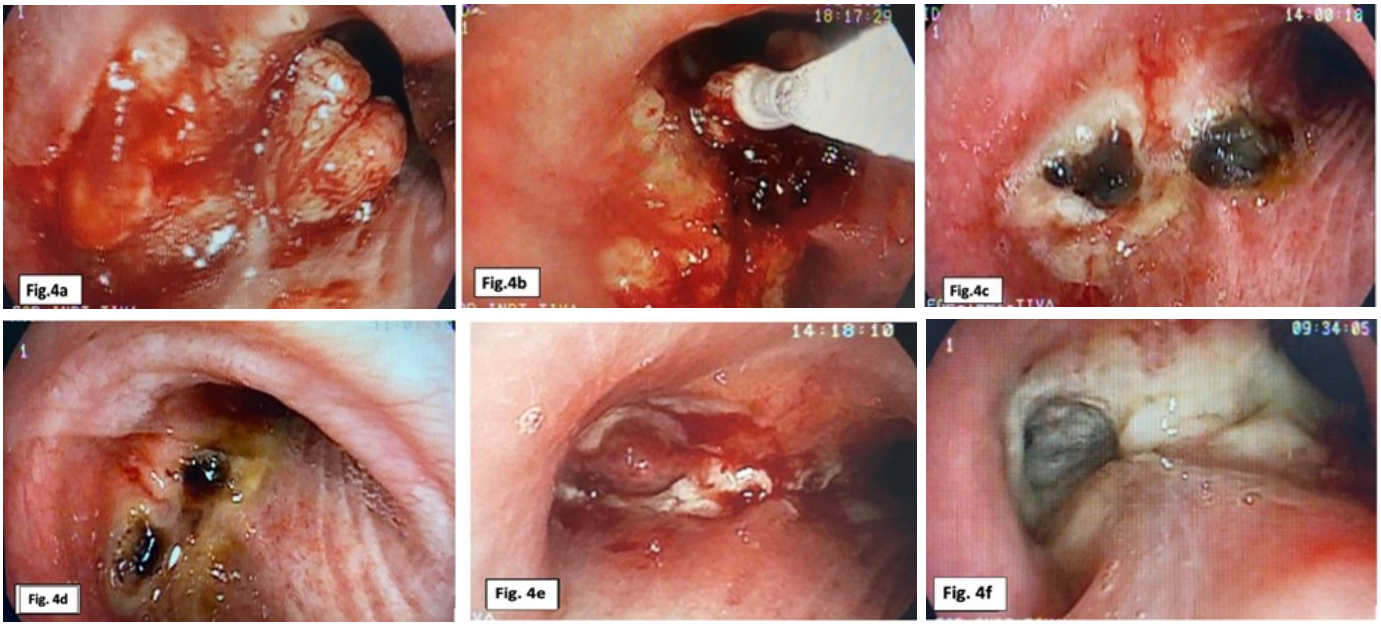

Figure 4. Bronchoscopy findings during treatment course. **4a:** Prior to FOB with thermal ablation, there was an irregularly-shaped friable mass occluding the RMB and LMB, at 70% and 100%, respectively. **4b:** Cryotherapy of the RMB and LMB. **4c:** Post-thermal ablation and cycle 1 cisplatin; irregularly-shaped necrotic mass completely obstructing the LMB extending to the opening of the RMB noted, with RMB now visualized. **4d:** For cycle 2 cisplatin; necrotic mass completely obstructing the LMB is again seen, the RMB is patent. **4e:** For cycle 3 cisplatin; no significant change in completely-occluded LMB; **4f:** For cycle 4 cisplatin; broad carina with presence of fibrin clot is noted. The LMB is now patent. FOB: fiberoptic bronchoscopy; RMB: right mainstem bronchus; LMB: left mainstem bronchus

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