

# Multimodality multistaged management of large endobronchial carcinoid causing respiratory failure: A case report with review of literature

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## ABSTRACT

We report the case of a 58-year-old female presenting with central airway obstruction leading to airway compromise thrice, first two times from endobronchial growth of typical carcinoid tissue and subsequently from granulation tissue at anastomotic site after left carinal pneumonectomy. Bronchoscopic resection of carcinoid tumor and granulation tissue was performed successfully with electrosurgical snaring through rigid bronchoscope. Cryodebridement using flexible cryoprobe of the tumor was done postembolization and of the remnant granulation tissue without any complication. A multimodality approach is required for favorable outcome as observed in this case.

**KEY WORDS:** Argon plasma coagulation, carcinoid, central airway obstruction, cryodebridement, granulation tissue, pneumonectomy

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## INTRODUCTION

Central airway obstruction (CAO) refers to obstruction of the central airways that include trachea, main stem, and lobar bronchi. It can result from a variety of malignant (locally advanced lung cancer, metastases to airway, and malignant primary tracheobronchial tumor) or nonmalignant (postintubation tracheal stenosis, posttracheostomy tracheal stenosis, posttubercular infection, lung transplant or thoracic surgery related, benign tracheobronchial tumor, and idiopathic) disease processes and is the cause of significant morbidity and mortality if left untreated.<sup>[1]</sup> It can present with varied clinical manifestations from gradually progressive dyspnea and cough, to rapidly developing respiratory distress and hypoxia irrespective of etiology. Therefore, relief of CAO should be immediate and should focus on securing and restoring of patency of central airways. A variety of interventional options are

available to relieve CAO. These options include mechanical techniques such as balloon bronchoplasty, stent placement, and microdebridement; hot therapies such as neodymium: yttrium-aluminum-garnet laser resection, electrocautery, and argon plasma coagulation (APC); and techniques such as cryodebridement or cryoavulsion and cryotherapy.<sup>[2-4]</sup> The evidence regarding efficacy of these techniques when used alone or in combination is limited.<sup>[5,6]</sup> We successfully used a combination of the aforementioned endoscopic techniques introduced through a rigid bronchoscopic barrel which was used to secure the airway in a 58-year-old female for relieving CAO. The procedure was carried out thrice, first two times to relieve obstruction from endobronchial growth of typical carcinoid tumor and subsequently from granulation tissue at anastomotic site after left carinal pneumonectomy.

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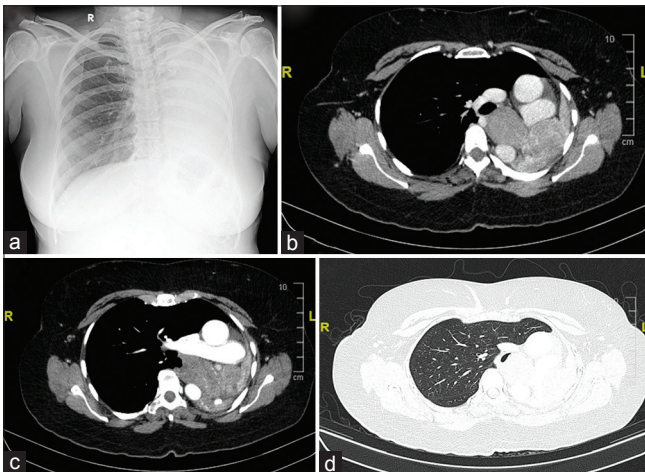
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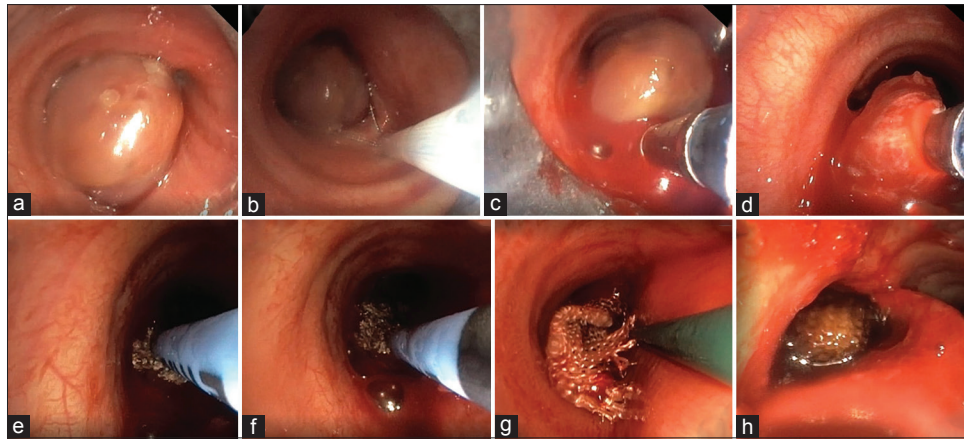
## CASE REPORT

A 58-year-old female was referred to our hospital in emergency state with complaints of gradually increasing breathlessness for 3 months and an audible wheeze for the past 1 month followed by worsening of symptoms and drowsiness for the past 2 days. She gave a history of an episode of pneumonia localized to her left lung 6 years ago for which she required inpatient care. She also gave history of recurrent respiratory tract infections over the past 5 years which were managed with over-the-counter medications, and no imaging had been performed. Her background history revealed that she was hypertensive and was taking antihypertensive medicines regularly for the past 5 years. On general examination, the patient had a Glasgow Coma Scale score – 13/15 (E3V4M6), arterial blood pressure – 140/80 mmHg, a heart rate – 128 beats/min, respiratory rate – 36 breaths/min, and oxygen saturation – 90% on room air. The arterial blood gas on room air showed a PaO<sub>2</sub> – 56 mmHg, PaCO<sub>2</sub> – 90 mmHg, HCO<sub>3</sub><sup>-</sup> – 28.2 mmol, and pH of 7.21 suggestive of acute hypercapnic respiratory failure. Respiratory system examination revealed absent left-sided air entry. Rest of the systemic examination and laboratory investigations were unremarkable. Chest radiography revealed complete haziness of the left hemithorax with abrupt cutoff of the left main bronchus and shifting of mediastinum to the left side suggestive of total left lung collapse secondary to suspected endobronchial growth [Figure 1a]. Computed tomography (CT) thorax showed total collapse of the left lung, enhancing lobulated soft-tissue density in the distal zone of the trachea extending to the left main bronchus and extraluminal component in the left hilar region measuring 5 cm × 3.8 cm × 5 cm [Figure 1b-d]. She was initially managed with noninvasive ventilation and then immediately shifted to the operation theater. She underwent diagnostic fiber-optic bronchoscopy (FOB)

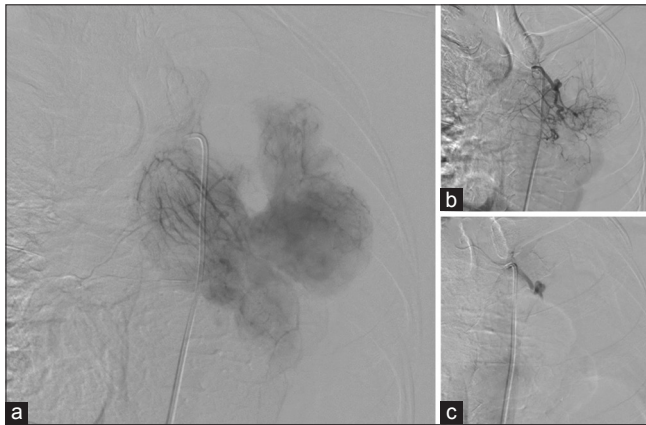


**Figure 1:** (a) Chest radiograph showing complete left homogeneous opacity with shifting of mediastinum to the same side. (b-d) Computed tomography scan thorax mediastinal (b and c) and lung (d) window showing total collapse of the left lung, enhancing lobulated soft-tissue density in the distal zone of the trachea extending to the left main bronchus

that showed complete occlusion of the left main and extension of growth over the carina to cause nearly 80% occlusion of the right main bronchi. Decision for tumor debulking with rigid bronchoscopy under general anesthesia was immediately taken under high-risk consent. Tumor was debulked with electrosurgical snaring (Olympus™ reusable electrocautery snare, Germany) using FOB (BF-1TQ190, Olympus Corp., Japan) introduced through rigid tracheobronchoscope of size 11 mm (KARL STORZ Endoskope, Germany), and patency of the right main bronchus was achieved [Figure 2]. The patient had significant bleeding despite the use of cautery from the cut surface of the residual tumor, and hence, mechanical debulking and cryodebridement were deferred. Hemostasis was secured with argon plasma photocoagulation (APC) (ERBE™ electrocautery and APC unit, Germany), adrenaline (1 ml of 1 in 10,000), tranexamic acid, and SURGICEL (Ethicon US, LLC). She had symptomatic relief as she got extubated next day of procedure and discharged with normal vital parameters under regular follow-up. Histopathology examination (HPE) of the biopsy specimens was suggestive of typical carcinoid (polypoid neoplasm with marked necrosis and hemorrhage and intervening stroma showing extensive hemorrhage and numerous blood vessels). Immunohistochemistry further supported the diagnosis (pan-cytokeratin, synaptophysin, and chromogranin positive with MIB-1 labeling index = 1%). As the tumor was potentially curable despite being extensive, it was decided to debulk further after embolization to assess possibility of left pneumonectomy. She underwent bronchial angiography, and vessels to the tumor were selectively embolized with polyvinyl alcohol and coils in order to minimize possibility of bleeding [Figure 3]. Rigid bronchoscopy and debulking were performed with cryoprobe (ERBE™ contact cryotherapy console; flexible cryoprobe with 2.4 mm tip, Germany) in addition to snare, and tumor was traced till about 1.5 cm distal to carina on the left side. Bleeding was minimal and hemostasis could be easily achieved. It was decided to seek thoracic surgery consultation for left pneumonectomy considering the bulk of the tumor and surgical accessibility. She underwent left posterolateral thoracotomy and left pneumonectomy with carinal resection and end-to-end tracheal–right main bronchus anastomosis without any complication after 1 month of discharge. Mediastinal lymph node sampling was also performed and findings were unremarkable. She remained asymptomatic for 2 months but again presented with stridor. Repeat FOB showed an eccentric exuberant growth seen at the anastomotic site narrowing the lumen to 5 mm. She underwent rigid bronchoscopic debulking of growth with electrosurgical snaring and cryoprobe [Figure 4]. HPE of growth revealed polypoid inflammatory granulation tissue with no evidence of neoplastic elements. She has been discharged in stable condition under regular follow-up with no recurrence of symptoms in the next 3 months.



**Figure 2:** (a) Bronchoscopic view showing endobronchial polypoid tumor growth causing complete occlusion of the left main with extension to distal trachea. (b) Electrosurgical snare placement around polypoid tumor pedicle. (c and d) Tumor removal (cryodebridement) with cryoprobe. (e and f) Argon plasma coagulation and (g) surgical application on tumor base for hemostasis. (h) Residual anatomy after tumor debulking



**Figure 3:** (a and b) Bronchial angiography of vessels supplying to the tumor. (c) Bronchial angiography postembolization showing reduction in vascularity

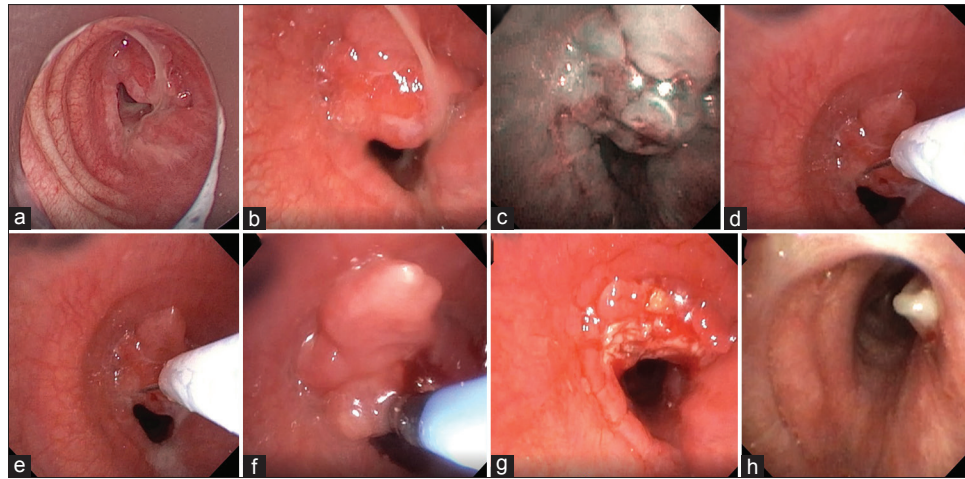
## DISCUSSION

The present report showed that a multimodality approach using combination of interventional bronchoscopic techniques (mechanical debulking, electrosurgical snaring, and cryodebridement) is a potentially useful method to manage CAO resulting from endobronchial carcinoid tumor and subsequently from granulation tissue developing at anastomotic site after left carinal pneumonectomy. The patient was successfully managed despite the complications and need for multistaged procedures. It has been previously reported that a multimodality approach to manage CAO offers the highest chance of successful immediate and long-term outcomes with minimal complications.<sup>[4-7]</sup> However, experience with endobronchial resection for carcinoid is relatively limited.

Endobronchial tumors are mostly malignant with benign ones being extremely rare. These tumors can cause CAO and threaten the life of patients irrespective of their benign or malignant character.<sup>[5]</sup> Our case initially presented to emergency with acute hypercapnic respiratory failure

secondary to endobronchial carcinoid with CAO. The objective in this setting was to select the appropriate technique for managing CAO in the emergent situation with minimal complications. Rigid bronchoscopic conduit was used to ensure adequate airway control, and electrocautery snare was used due to its ability to sever large polypoid mass quickly with concomitant hemostasis. Despite this, significant bleeding was encountered which was difficult to control. Once the emergency situation was handled, next step was to evaluate the need for further management. This depended on the histopathology which was consistent with typical carcinoid. In view of this, effort was made to look for the extent of tumor and assess possibility of curative resection. To assess this, a repeat rigid bronchoscopic debulking was done in a controlled setting after bronchial artery embolization (BAE) in view of excessive bleeding during the first time. It has been reported that this treatment modality is safe and feasible with the advantage of reduction of intraprocedural bleeding as well as occurrence of residual tumor postprocedure.<sup>[8-10]</sup> This allowed for the use of other debulking techniques including cryoprobe and mechanical obstruction with minimal bleed. BAE of tumor vessels immediately before endobronchial debulking is an excellent complementary technique to reduce bleed, especially in a resource-constrained country like India where laser is not easily available. Few studies have previously used BAE before debulking in order to reduce bleeding and reported favorable outcome.<sup>[8-10]</sup> Once adequate clearance for left pneumonectomy could be achieved with bronchoscopic techniques, the patient was subjected to surgery. Although the patient tolerated the procedure well, she developed a rare complication of resection surgery resulting in the need for another bronchoscopic intervention to remove granulation tissue at anastomotic site.

We performed a systematic search of the PubMed, Google Scholar, ScopeMed, and Embase databases (for years 1995–2018) to identify the studies reporting multimodality approach to manage CAO due to endobronchial carcinoid



**Figure 4:** (a and b) Bronchoscopic views showing an eccentric exuberant granulation tissue growth seen at the anastomotic site. (c) Narrow-band imaging showing branched vessels with intact tortuosity overlying growth suggesting benign nature. (d and e) Electrosurgical snare placement around granulation tissue growth. (f) Granulation tissue removal by cryodebridement. (g) Residual anatomy after granulation tissue resection. (h) Repeat bronchoscopy after 3 months showing no recurrence postresection

with successful outcomes and minimal complications using the following search terms (“BAE,” “Bronchial artery embolization,” “Bronchoscopic treatment,” “Carcinoid,” “Central airway obstruction,” “Endobronchial,” “Excision,” “Intraluminal carcinoid,” “Resection,” and “Typical carcinoid”). Thirty-one articles (case reports, case series, and observational studies) including the current case were identified. Four articles were excluded because neither the abstracts nor full texts were available. Articles pertaining to bronchoscopic resection of endobronchial tumors other than carcinoid were also excluded. The clinicodemographic profile of cases and types of bronchoscopic intervention including outcome of treatment has been described in Supplementary Tables 1 and 2, respectively.<sup>[7-36]</sup> Various bronchoscopic treatment options as mentioned in these studies were practiced depending on the physician’s discretion, expertise, and available resources. All studies have reported high success rates with minimal complications and good long-term outcome. Bronchoscopic treatment was considered to have curative intent if the carcinoid was exclusively intraluminal on radiological as well as bronchoscopic examination, associated with no metastasis, size < 20 mm, polypoid with narrow base, good bronchoscopic accessibility, and typical histology.<sup>[36,37]</sup> It was also used with palliative intent as it provided detailed anatomical information for the surgeon and relief from symptoms of postobstruction pneumonia and also decreased the extent of resection needed, thereby sparing valuable lung parenchyma providing better quality of life, especially in young patients. Few studies have termed the last advantage as procedure of endoluminal preparation for parenchyma-sparing surgery approach where bronchoscopic tumor debulking is performed before preparation for subsequent parenchyma-sparing surgery.<sup>[24,32]</sup> Extensive surgeries such as pneumonectomy and lobectomy were avoided whereas parenchyma-sparing surgeries such as sleeve lobectomies, segmentectomy, and main bronchial sleeve resections were encouraged

with favorable long-term outcome. Surgical resection or combined treatment was advised if there was extraluminal extension, typical carcinoid with size > 20 mm, atypical histology regardless of size, incomplete response with bronchoscopic therapy (BT), tumor with broad base, nodal involvement, metastasis, and residual disease as well as recurrence after BT.<sup>[36,37]</sup> However, few studies have reported BT to be curative even in atypical histology or in case of residual or recurrence.<sup>[17,17,22,23,33]</sup> Bleeding especially uncontrolled is considered to be one of major complications. Few studies including the current one have used BAE before BT in order to reduce the risk of bleeding.<sup>[8-10]</sup>

Obstructive granulation tissue at anastomotic site of tracheal resection followed by reconstruction is one of the postsurgical complications resulting in airway compromise with reported incidence of 7%–24%.<sup>[38-40]</sup> It generally occurs after few months of surgery but can develop as early as 2 weeks. Debulking with the use of flexible or rigid forceps using FOB or rigid bronchoscopy, respectively, for limited or nonobstructive granulation tissue that is eccentric in nature.<sup>[38,39]</sup> Extensive granulation tissue is best treated with cold therapies as the tissue is highly cryosensitive. Other modalities such as laser resection, APC, high-dose rate endobronchial brachytherapy, or PDT can also be used. Insertion of T-tube and re-surgery should be considered in cases with severe obstruction.<sup>[10]</sup> The recurrence of granulation tissue postresection has been reported in 10%–50% of cases. However, in our case, on follow-up of up to 3 months, there has been no recurrence.

Our experience supports that bronchoscopic treatment can be considered as a bridging therapy to definitive treatment such as surgery or chemoradiotherapy while managing endobronchial carcinoid with extrinsic component. Bronchoscopic resection alone may suffice if the tumor is small, typical, only endobronchial,

polypoid with small base and complete resection is achieved.<sup>[5-7,36,37]</sup> Bronchoscopic resection followed by surgical approach has gained attraction for treatment of endobronchial carcinoids with successful outcome as reported previously.<sup>[23,30,34]</sup> The advantages of this combined approach are recanalization of involved airway, resolution of inflammation, better assessment of the tumor base, allowing more accurate surgery planning with parenchymal sparing, reduction of postobstructive infections, and stabilization of patient in order to undergo surgery in better general condition. Bronchoscopic resection of endoluminal tumor provides larger tissue specimens for more accurate histological diagnosis between typical and atypical carcinoid which is an essential step before deciding for surgery.<sup>[7,34]</sup>

Periodic bronchoscopic surveillance is essential as endobronchial carcinoids are prone to recurrence and/or malignant transformation. This should be combined with radiological (chest X-ray, CT thorax, 68-Gallium DOTATATE positron emission tomography-CT, or somatostatin receptor scintigraphy) as well as biochemical markers (synaptophysin or chromogranin A) depending on the availability at the center. The European Neuroendocrine Tumor Society and National Comprehensive Cancer Network have provided surveillance recommendations for postprocedure resection of carcinoid tumors.<sup>[41]</sup> The surveillance should be frequent if there is nodal or distant metastasis and atypical histology in resected specimens. The management of large typical endobronchial carcinoid with extrinsic component is highly center and patient dependent. There is no gold standard due to rare nature of the tumor and lack of uniformity in expertise among centers managing such cases. Therefore, a larger prospective clinical trial is warranted in near future. Multimodality multistaged approach with curative intent seems most appropriate when dealing with such complex cases.

#### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

#### Conflicts of interest

There are no conflicts of interest.

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