Postobstructive pneumonia in lung cancer

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Abstract: Postobstructive pneumonia can complicate lung cancer, particularly in more advanced stages of the disease, producing significant clinical decline and a poorer prognosis. It can lead to complications such as empyema, lung abscess and fistula formation. Postobstructive pneumonia can also be the first manifestation of an underlying malignancy. There are multiple challenges in the management of these patients. Recognition and treatment of this entity can be complex and includes the use of imaging, administration of broad-spectrum antibiotics to cover the wide variety of microorganisms involved and the use of different interventional modalities to relieve the obstruction. Existing literature on postobstructive pneumonia is scarce. In this article, we review the pathophysiology, different diagnostic methods and the therapeutic options to treat this condition. The utility and efficacy of the various modalities that are currently available in clinical practice to the interventional pulmonologist are described in some detail.

Keywords: Postobstructive pneumonia; lung cancer; bronchoscopy; interventional pulmonology

Introduction

In the United States, more than 200,000 cases of lung and bronchus cancer are reported each year, along with an estimate of over 150,000 deaths (1). In patients with lung cancer, age and advanced stage of the cancer increase the risk of infection. In patients with an initial diagnosis of pneumonia, a diagnosis of lung cancer has been noted to be more frequent in patients older than 65 years and in those with nonresolving pneumonia (2).

Pneumonia has been reported to occur in 50–70% of patients with lung cancer (3). Derangements at the level of the immune system and lung architecture make patients with lung cancer more susceptible to infections. Changes in immunity include the immunocompromise from the malignancy itself and from side effects of the different treatment modalities used to treat it. Changes in lung architecture include structural abnormalities such as

airway obstruction. Postobstructive pneumonia is defined as an infection of lung parenchyma secondary to bronchial obstruction (4). It is often associated with lung malignancy (see *Figure 1*). The first documented cases were described in 1949 by McDonald *et al.*, who defined it as a radiographic opacity resulting from complete or partial obstruction of the airway by a lung tumor (5). Bronchial obstruction is more common with tumors arising centrally, such as small cell lung carcinoma (SCLC) and squamous cell carcinoma (SCC) (6). Airway obstruction has also been seen with carcinoid tumors, which usually have a more indolent presentation (7). Neoplasms that metastasize to the lungs such as carcinomas of the breast, ovaries, colon and kidney can also cause obstructive atelectasis, leading to poor airway clearance, microbial airway colonization and eventually pneumonia (8). Other malignancies with a propensity to cause airway obstruction include lymphomas and tumors of the neck, thyroid, larynx and esophagus (9).
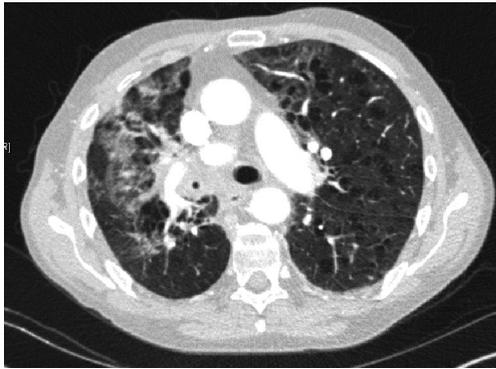
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Figure 1 Tumor obstructing the bronchus intermedius. There is evidence of postobstructive pneumonia affecting the parenchyma of the right lower lobe (courtesy of Dr. Kassem Harris, Interventional Pulmonology, Westchester Medical Center, Valhalla, NY, USA).

Postobstructive pneumonia can present at different stages of lung cancer and may occasionally be the initial manifestation of a malignancy (10). However, most cases are associated with advanced neoplasms. Up to 50% of patients with advanced lung cancer and pneumonia will have endobronchial compromise. This coexistence is associated with significantly increased morbidity and mortality (11). Pneumonia secondary to malignant obstruction is usually polymicrobial and difficult to eradicate with antibiotics alone (12). Infection distal to such obstructions can progress to complications like lung abscess, empyema or fistula formation in up to 10–15% of patients (4).

Besides the traditional treatments for cancer (surgery, chemotherapy and radiotherapy), additional therapeutic modalities are often required to overcome the obstruction. Improving endobronchial patency is usually needed to resolve such infections (13).

In this review, the key aspects of postobstructive pneumonia in lung cancer patients, including diagnostic evaluation and the most commonly used treatment modalities, will be described.

Epidemiology

Literature about postobstructive pneumonia in lung cancer patients is somewhat limited. Some reports suggest that 2–5% of cases of community acquired pneumonia are caused by an obstruction proximal to the site of infection, with an underlying malignancy in most of these cases. The majority of these patients also have a history of smoking, which further increases the risk of malignancy (14). Abers

et al. reported how malignancy was discovered to be the cause of the obstruction in approximately 50% of patients with postobstructive pneumonia (15).

Postobstructive pneumonia, however, is more common in patients with established lung cancer. About 45–50% of patients with advanced or rapidly progressing cancer will have a postobstructive pneumonia at some point (4). Other authors report that up to 80% of non-resectable lung cancers will manifest evidence of airway obstruction during the course of their disease (16,17).

Pathogenesis

The lung is a common site of infection in patients with cancer. In both, immunocompetent and immunosuppressed hosts, the initial pathophysiology of pneumonia is fairly similar and typically results from invasion and overgrowth of microorganisms in the lung parenchyma. Infectious organisms access the small airways via inhalation, aspiration, hematogenous spread or locoregional movement from larger airways. In order for bacteria to cause infection, they have to breach the patient's complex array of dynamic defense apparatuses that include architectural, cellular and humoral mechanisms (18). In immunocompetent patients, these defense systems are usually intact and capable of eliminating pathogens.

Multiple types of malignancies have been associated to postobstructive pneumonia (see *Table 1*). Along with the mechanical consequences of cancer-related airway obstructions, lung cancer patients frequently have a wide variety of immune defects, which increase their likelihood of developing lung infections. These changes in immunity are caused by both the malignancy and its treatment, including surgery, radiotherapy and chemotherapy (19). Lee *et al.* have described how the general debility from cancer and its treatment strongly influence the incidence of lung infections. An Eastern Cooperative Oncology Group (ECOG) score ≥2 has been identified as a risk factor for pneumonia. Nutritional deficiencies, commonly seen in patients with malignancy, typically have a deleterious effect (20). Other underlying lung diseases, such as chronic obstructive pulmonary disease (COPD), emphysema and bronchiectasis, commonly found in patients with lung cancer and smoking history, also increase the incidence of infections by affecting innate anatomical defense mechanisms resulting in poor clearance of secretions and bacteria.

Luminal airway obstruction due to malignancy can

Table 1 Malignant etiologies of postobstructive pneumonia

Primary lung cancer

    Lung adenocarcinoma

    Squamous cell

    Small cell

    Lung carcinoid

Metastatic carcinoma from other primary tumors in: head and neck, esophagus, colorectal, renal cell, melanoma, breast and esophagus

Lymphoma

Lymphadenopathy (from tumor spread) with airway compression

Mediastinal tumors: thymoma and thyroid cell carcinoma

Figure 2 Endobronchial squamous lung cancer obstructing the superior segment of the left lower lobe (courtesy of Dr. Kassem Harris, Interventional Pulmonology, Westchester Medical Center, Valhalla, NY, USA).

be due to different mechanisms, including extrinsic compression by a tumor or enlarged lymph nodes, endobronchial obstruction from an intraluminal mass (see *Figure 2*) or a combination of both (21). Smaller airways can get obstructed by lymphangitic spread of malignancy (22). These mechanisms have in common the stasis of secretions in bronchi and alveoli distal to the obstruction, formation of atelectasis and subsequent microbial colonization and infection (23). Established infections can cause extensive local destruction of the lung parenchyma, occasionally complicated by formation of lung abscess or empyema, often requiring invasive treatment modalities in addition to the use of antimicrobials (3).

Cancer treatments, such as chemotherapy, radiotherapy and surgery can also cause derangements of innate and adaptive immune defense mechanisms responsible for protecting the lungs from infections. Chemotherapy often leads to neutropenia, which when present, particularly with counts lower than 500 cells/μL, is associated with severe infections and poor outcomes. Functional neutropenia secondary to radiation, steroids and hyperglycemia also contributes to increased risk of pneumonia by impairing the phagocytic and chemotactic properties of neutrophils (24). Radiation and surgery can cause airway distortion and the risk of introducing microorganisms during surgical procedures. Presence of endobronchial stents used to open airways affected by extrinsic compression from lung tumors can also precipitate lung infections by different mechanisms, including the introduction of pathogens during the procedure or the colonization and growth of microorganisms on the stent (25).

Microbiology

There are not many studies describing the microbiology of postobstructive pneumonia in lung cancer patients, but those available have shown infections with a wide spectrum of microorganisms (see *Table 2*). The variability is particularly dependent on the immunologic defects related to the underlying neoplasm and the various treatment modalities that the patient has received (26). Bacterial, viral and fungal infections often coexist in these patients (27).

In patients with untreated cancer who are relatively non-immunocompromised, the predominant microorganisms are pretty similar to those affecting non-cancer patients with community acquired pneumonia. These include *Streptococcus pneumonia*, *Haemophilus influenza*, *Moraxella catarrhalis* and some viruses. Studies involving patients with advanced lung cancer that have received treatment, leading to multifactorial immunosuppression, describe a preponderance of other organisms such as *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Enterobacter cloacae* and *Acinetobacter* species (28). Oral anaerobes such as *Bacteroides*, *Prevotella*, *Fusobacterium* and *Actinomyces* have also been isolated from postobstructive pneumonias.

Once cellular immunity has been impaired, other viral infections such as cytomegalovirus and herpes can coexist with bacterial infections. Fungal organisms like *Candida*, *Aspergillus*, *Histoplasma* and *Coccidioides* cause pulmonary infections in these patients as well. *Pneumocystis jirovecii* pneumonia is also seen in this setting. Impaired humoral immunity increases susceptibility to infections

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Table 2 Microorganisms found in postobstructive pneumonia

Bacteria

  Gram-positive

    Staphylococcus aureus

    MRSA

    Enterococcus species

    Streptococci

      Pneumonia

      Viridans

    Peptostreptococcus species

    Nocardia

    Bacillus species

  Gram-negative

    Haemophilus influenzae

    Klebsiella species

    Pseudomonas aeruginosa

    Escherichia coli

    Acinetobacter

    Stenotrophomonas maltophilia

    Enterobacter species

    Citrobacter species

    Bacteroides species

Fungi

  Candida species

  Aspergillus species

  Zygomycetes

  Fusarium species

  Histoplasma

  Coccidioides

Virus

  Cytomegalovirus

  Other Herpes species

by encapsulated organisms. In neutropenic patients with postobstructive pneumonia, the spectrum of infection has shifted from a predominance of gram-negative bacilli to one of gram-positive cocci, particularly *Staphylococcus* (including methicillin-resistant *Staphylococcus aureus*), *Streptococcus*

and *Enterococcus*. In persistent neutropenia, superinfection with multidrug resistant (MDR) gram-negative organisms (*Pseudomonas*, *Stenotrophomonas*, *Acinetobacter* and *Citrobacter*) and fungi (*Aspergillus*, *Zygomycetes* and *Fusarium* species) is common.

Certain microorganisms have been found to be more commonly associated with complications. For example, the most commonly organisms seen in empyema include *Staphylococcus aureus* and gram-negative bacilli.

Microbiologic specimens, unfortunately, are difficult to obtain since infection is typically distal to the area of obstruction (29). Hsu-Kim *et al.* have described how the diagnostic yield is significantly increased by performing bronchoalveolar lavage (BAL) and needle aspiration (12).

Clinical presentation

The classic symptoms of postobstructive pneumonia are similar to that of any pneumonia. Fever, cough and dyspnea are present in the majority of cases. Cough is productive and purulent unless there is complete obstruction. Loss of appetite and weight loss may be due to the malignancy and is worsened by the development of pneumonia. Cachexia can be seen in >50% of cases. Hemoptysis and chest pain are not as common. Sometimes carcinoid tumors, especially if central, will present with hemoptysis, wheezing and bronchial obstruction. A proximal partial occlusion can manifest itself as localized monophonic wheezing.

The constellation of signs and symptoms also depends on whether the postobstructive pneumonia is diagnosed in the setting of a known advanced lung malignancy or if a non-resolving pneumonia led to the discovery of an underlying cancer. COPD is a common comorbidity in patients with postobstructive pneumonia in the setting of lung cancer and thus such a patient can present as an acute exacerbation of COPD with pneumonia.

In a prospective study, patients with postobstructive pneumonia due to malignancy, when compared to patients with bacterial pneumonia, had a longer duration of symptoms (14 *vs.* 5 days) and were more likely to have weight loss and cavitary lesions but less likely to have leukocytosis (15).

Evaluation

Postobstructive pneumonia is often initially described as "nonresolving pneumonia" and its evaluation generally requires a detailed workup. The presence of an underlying

malignancy should be suspected based solely on the clinical presentation. Suspicion should prompt the use of more advanced tools to look for an extrinsic or intrinsic airway occlusion as well as to obtain microbiologic and pathologic specimens. Imaging and bronchoscopy play key roles in diagnosing postobstructive pneumonia.

Pneumonia can be the first manifestation of a malignancy, and so a prompt diagnosis can be challenging unless a high degree of suspicion is maintained when evaluating such patients.

Imaging

Initial evaluation is typically with a chest radiograph, which is easily available and noninvasive (30). Its main disadvantage is its low specificity and poor negative predictive value. In addition, radiographic evaluation has been shown to have lower detection rates in immunocompromised patients with pneumonia (31). On plain radiographs, it is often difficult to differentiate tumor from postobstructive consolidation or atelectasis. However, it is helpful in determining when a patient has a "nonresolving pneumonia". In 1991, Kirtland and Winterbauer radiologically defined "slowly resolving pneumonia" as clearing of radiographic infiltrate <50% in 2 weeks or incomplete clearing at 4 weeks in a patient who has clinically responded to antibiotics (32). Other authors have defined it more broadly as radiographic infiltrate that is slow to resolve after optimal antibiotic therapy given for at least 10 days (33).

CT of the chest is not only more sensitive than plain radiography in detecting and characterizing of pneumonia (see *Figure 1*), particularly when intravenous (IV) contrast is used or when performed with high-resolution formatting (34). It helps determine the possible site of obstruction, distinguish consolidation from neoplasm or lymphadenopathy and evaluate the patency of distal bronchi, the relationship between mass and adjacent structures and the extent of pleural involvement (35,36).

New generation CT scanners, by acquiring thinner cuts, create better quality images and can generate a variety of two-dimensional multiplanar and three-dimensional reconstructions. These help direct bronchoscopic interventions that are aimed not only at obtaining diagnostic samples, but also to relieve the obstruction (37,38).

Ultimately though, fiberoptic bronchoscopy plays the central role in making a diagnosis of airway obstruction and malignancy (39). Better sputum samples can be obtained by protected specimen brushing (PSB) and BAL which is the diagnostic tool of choice (40).

Endobronchial ultrasound by identifying a lung mass or enlarged lymph node, followed by fine needle aspiration and/or transbronchial biopsy, is often invaluable in the diagnosis of a neoplasm and determining the extent of involvement.

Treatment

The management of postobstructive pneumonia is initially dependent on appropriate antibiotic therapy but will eventually require relief of the obstruction. The presence of the obstruction proximal to the infection predisposes to slow or even incomplete response to antibiotics, leading to frequent recurrence of the infection. Repeated treatments can then create significant resistance to antimicrobials (41). The duration of antibiotic regimen is usually more prolonged than pneumonia not associated with malignant obstruction and can last for 6 weeks or more.

Empiric broad spectrum antibiotics are usually selected initially since, at the initial evaluation, it is difficult to obtain information about the specific infection present distal to the obstruction. Antimicrobial regimens are typically guided by local prevalence and resistance patterns among MDR pathogens (41).

Response to antimicrobial therapy can be delayed and, therefore, it is not uncommon to observe persistence or recurrence of the pneumonia. If the infection progresses, it can lead to complications with serious consequences such as lung abscess, hemorrhage, empyema and formation of bronchopleural fistula (41). Estimated incidence of these complications is in the range of 10–15%. Due to their mixed bacterial etiology, their treatment is more challenging. Additionally, these complications can prevent prompt initiation of chemotherapy, thus further delaying resolution of the obstruction.

If the lesion is contained, surgery is usually the treatment of choice. If curative resection is not an immediate option, treatment should be attempted with one of several invasive methods available, individualizing decisions in each case. Interventional techniques allow treatment of the obstruction to facilitate drainage of secretions. With advances in interventional pulmonology, endobronchial treatment has become a safe, effective and important tool in the management of these patients.

Pleural effusion associated with ipsilateral malignancy and obstructive pneumonia can be paramalignant and transudative due to bronchial obstruction or parapneumonic

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and exudative secondary to pneumonia. Progressive pneumonia can lead to an infected pleural space and empyema. Management of the effusion includes evaluation of the pleural fluid and treatment of the obstruction. Manometry when available should be combined with the thoracentesis to evaluate for lung entrapment.

Fluid should be subjected to a thorough chemical, microbiological and cytological analysis. Benign transudative effusions can be managed by relief of bronchial obstruction and therapeutic thoracentesis. Small bore chest tube drainage, intra-pleural fibrinolytic therapy and decortication may be required for parapneumonic effusions or empyema. Surgical resection when undertaken in the presence of an infected pleural space carries a higher risk of bronchopleural fistula if the bronchial stump gets infected.

Tunneled pleural catheters combined with pleurodesis are indicated for confirmed malignant pleural effusions. Of note, application of talc under direct visualization achieves superior results compared to pleural catheter-directed application.

External beam radiotherapy (EBRT) for airway obstruction

Patients with advanced lung cancer, airway obstruction and poor performance status might not be suitable candidates for more invasive interventions. When immediate management of the airway is required, EBRT can be considered an alternative (42,43). Lee *et al.* evaluated the response to EBRT in 95 patients with obstructed airways due to different types of lung cancer. Not only did they find that EBRT was effective in resolving airway obstruction (reported response rate of 78.9%), but they also described a significant increase in 1-year survival rate in these patients. The type of tumor did not affect response to treatment but response was significantly better in tumors <6 cm (43). Application of local radiotherapy for 10–12 days at doses of 30–40 Gy have resulted in palliation of lung mass symptoms, including relief of obstruction. When compared to endobronchial brachytherapy, ERBT showed better outcomes (44).

Interventional modalities to relieve obstruction

Interventional pulmonology also offers different alternatives to manage external obstructions and to treat endobronchial lesions (45), leading to relief of obstruction, palliation of symptoms and treatment of infection. Because this condition is more commonly seen in advanced malignancy and in patients with a higher operative risk due to their poor pulmonary reserve, deconditioning and increased use of steroids, bronchoscopic procedures often become the preferred therapeutic option (17). There are multiple modalities available, including endobronchial laser therapies, brachytherapy, argon plasma coagulation (APC), cryotherapy, electrocautery, photodynamic therapy (PDT), airway dilatation and stent placement (46). Mechanical debulking and thermal techniques are usually preferred for intraluminal tumors, while stents are the preferred method to treat extrinsic obstructions. See summary of techniques in *Table 3*.

Laforet *et al.* first described the use of laser for the treatment of airway tumors in 1976 (47). Laser can be applied using both flexible and rigid bronchoscopes (17). This therapy targets endobronchial and endotracheal obstructions, enabling tumor destruction and appropriate hemostasis when needed (48). Laser has been shown to be beneficial to treat obstructions in proximal airways, ideally with a short length of involvement (<4 cm) and minimal submucosal infiltration. Treatment of obstructions in segmental bronchi is more difficult (49). Laser has been found to provide quick and meaningful improvement in symptoms, airway patency, hypoxemia, pulmonary function and quality of life when used for endobronchial obstructions (50). It has also often led to significant improvement in the drainage of mucus and resolution of the infectious process (51). Complications of laser are rare (around 2–3%) when the procedure is done by a trained operator, with procedural deaths less than 1%. Complications include hypoxemia, bleeding (severe hemoptysis reported in about 1% of cases), perforation, fistula formation and fire. The risk of fire can be decreased by using low inspired oxygen concentrations, not higher than 40% (52).

APC is a non-contact electrocoagulation that uses heated argon plasma as a conducting medium, offering a more uniform distribution of its therapeutic effect with less manipulation and trauma to the target tissue. This technique devitalizes tissue with high temperatures, coagulating and desiccating tissue. It is a good option for managing distal or extensively hemorrhagic tumors (53). It is also a good option for lesions that measure less than 3.5 cm in length that protrude within the lumen and do not extend beyond the cartilage of the airway (54). Complications rates are low given its superficial effect. Major complications occur in less than 5% of cases (55).

Table 3 Types of interventions for airway obstruction

Type of intervention	Principle	Indications	Advantages	Disadvantages	Complication rate
Rigid bronchoscopy and mechanical debulking	Rigid bronchoscope allows large entrance for debulking and suction of tumor	Central airway tumors	Low cost	Airway trauma, perforation	Less than 1%
		Proximal endobronchial lesions	More secure airway for ventilation		Teeth injury and airway injury by rigid bronchoscope and bleeding can be seen. Mortality risk is low
Laser (with rigid or flexible bronchoscopy)	Uses light to generate energy and heat to ablate tumors	Central airway tumors	Immediate and prolonged debulking	High cost	Around 2–3%
	Short pulsations of 20–40 W recommended in the bronchial axis	Intraluminal or mixed critical proximal obstructions	Good for short length tumors	Risk of perforation	Hypoxemia, bleeding, severe hemoptysis (1%), perforation, fistula formation, risk of fire (decreased when FiO_2 <40%)
Argon plasma coagulation (APC)	APC is a non-contact method that uses argon as a carrier gas	Intraluminal or mixed proximal lesions	Immediate efficacy	Risk of scarring stenosis if circumferential treatment	<2%
		Effective for vascular lesions	Cost	Risk of air embolism	Bleeding, hypoxemia and infections have been reported, including procedure-related bacteremia
		Hemostasis	Low risk of perforation	Very superficial. Not suitable for bulky exophytic tumors	
			Helpful for hemorrhagic lesions		
Electrocautery	Thermal tissue destruction using electric current	Ideal for superficial lesions. Intraluminal or mixed proximal lesions	Low cost, good efficacy	Risk of scarring stenosis if circumferential treatment	Rare
			Capability of coagulation in case of bleeding	Not suitable for bulky exophytic tumors	Bleeding has been seen, particularly during debulking of the mass. However, on most occasions, it can be controlled by the electrocautery itself

Table 3 (*continued*)

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Type of intervention	Principle	Indications	Advantages	Disadvantages	Complication rate
Cryotherapy	Cold cytotoxicity	Non-critical exophytic malignant obstructions	Low cost	Delayed effect (except cryoextraction and spray cryotherapy)	0–11%
			Easy procedure	Need for a subsequent cleaning	Hypoxia from tissue debris, bleeding, pneumothorax, benign airway obstruction
			No edema/perforation	Bronchoscopy to remove debris	
			Minimal scarring		
			No risk of fire		
			Prolonged efficacy		
			Synergistic action with Chemotherapy		
Photodynamic therapy	Phototoxic reaction using a photosensitizing agent and specific wave length	Non-critical exophytic malignant obstructions	Good symptom control	Delayed effect	15–20%
			Prolonged efficacy	Retention of tumor material	Photosensitivity, hypoxia may result from tissue debris and retained secretions. Airway narrowing from inflammation/edema
				Cleaning bronchoscopy	
				Phototoxicity	
				Constraining technique	
				Hemorrhagic complications	
Endobronchial brachytherapy	Delivery of radioactive isotopes (Iridium 192) in a localized manner	Exophytic malignant obstructions	Good for radio-occult lesion	Poor safety profile	10–20%
				Due to its rate of complications, it should not be considered first-line in the palliative treatment of malignant obstructions	Massive hemoptysis can occur. Radiation bronchitis

Table 3 (*continued*)

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Type of intervention	Principle	Indications	Advantages	Disadvantages	Complication rate
Stents	Stents are placed in the airway, inside the lesion. Can be placed using a prosthesis pusher inserted in a rigid tube or using a guidewire under direct visualization or using fluoroscopy	Extrinsic or mixed compression	Good tolerance	Altered ciliary clearance	Up to 10% complications, but serious ones are rare. Infection, migration, mucoid impaction, stent fracture, airway rupture, halitosis, tumor ingrowth and granulation formation
		Useful in highly necrotic lesions or large airway distortion	Few local granulomatous and ischemic reactions	Risk of migration (rare, except in cases of purely extrinsic compression)	
			Preserved clearance	Risk of misplacement	
				Metallic stents have more risk of granuloma, perforation, and rupture	

Electrocautery is the application of electric current to deliver thermal energy resulting in tissue destruction. At low power it can lead to coagulation and at high power it causes vaporization or carbonization. It can coagulate lesions, which can later be removed by suction or forceps. It is ideal for superficial coagulation and provides rapid results with relatively low risk of airway perforation. While responses are often similar, electrocautery is more economical than modalities such as laser, brachytherapy and cryotherapy. In case of endobronchial compromise by an extrinsic tumor, placement of a stent is usually considered complementary to thermocoagulation (56). Rates of complications with electrocautery are low, especially with the soft coagulation mode although scarring stenosis has been described, particularly after application of circumferential thermocoagulation (53).

Endobronchial brachytherapy involves applying radioactive isotopes (Iridium 192) in a highly localized manner to the tumor. It is usually given using a catheter under direct visualization with bronchoscopy. This allows preservation of surrounding healthy tissue (57). It can be used to treat lesions with endobronchial infiltration. Its use can improve symptoms and functional parameters. However, there is a significant rate of severe complications (reportedly as high as 10–20%) (58). Massive hemoptysis is one of the most feared complications and can occur in approximately 7% of patients. Other complications are radiation bronchitis, abscess formation, bronchial wall necrosis and esophago-bronchial fistula formation (59-61).

Cryotherapy uses very low temperature, causing dehydration and cellular crystallization of tissues in the short term and apoptosis and ischemia in the long term. It is useful in bleeding lesions especially when the exact site of hemorrhage is not known (62,63). Overall mortality is low (1–2%) with complication rates <10% (64) Cryotherapy has a favorable cost and risk benefit ratio and rarely causes stenosis secondary to scarring. Delayed effects give an additional benefit. Another advantage of cryotherapy is that it can be delivered near stents without damaging them.

PDT causes tumor destruction by activating a photosensitizing agent using a light source with a specific wavelength, depending on the agent selected for each case. This induces a phototoxic reaction and cell death (65). It can achieve marked, yet delayed, symptom improvement and is, therefore, not suitable for critical proximal obstructions (66,67). Hemoptysis has been reported as side effect (67). Since the collagen remains unaffected, the risk of perforation is almost nonexistent (68).
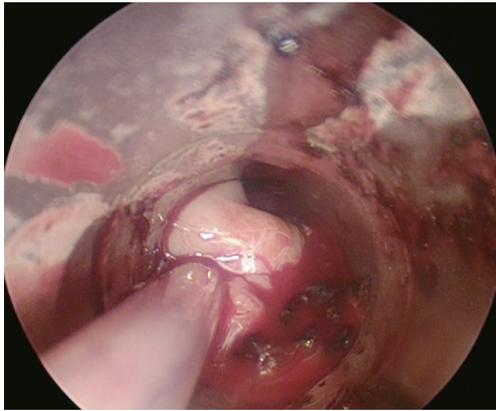
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Figure 3 Postobstructive pneumonia from tumor in the bronchus intermedius: rigid bronchoscopy view showing the suctioning of the purulent secretion after tumor ablation (courtesy of Dr. Kassem Harris, Interventional Pulmonology, Westchester Medical Center, Valhalla, NY, USA).

Airway dilatation or bronchoplasty can be achieved by different modalities, including rigid bronchoscopy, semi-rigid dilators and balloon dilators. Dilation of airway stenosis by rigid bronchoscopy is becoming less common, being replaced by flexible bronchoscopy and balloon dilatation, which has the advantage of producing less mucosal trauma and consequent granulation tissue. It also has an immediate effect of relieving extrinsic and intrinsic obstructions, sometimes preceding the insertion of a stent or the use of other interventions such as laser, electrocautery or APC, particularly if there is increased risk of airway restenosis. This can have an impact on the treatment of postobstructive pneumonia by further improving clearance of secretions. Hautmann *et al.* did a prospective study where 78 patients with malignant airway obstruction underwent bronchoscopic balloon dilatation (BBD) and an immediate improvement was reported in 79% of patients (69).

Stents (silicone or covered) are used to establish airway patency by counteracting extrinsic compression from a tumor or enlarged lymph nodes. They are also a complementary method after endobronchial debulking of a tumor. No clear advantage of one kind of stent over another has been described. After stent placement, patients usually have an improvement in their quality of life and pulmonary function. Some patients that suffered respiratory failure due to a malignant tracheobronchial lesion have been weaned off mechanical ventilation soon after implantation of a self-expandable stent under flexible bronchoscopy.

Combination of techniques

Depending on the mechanism of stenosis, various bronchoscopic techniques can be chosen from and performed alone or in combination. Some techniques are non-complementary like laser and thermocoagulation while other techniques can be complementary. An example of the latter is debulking followed by stent placement. Laser with its immediate effect can be synergistic with brachytherapy and data supports good symptomatic relief and extended survival (60% with combination *vs.* 30% survival at 7 months with laser only). Brachytherapy is marred by a high complication rate and that is the biggest hurdle in using the laser-brachytherapy combination widely. Cryotherapy can be used to desiccate the base of an intraluminal tumor following which mechanical debulking, laser or electrocautery can further improve the airway lumen.

The goal of all these techniques is to obtain the greatest relief of the airway obstruction as quickly as possible in order to palliate symptoms and to contribute to the treatment of a postobstructive pneumonia if present (see *Figure 3*).

Outcomes and prognosis

Postobstructive pneumonia significantly increases morbidity and mortality, particularly in advanced lung cancer. Its treatment often requires multiple long courses of antibiotics, thus contributing to the development of resistant organisms. The literature on the prognosis of postobstructive pneumonia is scant and is probably largely dependent on the primary malignancy and its stage. The response of the obstruction to interventional techniques is variable and exposes the patient to the risk of anesthesia, procedural complications and nosocomial infections.

Conclusions

Post-obstructive pneumonia in patients with advanced lung malignancy is a serious, often life-threatening development that occurs in approximately 50% of patients. Diagnosis of postobstructive pneumonia can be challenging. In some cases, infiltrates and consolidations distal to a lung tumor might not be infectious. Nevertheless, almost all patients are treated with broad-spectrum antimicrobial regimens and, when infectious, seldom resolve completely. Recurrent or refractory infections are common, and other serious

complications such as lung abscess, empyema, and fistula formation are also seen in this setting leading to rapid clinical deterioration.

Interventions to overcome obstruction are based on the nature of the obstruction, available techniques, quality of life concerns and physician expertise. No one modality is clearly superior to the others, and often multiple modalities need to be used in the same patient. In addition to relieving airway obstruction which will hasten resolution and prevent recurrence of infections, it is also helpful in decompensated patients by improving oxygenation and ventilation. If the stage of the malignancy is advanced, the primary goal is to improve quality of life and secondarily to potentially prolong survival.

Acknowledgments

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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