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Acute Care and Long-Term Results in Treatment of Tracheal Tumors: Monocentric Experience of the Last Seven Years

Abstract

Tracheal tumors are rare neoplasms with extremely heterogeneous histological aspects and can be potentially life-threatening, due to airway obstruction. We report our results in medical, endoscopic and surgical treatment of primary and secondary tracheal tumors. From January 2008 to June 2015, on 35 patients treated for various tracheal diseases, we observed 6 patients (2 males, 4 females; median age: 50, 5 years, range: 2 months-72 years) with tracheal tumors: 5 primary (subglottic hemangioma, inflammatory pseudotumor, condromatous hamartoma, squamous cell carcinoma, acinic cell carcinoma), 1 secondary (pulmonary adenocarcinoma). Treatments were: medical in 1 case (subglottic hemangioma), endoscopic in 2 (squamous carcinoma; metastatic adenocarcinoma), surgical in 3 (inflammatory pseudotumor; condromatous hamartoma; acinic cell carcinoma). Post-treatment course was uneventful and with radical results in all patients. At a median follow-up of 42 months (range: 11-89 months) five of six patients are alive, in good conditions and without local or distant recurrence. Treatment of tracheal tumors may vary in relationship to clinical condition of patients, grade of tracheal obstruction, tumor extension, stage, histology and biological behavior, which are factors affecting prognosis and long-term survival. Endoscopic evaluation and histological diagnosis are mandatory to select the most adequate treatment; whenever possible, radical surgical resection should be performed.

Keywords: Tracheal tumors; Airway obstruction; Bronchoscopy; Surgical resection

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Introduction

Tracheal tumors are extremely rare, representing less than 0.2% of all neoplasms of the respiratory system [1]. These tumors have a heterogeneous histology and are not easily classifiable, thus are reported in the Literature as part of large long-lasting studies or more frequently as case reports, focusing on peculiar and characteristic aspects [2].

Even if rare, tracheal neoplasms can be potentially lifethreatening, due to the involvement of the airway which may cause acute asphyctic syndromes, requiring a prompt diagnosis and correct treatment (endoscopic and/or surgical) in order to restore a normal air flow.

However, patients with tracheal tumors may present a long story of persistent cough and progressive respiratory symptoms such as dyspnea, stridor and wheezing, resembling asthmatic syndromes, which are misinterpreted and wrongly treated with Angela De Palma¹, Francesco Sollitto², Domenico Loizzi², Mariagrazia Lorusso¹, Francesco Di Gennaro¹, Giovanni Mercadante¹ and Michele Loizzi¹

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corticosteroids, causing a significant delay in diagnosis. This may lead to acute respiratory failure requiring emergency treatment.

Tracheal tumors can be distinguished in epithelial and nonepithelial, benign and malignant, primary and secondary. The majority of cases (90%) of primary tracheal neoplasms in adults are malignant and among these 75% are represented by epithelial histotypes (mainly squamous cell carcinoma and adenoid cystic carcinoma) [3, 4]. As concerns nonepithelial tracheal neoplasms, the distinction between benign and malignant forms is generally less evident than epithelial tumors [5], due to difficulties in histological classification of these rare tumors, thus hiding a potential malignant behavior. The distinction between benign and malignant neoplasms is usually based on morphological aspects, biological behavior, local invasiveness and metastatic spread.

In agreement with other Authors, we believe that some tracheal tumors, even if benign, for their characteristics of invasiveness and recurrency, should always be considered as potentially malignant and thus require a more aggressive treatment [2, 4]. In our experience, for the definition of benign or malignant tumor, the clinical behavior and the natural history of the tracheal lesion was determinant. Therefore, all tracheal tumors, also considering the involvment of the main airway and the severe associated symptoms, could be better classified in low, intermediate and high grade malignant neoplasms, as described by Grillo and Coll (**Table 1**) [1, 4, 6].

We report our experience about tracheal neoplasms, in order to assess the epidemiology, clinical presentation, diagnostic evaluation, treatment modalities, prognosis and short- and longterm results obtained with surgical, endoscopic and medical treatment of this rare disease.

However, it should be taken into account that the extreme rarity of these tumors makes difficult to obtain statistically significant data from the analysis of a single-center series and to the better of our knowledge the largest published series is that of Massachusetts General Hospital of the Harvard University in Boston (360 cases in a forty years' experience) [1, 6]. Thus, international guidelines to standardize the approach to this rare disease could only be achieved joining data of referral centres (multicenter studies).

Materials and Method

From January 2008 to June 2015 thirty-five patients with tracheal diseases (congenital, traumatic, inflammatory, idiopathic, postintubation stenosis and tumors) were treated at our Institution. We exclude from the present retrospective analysis 29 patients with non-oncologic tracheal diseases and focus our attention only on 6 patients with oncologic tracheal obstruction, requiring acute care treament. On 35 patients, 6 were suffering from tracheal neoplasms, 5 primary and one secondary (Table 2). There were 2 males and 4 females, with a median age of 50,5 years and a wide age range (2 months-72 years). Two cases were diagnosed in pediatric age and four in adult age, with no gender prevalence. In all cases symptoms were related to progressive obstruction of the airway: wheezing, stridor, cough, dyspnea and, in two patients, respiratory failure with oxigen desaturation. However, before being referred to our Institution, these aspecific respiratory symptoms had often been wrongly attributed to allergic disorders (bronchial asthma and asthma-like syndromes), except for patients with a known history of cancer. However, upon arrival to our attention, all patients had more or less severe acute asphyctic symptoms, requiring prompt and adequate treatment.

In each patient the diagnosis of tracheal tumor was obtained both with neck-chest computed tomography (CT) scan, with threedimensional (3D) reconstruction of the airway and bronchoscopy (flexible and/or rigid), allowing to precisely establish the site and characteristics of the neoplasm (size, shape, grade of stenosis of the tracheal lumen, possible presence of ulceration of the mucosa, etc.) and to obtain biopsies for histologic examination. In 2 cases rigid bronchoscopy represented both the diagnostic and therapeutical approach.

Table 1: Tracheal tumors classification. Forty years experience at Massachusetts General Hospital, Boston, USA (modified and adapted from [1, 6]).

Malignant tumors	N° of cases
Adenoid cystic carcinoma	135
Squamous cell carcinoma	135
Nonsquamous bronchogenic carcinoma	15
Small cell carcinoma	5
Adenocarcinoma	4
Large cell carcinoma	4
Adenosquamous carcinoma	2
Mucoepidermoid carcinoma	14
Carcinoid tumors	11
Typical	10
Atypical	1
Lymphoma	2
Melanoma	1
Sarcoma	13
Spindle cell sarcoma	6
Chondrosarcoma	3
Leiomyosarcoma	1
Carcinosarcoma (pseudosarcoma)	1
Invasive fibrous tumor	1
Malignant fibrous histiocytoma	1
Total of malignant tumors	326
Benign tumors	2
Pleomorphic adenoma	3
Squamous papilloma	9
Mulitiple	5
Solitary	4
	1
Capillary Hernangiorna Chondroblastoma	1
Chondroma	2
	1
Glomus tumor	1
Granular cell tumor	2
Hamartoma	2
Hemangiomatous malformation of mediastinum	1
	3
Paraganglioma	1
Neurogenic tumor	3
Schwannoma	1
Peripheral nerve sheath tumor	1
Atypical schwannoma	1
Total of benign tumors	31
Intermediate malignancy tumors	
Vascolar tumor of borderline malignancy	1
Inflammatory pseudotumor (plasma cell granuloma)	1
Plexiform neurofibroma	1
Total of intermediate malignancy tumors	3
Total	360

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Table 2: Tracheal tumors	Our experience of the	last seven years.
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Case n.	Tumor histology	Year	Age	Sex	Tumor size	Symptoms	Treatment	Techniques	Follow-up
1	Subglottic hemangioma	2011	2 months	F	10 × 10 mm	Stridor, dyspnea and oxigen desaturation	Medical	Oral propranolol	Alive at 4 years, no recurrence
2	Inflammatory pseudotumor	2008	12 years	Μ	15,2 × 13,8 mm	Dyspnea and wheezing	Endoscopic and surgical	Rigid bronchoscopy+Nd- YAG laser+tracheal resection and termino- terminal anastomosis	Alive at 7 years, no recurrence
3	Chondromatous hamartoma	2012	39 years	F	90% stenosis of tracheal lumen	Dyspnea and stridor	Surgical	Tracheal resection and termino-terminal anastomosis	Alive at 3 years, no recurrence
4	Squamous cell carcinoma	2012	62 years	F	9 × 5 mm	Stridor and dyspnea	Endoscopic	Rigid bronchoscopy+Nd- YAG laser	Alive at 3 years, no recurrence
5	Acinic cell carcinoma in previous (2004) tracheal pleomorphic adenoma	2011	69 years	F	30% stenosis of tracheal lumen	Dyspnea	Surgical	Resection through transcervical- transtracheal approach	Alive at 4 years, no recurrence
6	Secondary adenocarcinoma in previous lung squamous cell carcinoma (2010-2012) and adenocarcinoma (2013)	2014	72 years	М	1 cm	Dyspnea and respiratory failure	Endoscopic	Rigid bronchoscopy+coring, biopsy forceps and Nd- YAG laser	Dead at 1 year for ictus cerebri

As concerns histology, three cases were classified as nonepithelial (subglottic hemangioma, inflammatory pseudotumor, chondromatous hamartoma) and the other three as epithelial tumors (squamous cell carcinoma, acinic cell carcinoma in previous pleomorphic adenoma, high grade adenocarcinoma in previous squamous cell carcinoma and adenocarcinoma of the lung).

The type of treatment was decided considering the underlying clinical condition of patients, grade of tracheal obstruction, neoplastic extension and infiltration and histotype, using from simple medical therapy to invasive technique, such as endoscopic treatment (laser, coring with rigid bronchoscope, biopsy forceps) or tracheal surgical resection (limited resection and reconstruction with simple suture and/or tracheoplasty, complete circumferential resection followed by termino-terminal anastomosis).

Due to the extreme histological variety and the different treatment options which were adopted, each case with its specific and peculiar clinical history and diagnostic-therapeutic approach is described below.

Case N. 1

In 2011 we observed a subglottic hemangioma (SGH), a rare and benign vascular tumor of the head and neck in children, in a 2-month old infant girl. She was admitted to our Institution with \odot Under License of Creative Commons Attribution 3.0 License

stridor, severe dyspnea and oxygen desaturation. Neck-chest CT scan and fiberbronchoscopy revealed a contrast-enhancing, 10 mm, subglottic bluish elliptic lesion, referable to a sub-occlusive SGH, closing more than 75% of the laryngotracheal airway.

After multidisciplinary discussion, in agreement with our neonatologists and ear, nose and throat (ENT) specialists, we decided to begin oral propranolol therapy (0,4 mg/kg/die for 14 days), which rapidly and dramatically improved respiratory symptoms, avoiding the need for a tracheostomy.

Fiberbronchoscopy six days after treatment confirmed a reduction of the size of the tumor and of the subglottic narrowing. The patient is doing well, without respiratory symptoms four years after treatment with propranolol.

This is the first reported case of successful treatment with propranolol of an SGH obstructing more than 75% of the airway [7]. The case underscores the effectiveness of oral propranolol as first-line treatment in the management of severely-obstructive paediatric SGH and the importance of CT and fiberbronchoscopy in the diagnosis; it also highlights the importance of multidisciplinary cooperation between thoracic surgeons, anaesthesiologists, neonatologists and ENT specialists in the treatment of these patients.

Case N. 2

A rare case of tracheal inflammatory pseudotumor (IPT), usually affecting pediatric and young patients and with a still unclear pathogenesis, was diagnosed in 2008 in a 12-year-old boy, who had received corticosteroid therapy for two years. He presented to our institution with sudden dyspnea after months of wheezing and cough, wrongly considered and treated as asthma.

Neck and chest CT scan revealed an intraluminal pedunculated tracheal mass (diameter 15.2×13.8 mm), originating from the left antero-lateral tracheal wall, at 5,2 cm from the main carena and 4,6 cm from the glottis (**Figure 1A**). Fiberbronchoscopy confirmed the lesion at the level of the fifth cartilagineous tracheal ring, involving three rings.

At first, considering the young age of the patient and the typical benign behavior of this kind of lesions, after endoscopic biopsy and pathological diagnosis, the mass was removed with coring (to transect the pedicle), endoscopic forceps (to take the resected mass away) and Nd-Yag laser (to treat the base of implant) in rigid bronchoscopy.

However, due to a rapid tendency to recurrence of the lesion,

two more endoscopic recanalizations, at one and three months from the first one, were performed. Nevertheless, as a new recurrence appeared at bronchoscopy and CT showed transmural involvement of the tracheal wall (**Figure 1B**) at about four months from the first observation, we decided to perform a tracheal surgical resection.

Through cervicotomy and sternal split the three involved tracheal rings (V–VII) were circumferentially resected and a termino-terminal tracheal anastomosis was accomplished with a continuous running suture (PDS 4-0) posteriorly and interrupted sutures (Vicryl 3-0) anteriorly (Figures 1C-1E). Follow-up with CT scan and fiberbronchoscopy shows a stable tracheal lumen without signs of recurrence, seven years after surgery [8].

Case N. 3

A 39-year-old woman came to our attention in 2012 for a tracheal chondromatous hamartoma. The patient presented with a 2-year



history of dyspnea and stridor, at first attributed to an asthma-like syndrome, because of a medical history of allergic diathesis.

Neck and chest CT scan showed a subglottic intraluminal tracheal mass causing a 90% stenosis of the airway lumen, at 2 cm from the cricoid cartilage. Fiberbronchoscopy confirmed the presence of the tumor, originating with a broad base of attachment from the right lateral tracheal wall.

Due to the extent of the lesion (90% stenosis) we decided to perform surgical resection: through cervicotomy the patient underwent tracheal resection and end-to-end anastomosis. In particular, in this patient the operation was performed under monitored local anesthesia (stepwise local infiltration of 2% lidocaine and 7,5 mg/ mL ropivacaine) and conscious sedation, which was achieved by boluses of ketamine and midazolam. The patient remained awake during the entire procedure, thus permitting the movement of the vocal cords to be monitored. Mechanical ventilation was not required. The postoperative period was uneventful and at three years from surgery bronchoscopy shows a stable tracheal lumen without signs of recurrence [9].

Case N. 4

In 2012 a 62-year-old woman came to our attention for stridor and dyspnea. Neck and chest CT scan and fiberbronchoscopy revealed a subglottic intraluminal squamous cell carcinoma originating from the right lateral tracheal wall, causing laryngotracheal stenosis.

Considering the comorbidities of the patient (fatty liver disease, diabetes mellitus, hypertension, depressive syndrome) and the resulting contraindications to surgery, rigid bronchoscopy with Nd-Yag laser treatment of the subglottic tracheal lesion was performed.

Postoperative bronchoscopy some days later showed an improvement of the subglottic tracheal lumen, but the presence of a little flap of mucosa moving with breaths. Thus a fiber-bronchoscopy was performed and the flap simply removed with biopsy forceps.

Endoscopic treatment in this patient allowed to obtain the resolution of respiratory symptoms. At three years from treatment the patient is doing well and bronchoscopic and CT scan follow-up shows no recurrences of the tracheal tumor.

Case N. 5

A 69-year-old woman was treated at our Institution in 2011 for an acinic cell carcinoma (histological subtype of tracheal adenocarcinoma). She had already undergone surgical resection through cervicotomy of a tracheal pleomorphic adenoma in 2004 and came to our attention for inspiratory and expiratory dyspnea 7 years after surgery.

Neck and chest CT scan and fiberbronchoscopy showed an intraluminal tracheal tumor originating from the posterior wall of the upper third of the trachea, causing a stenosis of 30% of the tracheal lumen (**Figure 2**). At first the tumor was interpreted as a recurrence of the previous pleomorphic adenoma, however histological examination of biopsies collected during fiberbronchoscopy revealed a different histotype from the © Under License of Creative Commons Attribution 3.0 License

previous one: acinic cell carcinoma of minor salivary glands.

Surgical resection of the tumor was performed through a recervicotomy and longitudinal incision of the anterior tracheal wall (transcervical-transtracheal approach) at the level of the first five cartilagineous tracheal rings. Four years after surgery the patient is doing well, without respiratory symptoms, and CT and bronchoscopic follow-up do not show any other recurrence.

Case N. 6

A 72-year-old man, in follow-up at our Institution after a right lung lobectomy for a squamous cell carcinoma and subsequent resection of an ipsilateral lung adenocarcinoma, came to our attention again in 2014 due to severe dyspnea and respiratory failure.

In particular, the patient had been submitted to right lower lobectomy in 2010 and to medium lobectomy with resection of the main carina in 2012 for a squamous cell carcinoma; in 2013 a wedge pulmonary resection of the right upper lobe for an adenocarcinoma had been performed.

Neck and chest CT scan allowed diagnosing an intraluminal tracheal mass of about 1 cm located at the medium third of the trachea and right paratracheal lymph nodes, in addition to left multiple pulmonary nodules and a right lung nodule. PET-CT scan was positive both at the level of the tracheal mass and of the lung nodules.

Fiberbronchoscopy confirmed the pedunculated intraluminal tracheal tumor, almost totally obstructing the airway lumen, with base of attachment on the left posterior wall of the upper third of the trachea (**Figure 3A**).Considering the clinical situation (multiple and recurrent lung cancers) and the comorbidities of the patient (hypertension, ischemic heart disease, bilateral carotid stenosis, chronic respiratory failure in COPD and dysthyroidism), we decided to perform a less invasive, endoscopic treatment.

Tracheal obstruction was removed in rigid bronchoscopy with mechanical coring and biopsy forceps and the base of implant



Figure 2 Neck and chest CT scan of a 69-year-old woman, showing an intraluminal tracheal tumor (arrow) originating from the posterior wall of the upper third of the trachea, causing a stenosis of 30% of the tracheal lumen (acinic cell carcinoma of minor salivary glands).

of the tumor was treated with Nd-Yag laser (**Figures 3B-3D**). Definitive histological diagnosis revealed a secondary tracheal tumor from lung adenocarcinoma. The patient died at one year from surgery due to a stroke (ictus cerebri).

Results and Discussion

Whatever was the approach (medical, endoscopic and surgical), in all patients post-treatment course was uneventful. At a median follow-up of 42 months (range: 11-89 months) five of the six patients are alive, in good health condition and without local or distant recurrence. Only one patient died, one year after bronchoscopic treatment, for causes unrelated to the history of cancer (ictus cerebri).

Due to the rarity of tracheal tumors, few studies have been published in the Literature concerning histological classification [10], staging, strategies of treatment, short and long-term results and survival rates [11]. The lower incidence of primary tracheal tumors compared to primary lung and bronchial ones could be explained by the reduced surface of the tracheal epithelium (ciliated pseudostratified), the presence of mucinous secreting cells (ensuring a continuous muco-ciliary clearance and thus a better defense action against external insults) and the tracheal laminar air flows (unlike those turbulent of the bronchial tree).

Among malignant tracheal neoplasms, the epithelial ones prevail in term of incidence, mainly the squamous histotype and secondarily the mucinous or glandular (adenoid cystic carcinoma) one. This particular aspect has been attributed to the metaplastic transformation of the respiratory epithelium in a squamous one, as a consequence of the action of damaging agents (such as cigarette smoke) on the mucosa, although to date etiologic factors related to the origin of tracheal tumors are still unclear [12].

As concerns benign tracheal tumors, etiology is unknown both for epithelial and nonepithelial histotypes, except for squamous papilloma, which is associated to infection by human papilloma virus 6 and 11 [13]. Squamous papilloma (multiple or solitary) and



(A) Fiberbronchoscopy of 72-year-old man, in follow-up for squamous cell carcinoma and adenocarcinoma of the lung, showing a pedunculated intraluminal tracheal tumor, almost totally obstructing the airway lumen, with base of attachment on the left posterior wall of the upper third of the trachea; (B,C) considering the clinical situation (multiple and recurrent lung cancers) and the comorbidities of the patient, endoscopic treatment was performed and tracheal obstruction removed in rigid bronchoscopy with mechanical coring and biopsy forceps and the base of implant of the tumor was treated with Nd-Yag laser; definitive histological diagnosis revealed a metastasis from lung adenocarcinoma; (D) bronchoscopic control after endoscopic treatment.

pleomorphic adenoma are the most common benign epithelial neoplasms. Most of nonepithelial tracheal neoplasms are benign, arising from soft tissue cells (fibroblasts, smooth muscle cells, chondrocytes, nerve sheaths cells, adipocytes), thus there is a considerable variety of extremely heterogeneous histotypes (fibromas, fibromatosis, fibromatous histiocytomas, leiomyomas, lipomas, chondromas, chondroblastomas, hemangiomas, hamartomas, neurofibromas, etc.) [12], with a rare, but possible, potential for malignant transformation.

Prognosis and survival of primary tracheal neoplasms are related to several elements, mainly the histotype: low survival rates for squamous cell carcinoma have been reported, while a better survival for adenoid cystic carcinoma has been described, with a poorer prognosis in case of lymph node involvement. In case of positive lymph nodes, survival in epithelial tumors is reduced by 50% [11].

Secondary tracheal neoplasms are extremely rare, often presenting as direct invasion of the trachea by tumors of adjacent organs, such as the larynx, thiroid, esophagus, lung or mediastinal structures [14]. Strictly speaking, tracheal metastases are really sporadic, in comparison to the bronchial tree, which is more frequently site of metastases from primary tumors in distant organs; breast, kidney and colon cancers and melanomas are those most commonly metastatizing to the trachea [15].

Clinical presentation of tracheal tumors is typically characterized by obstruction symptoms (asthma-like syndromes, dyspnea, wheezing, cough and hemoptysis) which may vary based on the location and extent of the mass. Hemoptysis is generally associated to epithelial tumors in an advanced stage. A severe obstruction may occur when the percentage of stenosis is one third or a half of the total lumen [16]. The diagnosis is often delayed because at the beginning symptoms are underestimated or wrongly attributed to COPD or asthma. Thus, a tracheal neoplasm should always be suspected in any patients with asthmatic symptoms unresponsive to drug treatment [1, 9].

In our patients, symptoms were related to obstruction of the airway: wheezing, stridor, cough, dyspnea and, in two cases, respiratory failure with oxygen desaturation. However, in most patients these aspecific respiratory symptoms had been wrongly attributed to allergic disorders (except for patients with a known history of cancer), thus causing some delay in diagnosis.

The site and characteristics of tracheal tumors should be studied by imaging (CT) at first, but the gold standard remains bronchoscopy, which can be used both for diagnostic and thrapeutical aims. In fact, tracheo-bronchoscopy, with rigid and/ or flexible instrument, under local anesthesia (with or without sedation) or general anesthesia, is fundamental not only to directly visualize the intraluminal tracheal neoplasm and evaluate its morphology and development, grade of obstruction of the airway and surgical resectability, but also to define the histotype by biopsies [4, 13].

At endoscopic examination these tumors usually present a polypoid growth within the tracheal lumen, often showing a subepithelial growth pattern and sometimes infiltrating the tracheal wall and the adjacent soft tissues. The lining epithelium may appear hyperplastic and ulcerated.

In our experience, the diagnosis of tracheal tumor was obtained in all patients both with neck-chest CT scan with 3D reconstruction of the airway and bronchoscopy (flexible and/or rigid), allowing to precisely establish the site and characteristics of the neoplasm (size, shape, grade of stenosis of the tracheal lumen, presence of ulceration of the mucosa, etc.) and to obtain biopsies for histologic examination.

Treatment and prognosis depend on various factors, such as the site and histotype of the tumor, the staging, the clinical condition and the degree of impairment of the respiratory function and the entity of stenosis of the tracheal lumen [12]. Treatment includes conservative (medical, endoscopic) and surgical procedures.

In selected cases, treatment of tracheal neoplasms can be performed with conservative modalities, mainly endoscopic procedures. As concerns tracheal operative endoscopy, flexible and/or rigid bronchoscopy may be used and the latter is to be preferred to treat neoplastic obstruction, as it allows a better control of the airway and ventilation of the patient. Flexible bronchoscopy, alone or in association to rigid bronchoscopy, can be useful for laser treatment or other techniques (brachytherapy, electrocoagulation, cryotherapy) to rapidly remove acute local obstruction, with the aim of restoring an adequate airway lumen, improving respiratory symptoms [13].

In malignant tumors which are not completely resectable by endoscopic procedures, stabilization of the tracheal lumen and permanent palliative treatment can sometimes be achieved with the implant of stents (self-expandable or non-expandable, metallic or silicone) [13].

However, surgery still represents the treatment of choice for primary tracheal tumors and should always be preferred, whenever possible, as it allows to obtain radical oncological resection [1, 4]. The main aims are to completely resect the tumor, eliminate obstruction and permanently restore airway patency, improving long-term survival [16].

Surgical techniques may include: limited resection and reconstruction with simple suture and/or tracheoplasty, wedge resection, complete circumferential resection followed by termino-terminal (end-to-end) anastomosis. Surgical resection definitely represents the best therapeutical option for primary tracheal tumors, being curative for benign and low/intermediate grade malignant neoplasms and improving survival of high grade malignant ones [16].

As regards surgical approach, tumors of the subglottic region and of the upper third and middle third of the trachea can be treated by a cervicotomy (sometimes with a sternal split), while those of the lower third of the trachea and/or of the main carina by a sternotomy or right thoracotomy [13].

The most frequent type of tracheal resection is a circumferential resection followed by a reconstruction with a termino-terminal anastomosis [13]. The success of this surgical technique is related to the respect of the vascularization of the tracheal stumps and the realization of a tension-free anastomosis, in order to avoid necrosis and diastases/dehiscence of the sutures. About 3-5 cm

of the total lenght of the trachea can be resected, then using a postoperative forced flextion of the neck according to the technique of Grillo (chin-pectoral sutures) [4].

During surgery, the trachea is opened immediately below the tumoral lesion (being careful to leave negative histologic margins) and the tracheo-bronchial tree usually ventilated through a standard Magill endotracheal tube [17] or, in selected cases, jetventilation [13].

The anastomosis is generally accomplished with a continuous running suture (PDS 4-0 or 3-0) of the posterior tracheal wall and interrupted sutures (Vicryl 3-0) of the anterior one [13, 17].

In our experience conservative treatment was performed in 3 patients: medical treatment with propranolol in one case (subglottic hemangioma) and endoscopic treatment in two cases (primary squamous cell carcinoma, removed by Nd-YAG laser, and secondary adenocarcinoma, resected by coring, biopsy forceps and Nd-YAG laser). The other 3 patients underwent surgical resection (inflammatory pseudotumor, chondromatous hamartoma and acinic cell carcinoma of minor salivary glands).

Data of our series are in agreement with those reported in bigger series. In fact, in the two youngest patients (a 2-month-old infant girl, a 12-year-old boy and a 39-year-old woman) benign or low grade malignant neoplasms (subglottic hemangioma, inflammatory pseudotumor and chondromatous hamartoma, respectively) were diagnosed, while adult patients (>60 years of age) mainly presented malignant epithelial tumors (primary squamous cell carcinoma, acinic cell carcinoma of minor salivary glands and metastatic adenocarcinoma).

The acinic cell carcinoma was diagnosed in a patient with a previously resected pleomorphic adenoma of the trachea, confirming that tracheal tumors may recur and have a malignant transformation, even after a long time from first treatment, thus requiring a long-term follow-up.

In our experience, a better prognosis was found in young patients, in neoplasms limited to the trachea at diagnosis (early stage tumors) and in absence of comorbidities. In order to provide the patient with a higher probability of cure, a strict multidisciplinary cooperation of various specialists (surgeon, anesthesiologist, oncologist, radiotherapist, ENT specialist, pediatrician and neonatologist) is essential. Moreover, some specific aspects of our series of patients should be considered and analyzed.

Our case of subglottic hemangioma was the first, reported in the Literature, with severe tracheal stenosis (>75%), successfully treated with medical therapy (propranolol). Subglottic hemangioma is a benign tumor of childhood; however, as observed in our patient, it can be potentially life-threatening in case of severe airway obstruction [7]. Approximately 50% of affected children also have cutaneous hemangiomas. It is usually not evident at birth, but grows rapidly during the first year of life and the proliferation phase begins around 1-2 months of age, causing intermittent airway obstruction with stridor, dyspnea and respiratory distress [7]. The management may vary depending on the dimensions and site of the tumor and the symptoms of the patient, thus a standard method has not been established. Alternatives are conservative treatment ("wait and see", with or without tracheotomy; systemic and intralesional steroid; interferon; propranolol; CO2 laser) or open surgical approach (laryngotracheoplasty, submucous resection, tracheostomy). In our patient medical therapy alone with oral propranolol allowed to obtain a rapid improvement of respiratory symptoms and permanent successful results at four years from diagnosis. Therefore, an extensive knowledge of medical drugs and their alternative indications may be useful even for treatment of diseases in surgical/endoscopic field and a multidisciplinary approach is mandatory. Moreover, an early diagnosis by bronchoscopy is fundamental to precociously start treatment with propranolol, avoiding more invasive surgical approach, such as tracheotomy, in pediatric patients [7].

As concerns tracheal inflammatory pseudotumor, this is generally a benign, polypoid or sessile, reactive lesion, characterized by proliferation of myo-fibroblastic cells associated with a variable number and type of inflammatory cells; however, some Authors believe that it is a low grade fibrosarcoma with inflammatory (lymphomatous) cells, thus it is still not clear if it should be considered as a real tumor or an entity of inflammatory nature [8]. It usually affects pediatric and young patients, as in our experience, and has an unpredictable biological course. Modality of treatment can vary from a conservative approach (endoscopic resection with coring and laser; corticosteroids; radiation therapy) to surgical resection and termino-terminal tracheal anastomosis, which may sometimes be necessary, even in pediatric age, in case of transmural extent or tendency to recurrence after endoscopic removal, as occurred in our patient. When he came to our attention, due to the young age, we decided to perform a conservative treatment; however, after three endoscopic resections a new recurrence appeared with infiltration of the tracheal wall. Surgical treatment became mandatory and allowed to obtain a radical oncological resection. CT scan and bronchoscopy follow-up shows a stable tracheal lumen without signs of recurrence at seven years from surgery. Therefore, radical resection of inflammatory pseudotumor represents the gold standard of treatment, to prevent not only recurrences, but also any sarcomatous transformation [8].

In our series a case of chondromatous hamartoma was described, causing a tracheal stenosis of 90% in a young woman. This is a rare benign tumor which is typically localized in the lung parenchyma; less than 2% of cases have an endobronchial localization and extremely rare are the tracheal ones. Differently from pulmonary hamartoma, predominantly containing cartilaginous elements, tracheal hamartoma mainly consists of lipomatous tissue, with a minimal part of cartilagineous tissue, smooth muscle cells, mucinous and inflammatory cells [18]. Even if this is a benign, slow-growing tumor, without potential malignant transformation, considering the extent of tracheal stenosis (>90%) and the transmural involvment at the base of implant, the treatment of choice in our patient was surgical resection with termino-terminal anastomosis, as it had already been described in the experience of Massachusetts General Hospital [1, 6]. The peculiarity of our case is represented also by the type of surgical approach: in fact, due to the intraluminal involment and the grade of tracheal obstruction, surgical resection under local anesthesia and conscious sedation was performed, this case being the first reported in the Literature [9]. Tracheal surgery is usually performed under general anesthesia: however, there are some disadvantages, that is the impossibility to control the condition and movements of the vocal cords (which may be checked only at the end of surgical operation and tracheal intubation) and the difficulty to have a satisfactory vision of the operating field due to the presence of the endotracheal tube. In 2010, a series of 21 tracheal resections performed with cervical epidural anesthesia and conscious sedation was descibed by Macchiarini and colleagues [9, 19]. In our patient we used local anesthesia and conscious sedation [9]. Advantages of these techniques are the optimal vision of the operating field (as no tracheal tube is present) and the possibility of monitoring the voice of the patient and the movements of the vocal cords at any time during surgery (without having to wait for extubation) [9]. Unfortunately, this therapeutic option and approach is applicable only in selected, cooperative patients. Moreover, local anesthesia infiltration of the tracheal wall may cause a temporary postoperative paralysis of the vocal cords, while cervical epidural anesthesia may be complicated by accidental intrathecal administration of the local anesthetic with consequent spinal block, epidural hematoma, spinal cord injury and phrenic nerve block [9].

In our experience we observed one case of primary tracheal squamous cell carcinoma, epithelial tumor mainly affecting male smokers, in an age range comprised between the fifth and sixth decades of life. As the patient suffered from various comorbidities contraindicating surgery, a conservative approach was chosen and rigid bronchoscopy with Nd-Yag laser treatment of the subglottic tracheal lesion was performed. This is important to emphasize the principle of personalization of therapy in these patients (surgical resection would have probably been performed as treatment of choice in another patient with the same tumor, but without comorbidities).

Acinic cell carcinoma, commonly considered a low grade malignant tumor, originates from the minor salivary glands [20]. Serous and mucinous submucosal epithelial glands of the tracheobronchial tree are similar to salivary glands. Therefore, the natural history, morphological aspects and biological behavior of neoplasms originating from tracheobronchial glands are similar to those of salivary gland tumors, thus explaining why adenoid cistic carcinoma, mucoepidermoid carcinoma and acinic cell carcinoma of the trachea are usually called "salivary gland-type tumors". These tumors generally involve the upper part of the trachea, differently from the squamous cell ones which usually originate from the lower part of the trachea. Concerning our case of acinic cell carcinoma, diagnosed in a 69-year-old patient who had already undergone surgery to resect a pleomorphic adenoma 7 years earlier, we had the confirmation that some tracheal neoplasms, even if benign, may recur and/or have a malignant transformation years after treatment [21]. This emphasizes the importance of regular and long-term follow-up with CT scan and bronchoscopy in patients treated for tracheal tumors, for early detection of possible local or distant recurrences. In our patient, surgical resection of the acinic cell carcinoma through a transcervical-transtracheal approach was successfully performed, without any recurrence four years later, thus pointing out that even repeat tracheal resection may be indicated, in selected patients, to obtain positive long-term results.

In our experience we only found one patient with secondary tracheal neoplasm, confirming the extreme rarity of tracheal metastases from primary tumors in adjacent or distant organs, as reported in the Literature. Less than 1% of lung tumors during their natural history may cause a secondary localization to the trachea. Due to the rarity of these conditions, it is difficult to standardize treatment. Moreover, considering the advanced age and the severe comorbidities of our patient, (including previous major lung resections for two different tumors, squamous cell carcinoma and adenocarcinoma), contraindicating surgery, we decided to choose conservative treatment. Rigid bronchoscopy with coring, biopsy forceps and Nd-Yag laser allowed obtaining successful complete resection of the tracheal metastasis from lung adenocarcinoma. The patient died one year later for a stroke, thus for causes unrelated to the underlying disease. This fact underscores that an experienced surgical staff, providing the correct treatment, can achieve good results in terms of survival even in selected cases of solitary tracheal metastasis.

Conclusion

In conclusion, treatment of tracheal tumors may vary in relationship to the clinical conditions of the patient, the grade of tracheal obstruction, the extension and stage of the tumor, its histology and biological behavior, which are factors affecting the prognosis and long-term survival.

Bronchoscopic evaluation and histological diagnosis are fundamental to choose the most appropriate treatment; whenever possible, surgical resection should be performed to obtain the oncological radicality. Conservative treatment is preferred in very young patients and in those with significant comorbidities. In our experience, whatever was the approach (medical, endoscopic and surgical), in all patients post-treatment course was uneventful.

As nowadays no international guidelines are available, further and multicentric studies by experts in this rare disease are needed, to standardize treatment and improve prognosis.

Moreover, in order to increase the number of patients candidates to surgical resection, it is recommended to centralize tracheal tumor care in a small number of highly specialized referral centers, each of which, according to expert estimates, should be working for a population of about ten/twenty million units [22, 23]. In this way it would be possible to greatly improve the quality of care and the experience of the operating team, which should be able to deal with the presenting cases with greater competence and professionalism, thus achieving levels of excellence.

References

- 1 Gaissert HA, Mathisen DJ (2008) Primary tumors of the trachea. In: Patterson GA, Pearson G, Cooper JD, Deslauriers J, Rice TW, Luketich JD, Lerut AEMR (eds), Pearson's Thoracic and Esophageal Surgery, Vol.1 (3rdedn) Churchill Livingstone Elsevier ed, Philadelphia, PA, USA 312-20.
- 2 Gaissert HA, Grillo HC, Shadmehr MB, Wright CD, Gokhale M, et al. (2006) Uncommon primary tracheal tumors. Ann Thorac Surg 82: 268-73.
- 3 Compeau CG, Keshavjee S (1996) Management of Tracheal Neoplasms. The Oncologist 1: 347-53.
- 4 Grillo HC (2004) Primary tracheal neoplasms. In: Grillo HC (ed), Surgery of the trachea and bronchi. BC Decker ed, Hamilton, Ontario 207-47.
- 5 Beheshti J, Mark EJ (2004) Mesenchymal tumors of the trachea. In: Grillo HC (ed). Surgery of the trachea and bronchi. BC Decker ed, Hamilton, Ontario 86-97.
- 6 Gaissert HA, Burns J (2010) The compromised airway: tumors, strictures and tracheomalacia. Surg Clin N Am 90: 1065-89.
- 7 Loizzi M, De Palma A, Pagliarulo V, Quaranta N (2013) Propanolol as first-line treatment of a severe subglottic haemangioma. Eur J Cardio-thorac Surg 43: 187-9.
- 8 De Palma A, Loizzi D, Sollitto F, Loizzi M (2009) Surgical treatment of a rare case of tracheal inflammatory pseudotumor in pediatric age. Interact Cardiovasc Thorac Surg 9: 1035-7.
- 9 Loizzi D, Sollitto F, De Palma A, Pagliarulo V, Di Giglio I, et al. (2013) Tracheal resection with patient under local anesthesia and conscious sedation. Ann Thorac Surg 95: e63-5.
- 10 Heffner DK (1990) Classification of human upper respiratory tract tumors. Environmental Health Perspectives 85: 219-29.
- 11 Bhattacharyya N (2004) Contemporary staging and prognosis for primary tracheal malignancies: a population-based analysis. Otolaryngol head neck surg 131: 639-42.
- 12 Beheshti J, Mark EJ, Graeme-Cook F (2004) Pathology of tracheal tumors, In: Grillo H (ed), Surgery of the trachea and bronchi. BC Decker ed, Hamilton, Ontario 73-85.

- 13 Loizzi D, De Palma A, Quercia R, Sollitto F (2008) Affezioni della via aerea principale di interesse chirurgico. In: Gramiccioni E, Loizzi M, Foschino Barbaro MP, Resta O, Sollitto F (ed.), Malattie dell'apparato respiratorio. Edizioni Minerva Medica, Torino, Italia 113-23.
- 14 Wigle DA, Keshavjee S (2008) Upper airway tumors: secondary tumors. In: Patterson GA, Pearson G, Cooper JD, Deslauriers J, Rice TW, Luketich JD, Lerut AEMR (eds). Pearson's Thoracic and Esophageal Surgery, Vol.1 (3rd edn), Churchill Livingstone Elsevier ed, Philadelphia, PA, USA 321-5.
- 15 Grillo HC (2004) Secondary tracheal neoplasms. In: Grillo HC (ed), Surgery of the trachea and bronchi, BC Decker ed, Hamilton, Ontario 249-69.
- 16 Wang H, Du Z, Ren H, Zhang C, Song J, et al. (2010) Surgical treatment of primary tracheobronchial malignant tumors. Chinese-German Journal of Clinical Oncology 9: 97-100.
- 17 Borasio P, Ardissone F (2000) Resezioni tracheali. In: Paletto AE (ed) Nuovo trattato di tecnica chirurgica, Vol.3, Parete toracica, pleura, polmoni, trachea, bronchi, UTET, Italia 219-28.
- 18 Cetinkaya E, Gunluoglu G, Eyhan S, Gunluoglu MZ, Dincer SI (2011) A hamartoma located in the trachea. Ann Thorac Cardiovasc Surg 17: 504-6.
- 19 Macchiarini P, Rovira I, Ferrarello S (2010) Awake upper airway surgery. Ann Thorac Surg 89: 387-91.
- 20 Tsukayama S, Omura K, Kanehira E, Kawakami K, Oda k, (2004) Acinic cell carcinoma of the trachea: report of a case. Surg Today 34: 764-8.
- 21 Demira`g F, Topcu S, Kurul C, Memis L, Altınok T (2003) Malignant pleomorphic adenoma (malignant mixed tumor) of the trachea: a case report and review of the literature. Eur Arch Otorhinolaryngol 2003; 260: 96-9.
- 22 Honings J, Gaissert HA, Verhagen AFTM, van Dijck JAAM, van der Heijden HFM, et al. (2009) Undertreatment of tracheal carcinoma: multidisciplinary audit of epidemiologic data. Ann Surg Oncol 16: 246-53.
- 23 Nouraei SM, Middleton SE, Reza Nouraei SA, Virk JS, George PJ, et al. (2014) Management and prognosis of primary tracheal cancer: a national analysis. The Laryngoscope 124: 145-50.