Tracheal and bronchial tumors

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Abstract: Although primary tracheobronchial tumors are extremely rare in children, recurrent respiratory symptoms resistant to conventional therapy require further investigations to exclude possible malignant obstructive causes. As the matter of fact, early diagnosis may allow minimally invasive surgeries, improving the standard of living and the globally survival rate. The aim of this article is to provide an overview of diagnosis and management of tracheobronchial tumors in the early age, since only few reports are reported in the worldwide literature.

Keywords: Primary tracheobronchial tumors; pediatric tumors; subglottic hemangioma; fibro-bronchoscopy; sleeve resection

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Introduction

Tracheobronchial tumors are extremely rare in the paediatric population, accounting for 0.2% of all cancers in this range of age (1). They include both benign and malign lesions (Table 1). In the former group, the most common histological entities are represented by infantile hemangioma and squamous papilloma, while inflammatory pseudotumors, leiomyomas, granular cell tumor, juvenile xanthogranuloma, tracheal lipoblastoma and laryngotracheal chondromas occur more sporadically. The latter group includes carcinoids, mucoepidermoid carcinomas and less frequently rhabdomyosarcoma, leiomyosarcoma and adenoid cystic carcinoma (2,3). Because of their low prevalence in the paediatric age and the absence of specific signs and symptoms, primary tracheobronchial tumors are often not suspected or misdiagnosed. This inevitably leads to delayed definitive diagnosis and treatment (4). In the worldwide literature, relative little attention has been provided to their management and only few studies are reported. The aim of this article is to review the current literature, producing a complete overview with regards to their pathological and clinical features, requirement of diagnostic imaging, surgical treatments and follow up.

Pathologic classification and tumoral behavior

Primary tracheobronchial tumors include a broad spectrum of pathologic entities arising from the respiratory epithelium, the salivary glands or the mesenchymal tissue of the tracheobronchial tree. In literature great confusion exists about their real prevalence. Several studies report a clear predominance of the malignant forms (65% of cases, approximately) but infantile hemangioma and papilloma are often excluded in these epidemiological analyses (3,5,6).
Malignant tumors

In these forms, the survival rate is mainly influenced by histological type, lymph node involvement and by the type of surgery (7).

Bronchial carcinoid and mucoepidermoid carcinoma are the most common histopathological type, with a good prognosis overall. The former accounts for 80% of all malignant forms. It arises from the neuroendocrine cells of the respiratory epithelium, mainly from the lobar bronchi of the right side (75% of case, approximately). Basing on the mitotic activity rate and on the grade of tumour necrosis, they are usually classified as typical and atypical, with the latter one showing a more aggressive behaviour and a worse prognosis. Lymph nodes metastases are frequently described, while local recurrences and distant metastasis rarely occurred (2).

Mucoepidermoid carcinoma appears as an exophytic mass originating from the submucosal bronchial glands of the tracheobronchial tree. They are classified into low, intermediate and high grade tumors, in relation to cell type and pleomorphism, mitotic index and the presence of cystic structures. The most common in children is the low-grade type which is primarily composed of mucous cells (4).

Rhabdomyosarcoma and leiomyosarcoma along with adenoid cystic carcinoma are the less frequent malignant form reported in the paediatric population. The former accounts for 5.8% of all paediatric endobronchial tumors (8) with previous radiation therapy, genetic predisposition and immunological factors as main documented risk factors for its occurrence (9). Leiomyosarcoma is even more sporadic, making up 3.8% of all paediatric forms (8). Adenoid cystic carcinoma shows an aggressive attitude, with local relapse and local lymph nodes metastases (10) but it is infrequently described in children.

Benign tumors

In children infantile hemangioma is a relatively frequent and well-known airway tumour. It consists of a vascular proliferation of packed endothelial cells with a lobular architecture. It typically look like as localized, smooth, compressible mass arising from the subglottic area, but sometimes it could be diffuse without any mucosal elevation (3). Because of its localization, it may become potentially life-threatening especially during the proliferative phase of its growth. Conversely to congenital hemangioma and other vascular anomalies, the immunohistochemical staining for glucose transporter-1 protein (GLUT-1) is usually positive in the endothelial cells (11).

Granular cell tumours are soft tissue neoplasms probably derived from Schwann cells. Approximately half of all cases originates in the head and neck, with 10% of these one having a laryngeal involvement (12,13). In children, surgical resection should be considered because of recurrent obstructive symptoms, although malignant transformation has never been documented (14).

Inflammatory myofibroblastic tumor, also known as inflammatory pseudotumor, consists of a variable mixture of myofibroblastic mesenchymal spindle cells accompanied by inflammatory cells and collagen. Found most frequently in upper trachea it could occur anywhere else. Metastases are occasionally referred (15).

Usual manifestations of the juvenile xanthogranuloma are cutaneous lesions appearing in the first year of life. Airway involvement is rarely described but it can result in severe respiratory obstruction. Since most of them regress spontaneously, endoscopic or surgical excision is required only in case of involvement of vital structures (3).

In addiction also laryngotracheal chondromas and tracheal lipoblastoma are reported although their appearance in children is extremely rare (16).
Sign and symptoms

Sign and symptoms depend on tumor histology and localization. In case of involvement of the upper respiratory tract, when more than 50% of the lumen is interested, obstructive symptoms such as stridor, wheezing and dyspnoea appear. Furthermore patients frequently experience chronic cough due to persistent mucosal irritation or inadequate clearance of distal airway secretions (5). Depending on the degree of the lumen obstruction, bronchiectasis and pulmonary atelectasis could appear, leading to chronic pneumonia (5). Haemoptysis could also appear as consequence of mucosal ulceration and bleeding (14). In relation to each histological type, the lack of pathognomonic symptoms lead to frequent misdiagnoses with other conditions (such as bronchitis, pneumonia or asthma) causing diagnostic delayed (2). Consequences are cancer spreading and metastases with permanent pulmonary damage following radical surgery (2). Actually, fewer than 10% of patients with bronchial carcinoid develops the typical syndrome characterized by hypotension, diarrhea and flushing (17,18). The more insidious and life-threatening neoplastic growth of the upper airway is the hemangiomatous proliferation. Subglottic involvement may be asymptomatic at birth, but later in life inspiratory stridor usually occurs, especially during feeding or crying. For these reasons, children younger than 6 months with biphasic stridor should be evaluated with nasopharyngolaryngoscopy or rigid bronchoscopy (19). Persistent respiratory tract infections are also common. Regarding mediastinal infantile hemangioma, it can also occur as an extension from the primitive site, adding an extrinsic compression to the airway (2).

Imaging and endoscopic assessment

Because of the not-specific presenting respiratory symptoms, patient evaluation usually begins with a chest X-ray. Although it is not diagnostic in most cases, it usually shows indirect signs of bronchial obstruction (such as segmental atelectasis, bronchial dilatation or distal air trapping) which compel further evaluations. The evidence of persistent infiltrate advocate chest CT scan or bronchoscopy in order to distinguish between congenital lung defects, external compression of the airways, intraluminal foreign bodies or endobronchial masses (4). Actually the gold standard for primary tracheobronchial tumors detection is CT scan with intravenous contrast administration. Although the high radiation exposure, it is a fast diagnostic technique with great spatial resolution that allows the clear identification of primary tumor site and extension, the anatomic relation with adjacent organ and vessels and the presence of synchronous lesions distally to primary obstructive site (3). Magnetic resonance is useful for staging malignancies and detecting distant spread without exposing the body to ionizing radiation (20).

Bronchial carcinoids are usually described as well-defined exophytic masses which could entirely occupy the airway lumen causing obstructive symptoms. Full thick involvement of the bronchial wall and extraluminal extension are also possible. They tend to be highly vascularized, showing homogenous contrast enhancement on the CT scan images. Different patterns of calcification are described in 30% of cases (3). Cells expression of somatostatin receptors is a distinctive feature of carcinoid tumors so that radiolabeled somatostatin analogues are usually used in scintigraphy as complementary study for diagnosis and follow up (6). Mucoceridermoid carcinomas appear as intraluminal slow-growing vascular polypoid masses with a high rate of calcifications (50% of cases) (6).

Infantile hemangioma shows different features on CT scan images in relation to their phases. During the proliferative growth it appears as a uniform enhancing soft-tissue mass while during the involution phase the contrast enhancement varies due to its fibrofatty infiltration (3). In any case, endoscopy with biopsy remains crucial for definitive diagnosis based on histological type (21). Both flexible endoscopy and rigid bronchoscopy are used to explore the lumen of the airway, in order to identify tumor location and get tissue samples (22,23). Operative maneuvers such as hemostasis, tumor debulking or airway stenting can also be provided (23).

Treatment

Removing the lesion with great spare of the functional parenchyma is the goal of the surgical treatment. Although several reports referees about endoscopic resection of tracheobronchial tumors, this approach remains controversial in favour to radical surgery (22-24). Conversely, the mainstay of the therapy of infantile hemangioma is medical. Literature supports the prompt initiation of propranolol, which should be continued until the involution phase, which usually occurs at the end of the first year (25).
Endoscopic treatment

Endoscopic treatments are used to ablate endobronchial tumors. In 2013, Sjogren and colleagues published the largest series of endoscopic treatments of tracheobronchial using the carbon dioxide laser. Although the first results were encouraging, several limitations were identified and different surgical complications were highlighted: bleeding, transmural injuries, fibers ruptures and dislocations. Repeated endoscopic treatments were required to remove completely the neoplastic mass exposing each patient to several anesthesiological procedures (24,26,27).

Jaramillo and colleagues reported that endoscopic treatment of mucoepidermoid carcinoma makes really arduous their complete excision, preventing lymph node staging (4). Endoscopic treatment of bronchial carcinoid was also controversial: guidelines considered it only in selected patients with typical carcinoid localized proximal to subsegmental level with polypoid growth and no signs of bronchial wall infiltration or lymph node involvement (6).

As mentioned above, endoscopy has a few utilities in the treatment of infantile hemangioma, which use is limited to the evaluation of the pharmacological response. Laser ablation is a second line therapy in order to allow an adequate airway lumen. However circumferential coagulation must be avoided because of the risk of subglottic stenosis due to scar formation (19).

Surgical treatment

Aim of surgical treatment is complete tumor resection. In order to prevent later functional limitations, normal lung tissue must be spared as much as possible. Although pneumonectomies and lobectomies have been typically performed for bronchial tumours, parenchyma-saving procedures, such as sleeve resections and bronchoplasties, are the main procedures performed recently (28). Bronchial carcinoid and mucoepidermoid carcinoma are reported to metastasize to the lymph nodes so that their biopsy is strictly recommended (14,24,29).

Preventive tracheotomy is not usually recommended. Also in case of in case of infantile hemangioma, tracheostomy, which was commonly used in the past, is not required now. It should be performed in selected cases of severe tracheal obstructive symptoms, however it should be avoided when primary resection of the tumor or biopsy with endoscopic debulking could be possible (14).

In case of lesions located in the laryngeal tract an anterior transverse collar incision is indicated. During surgery a temporary intra-operative tracheotomy could be useful in order to remove the tracheal tube. After dissection of the subcutaneous tissue and the platysma muscle, the infrahyoid muscles and the thyroid isthmus are retracted in order to obtain free access to the airway. A laryngofissure may help to reach the site of the lesion, depending on its localization. Radical tumorectomy can be safely performed, if there is no infiltration of the cartilaginous tissue with clear cleavage planes. Partial resection is mandatory in case of larynx infiltration. Laryngotracheal defect can be repaired by rib graft (30). Huge neoplastic masses required cricotracheal resection with an end-to-end anastomosis. Extubation is usually carried out at the end of surgery, except for selected cases (14). Postoperative complications such graft infection or collapse, excessive proliferation of the granulation tissue, extensive malacia, vocal fold palsy or laryngotracheal stenosis could occur rarely (14).

Neoplastic lesion involving the upper trachea can be approached by transverse cervical incision, while sternotomy is usually not required. Flexible intraoperative bronchoscopy is performed to identify the tumor site. The neoplastic mass is then removed through a tracheal window or a cylindrical resection. In the latter case an end-to-end tension free anastomosis is advocated. Lymph nodes biopsy is mandatory (7).

Conversely, when the tumor is identified in the inferior part of the trachea, a sternotomy is usually required. Each surgical approach must be individualized depending on the tumor site and extension (31).

In case of masses localized in the main bronchi, with proximal and distal stumps free from neoplastic lesions proved by frozen sections, the gold standard is the sleeve resection. Intra-operative bronchoscopy and endobronchial ultrasound may help to guide the appropriate bronchial resection. Entire preservation of health lung parenchyma is the clear advantage of this approach (27,32).

Although for congenital pulmonary malformation thoracoscopic lobectomy and segmentectomy are now generally accepted (33), the same procedures for tracheobronchial tumors have not been attempted in the pediatric population yet (34,35).

Medical treatment

Given the benign course of the most common tumours
when radical resection is achieved, conservative treatment is not usually performed (36). Conversely, regarding the management of tumour relapses, both chemotherapy and radiation therapy are required (14).

Follow up

Pediatric oncological guidelines are lacking and no recommendations exist on medical, radiological and endoscopical follow-up. Primary surveillance should identify the related symptoms of neoplastic relapses. Al-Qahtani and colleagues propose clinical examination and chest X-ray every 3 months for the first year and every 6 months thereafter. Carcinoid tumors required abdominal ultrasound, chest computer tomography and urine and serum 5-HIAA every 6 months to exclude metastases. Bronchoscopy should be performed every 6 months for the first year and then yearly, especially in case of partial surgical resection (37).

Conclusions

Tracheobronchial tumours usually are not suspected in children experiencing recurrent respiratory symptoms. This is often cause of delayed diagnosis. Conversely, respiratory symptoms resistant to pharmacological treatment should deserve further investigations to early identify possible obstructive causes. Early diagnosis may allow to perform parenchyma-saving surgeries, avoiding the functional problems related to extensive lung resection.

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Footnote

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

References

18. Wang LT, Wilkins EW Jr, Bode HH. Bronchial carcinoid


