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Case Report
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Endobronchial Carcinoid in an 11-Year-Old Child with Indication for Pneumonectomy

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Abstract

We present a case of an eleven-year-old girl with one-year persistent infectious symptoms of the respiratory tract. She was treated for an extended period as recurrent pneumonia, which resulted in destroyed lung and the necessity of right pneumonectomy due to a 30 mm endobronchial typical carcinoid tumor, with the involvement of the right main bronchus.

Keywords: Neuroendocrine tumors; Pediatric malignant tumor; Pediatric thoracic surgery

Introduction

Carcinoid tumor is relatively rare, comprising less than 5% of all bronchopulmonary tumors and even rarer in the pediatric population, accounting for 0.6 cases per million people under 30 years of age [1-3]. Although it is the most common malignant tumor in children, with the incidence of 63% to 80% of all malignant neoplasms (7, 10, 12), it usually presents as slow growth neoplasia, derived by neuroendocrine Kulchitsky cells of the respiratory tract. Its classification, based on necrosis and mitosis rate, is divided into two variants named typical carcinoid (no necrosis and <2 mitoses/2 mm^2) and atypical carcinoid (>2 mitoses/2 mm^2 or necrosis). This classification helps to understand their malignancy potential and is a strong prognostic factor, in favor of the typical carcinoid [4-6]. When discovered early, carcinoid tumors are associated with excellent survival and a low recurrence rate. In selected cases, it is possible to do an endobronchial resection without any loss of lung parenchyma and lung function. Quite often, delay in diagnosis of this entity occurs due to nonspecific symptomatology related basically to endobronchial obstruction, as asthma-like symptoms, or recurrent pneumonia. In these cases, with a more advanced local disease, radical treatment is necessary, including lobectomy and bronchoplasty, bilobectomy, or even pneumonectomy, also achieving a good outcome [1,3,6,7]. We present a case of an 11-year-old girl with a one-year persistent respiratory tract infection treated as pneumonia, which resulted in destroyed lung and the necessity of a right pneumonectomy due to an endobronchial carcinoid.

Case Presentation

An eleven-year-old girl was seen at the Pediatric Hospital (Hospital Pro- Criança - Rede D'Or - Rio de Janeiro) with pneumonia. It was her 4th episode of pulmonary infection in the past year. A CT-scan with coronal reconstruction showed right lung atelectasis with mediastinal shift to the right (Figures 1A-1C). The CT scan showed pleural thickening, destruction of the right lung with bronchiectasis, a mass obstructing the right main bronchus, and lymphadenomegaly (>2.0 cm) in the mediastinum in chains 2R, 4R, 7, and 10. A bronchoscopy was performed, and an obstructing mass was seen in the right main bronchus, 1 cm distal to the main carina, with strawberry-like appearance, suggestive of endobronchial carcinoid, as well as a small amount of purulent secretion around the mass (not seen in the picture) (Figure 2). Several biopsies were done but were inconclusive (inflammatory reaction).

At this point, a DOTATOC PET was ordered and confirmed that the lesion was a neuroendocrine tumor, and the multiple lymphadenomegaly did not have any uptake of the radiotracer (Figure 3).

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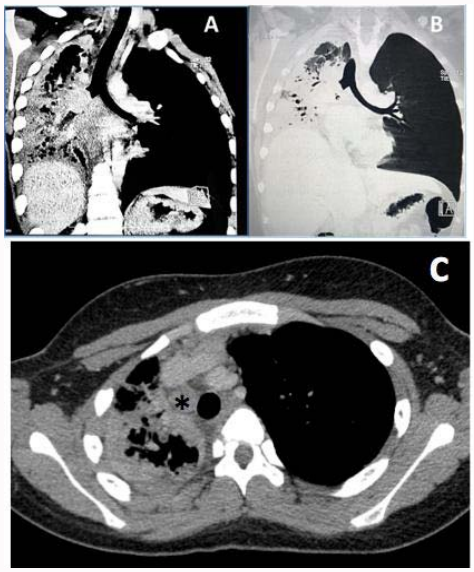

Figure 1A: Rounded lesion in the right main bronchus.
Figure 1B: Pleural thickening and bronchiectasis with pulmonary atelectatic destruction.
Figure 1C: Axial mediastinal window shows an enlarged 4R lymph node (*).

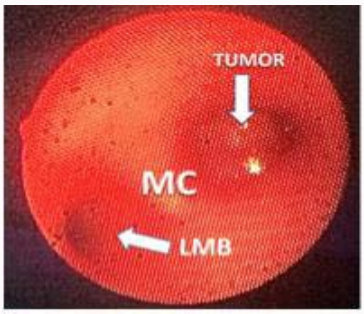

Figure 2: Tumor obstructing the right main bronchus.
MC: Enlarged Main Carina; LMB: Left Main Bronchus

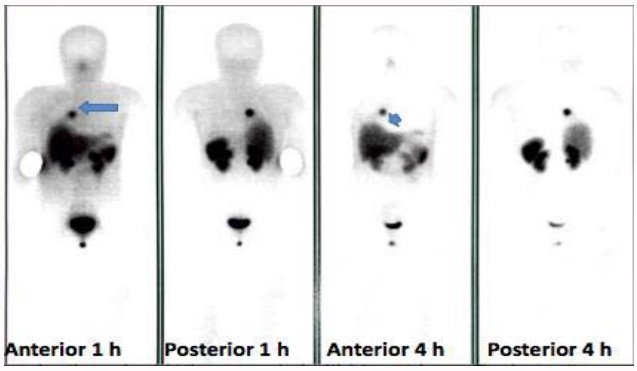

Figure 3: DOTATOC-PET with heavy uptake only in the endobronchial lesion (arrow), and no uptake in mediastinal nodes. There is some uptake in the right lower lobe due to obstructive pneumonitis (arrowhead). This figure shows early (1 hour), and late (4 hours) images.

The case was discussed in the multidisciplinary conference, and it was decided to do a resection, a possible *right sleeve pneumonectomy*. After 15 days of intensive treatment, the patient was brought to the OR, and under general anesthesia and selective intubation of the left main bronchus with bronchoscopic orientation, the patient was put

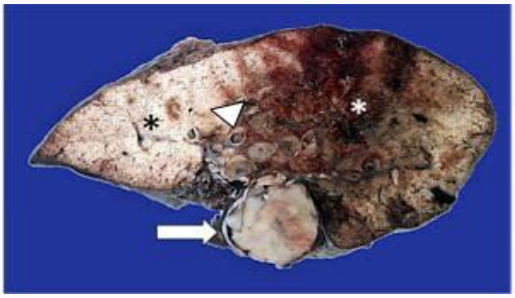

Figure 4: Tumor into the right main bronchus, measuring 30 mm (arrow), extensive consolidation of the lung (**) and bronchiectasis (arrowhead).

in left lateral decubitus and operated on through a right thoracotomy in the 4th intercostal space. The chest cavity was almost totally free of adhesions. The right middle and lower lobe were entirely collapsed, and the right upper lobe was hyper-inflated with significant consolidation (hepatization). We did a radical lymphadenectomy, and all the resected nodes were inflammatory at the quick section. We then proceeded to the right pneumonectomy by stapling the lower lobe vein, upper lobe vein, and the right main pulmonary artery, and then we opened the right main bronchus for direct vision and inspection. The lesion was coming from the right upper lobe bronchus, and it was possible to resect the lung and to close the right main bronchus manually with separated "X" shaped stitches of 3-0 Polyglycolic Acid. The bronchial margin was free of tumor. The bronchial suture was covered entirely with a pediculated graft of the right thymic lobe that was dissected down from the pericardium. We did an intercostal nerve block in 6 interspaces and put a chest tube 16 Fr at the top of the pleural cavity. The chest tube was maintained open until the patient was returned to the supine position, and it was closed with a tube clamp and monitored every 2 h in the pediatric ICU. The right lung and the chains 10R, 9R, 7R, 8R, 4R, and 2R lymph nodes were sent to pathology together with the right lung (Figure 4), which at the pathology confirmed the presence of a unifocal, well-differentiated, 30 mm in diameter, typical endobronchial carcinoid tumor without lymph-node metastasis. The tumor originated in the right upper lobe bronchus and invaded the intermediate bronchus. Extensive chronic obstructive pneumonitis and bronchiectasis were present in the remaining lung (the tumor was in stage IB - T2a N0 M0). The PO course was relatively uneventful, the chest tube was withdrawn in the 8th PO, and she was discharged on the 28th PO. The admission was long because of difficult pain and psychological control, the chest tube was in place for 8 days because of a PO fever (that was urinary tract infection), but the patient was in excellent shape after 1 month of her discharge. The Figures 5A-5C shows the pathology study, with Hematoxylin/Eosin (HE) and immunohistochemistry of the tumor.

Discussion

Neuroendocrine carcinomas are rare malignant neoplasms derived from neuroendocrine epithelial cells, with the potential to secrete bioactive peptides. It was first described in 1888 and denominated 'karzinoid' by Oberndorfer in 1907. Lung carcinoid tumors derive from the neuroendocrine cells of the bronchial wall. Its exact incidence over the years is not well defined. The 2015 WHO has classified neuroendocrine tumors of the lung into four histological variants: 1- Typical Carcinoid (TC), 2- Atypical Carcinoid (AC), 3- Large Cell Neuroendocrine Carcinoma (LCNEC), and 4- Small Cell Lung Carcinoma (SCLC). The histopathological defining criteria of typical carcinoid tumors are low mitotic count in 2 mm^2 and

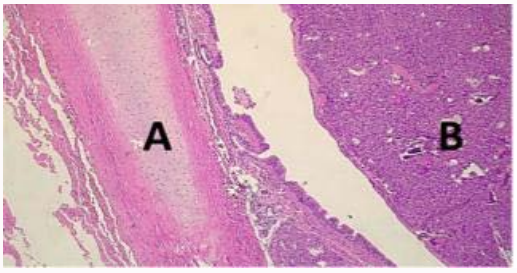

Figure 5A: Image at the level of the lesion. Cartilage and bronchial mucosa on the left (A) and tumor on the right (B) Hematoxylin-Eosin stain - 40x.

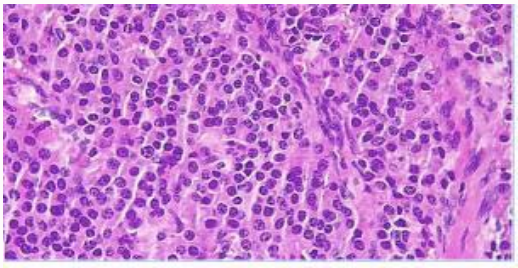

Figure 5B: Classic histopathologic features of typical carcinoid: Cells in uniform arrangement with nuclei in salt and pepper pattern, high vascularized stroma and absence on necrosis and mitosis.

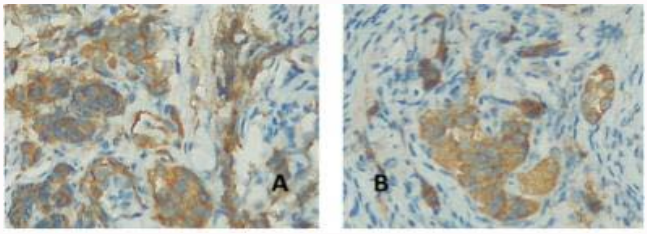

Figure 5C: In A - Chromogranin A immunohistochemistry neuroendocrine marker - positive in brown (40x) and in B – Synaptophysin stain, also a neuroendocrine marker – positive in brown (40x).

the absence of necrosis as already pointed out [8]. Despite having indolent behavior these tumors have the potential to metastasize, especially the atypical ones, characterized by high mitotic count and the presence of necrosis [2,5,6]. These tumors are uncommon, usually seen in the fourth to sixth decade of life. In children, it comprises the most common primary lung malignancy, but with *rare prevalence* and restricted literature data. It is estimated to represent about 80% of primary lung malignancies, and 75% of them are typical carcinoids. Usually, diagnosis is made at ages between 10 and 15 years old, and sometimes its diagnosis can be delayed due to its slow growth pattern and nonspecific symptoms. Clinical features are related to endobronchial infiltration, leading to obstruction. Younger patients can present cough, wheezing, hemoptysis, or respiratory distress, often treated as other reactive airway disorders. Some symptoms are associated with paraneoplastic syndromes, as the lesion can secrete hormones (mainly when metastatic). So, suspicion of bronchial carcinoid tumor is challenging, because the symptoms are often related to different conditions than lung malignancy. Due to its low prevalence in children. It is common to see younger patients being treated recurrently for pneumonia, or asthma, undergoing more sensitive diagnostic workup only after being symptomatic for several months [2,3,7-13]. The diagnostic workout is selected basically to characterize the airway obstruction. These tumors tend to present as an endobronchial polypoid lesion, with an intraluminal and an extraluminal component, involving the main stem or lobar bronchus in 85% of cases, but may eventually be discovered in the peripheral lung. Chest radiography may visualize atelectasis or obstructing pneumonia, indicating a Computerized Tomography (CT) of the chest. CT is a more sensitive noninvasive modality of exam, and it is mandatory to characterize and locate the lesion, as well as searching for signs of advanced disease, like additional lung nodules, pleural effusion, nodal enlargement, and invasion of adjacent structures. The use of contrast turns possible to observe an avid enhancing lesion due to the common hypervascularization of these tumors. Bronchoscopy is the preferred method for evaluating endobronchial lesions. With bronchoscopy, it is possible not only to visualize the obstruction but also to biopsy the lesion, including treating symptomatic obstruction if present by endoscopic resection [3,5,6,9]. Limitations of these modalities are observed when trying to detect small and low metabolic lesions, with a low sensibility of computerized tomography, magnetic resonance imaging, somatostatin receptor scintigraphy, or even Positron Emission Tomography (PET) with 18-F-fluorodeoxyglucose. The widespread use of more sensitive and new imaging modalities with outstanding results can change this scenario. 68Ga-DOTATATE, 68Ga-DOTATOC, and 68Ga-DOTANOC PET and PET/CT, notably the first one, have been associated with a marked improvement in detecting small metastatic lesions, being superior to other imaging tools for correct staging these patients. At the same time, it has low toxicity, uses less radiation, and has fast administration, being a reliable method to use in the pediatric population. Genetic testing may be considered, as some cases are related to Multiple Endocrine Neoplasia 1 (MEN1) syndrome [2,5,10]. Classic histopathological features of carcinoid tumors are size more than 5 mm (lesions with less than 5 mm are considered tumorlets), cells uniform with nuclei in salt and pepper fashion, and high vascularized stroma. Differentiation between typical and atypical forms is based on mitosis count and the presence of necrosis: Typical carcinoid has lower than 2 mitoses/2 mm^2 and absence of necrosis and atypical with 2 to 10 mitoses/2 mm^2 or presence of necrosis. Immunohistochemistry can be helpful in the diagnosis, but it is not pivotal: Neuroendocrine immunohistochemistry markers (chromogranin A, synaptophysin, and CD56) are usually positive, but not always. Ki67 proliferative index is not recommended by WHO 2015 to distinguish typical and atypical carcinoids. Surgical resection of carcinoid tumors has been the treatment of choice, and it is associated with a good prognosis, especially in cases of typical carcinoids. Lymph node sampling or dissection is crucial since up to 20% of the cases have metastasis to mediastinal nodes. To preserve lung function is expected to resect the lesion and preserve as much viable parenchyma as possible. In cases with pure endobronchial involvement, it is feasible and effective to perform pure bronchoplasties, without any lung resection, achieving excellent oncologic outcomes, as reported by Pikin. Usually, lesions are more extensive, so sleeve resections and lobectomy with bronchoplastic procedures are the standard approaches, as seen in reported cases and series. However, in late and not uncommon diagnosticated cases, like ours, the extensive destruction of the lung or involvement of the central tracheobronchial tree requires pneumonectomy to achieve complete resection, which can carry increased morbidity and mortality rates [11]. In our case, we performed a right pneumonectomy due to destroyed lung. Five-year survival rates for typical carcinoids can be as good as 90%. On the contrary, in nodal metastatic disease or atypical carcinoids, a poorer

clinical prognosis is seen, with 40% to 75% of patients alive after five years. In these cases, adjuvant chemoradiotherapy may have a positive role in defining the prognosis. In metastatic diseases, temozolomide and 177-lutetium-DOTATATE can be used for disease control.

Conclusion

Carcinoid tumors of the lung are particular neuroendocrine bronchial tumors that are well-differentiated, have an indolent course, and in the typical type has an excellent prognosis. Besides its rarity, they are the most common primary lung malignancy in children. When suspected and discovered early, good oncologic outcomes can be achieved with conservative resections and without significant consequences to lung function and quality of life. Early referral for computerized chest tomography and bronchoscopic evaluation of suspected cases may impact on the management and the prognosis of these patients.

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