Pediatric endobronchial inflammatory myofibroblastic tumor: a case report and review of the literature

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Abstract

Inflammatory myofibroblastic tumor (IMT) belongs to the group of soft tissue tumor and could occur at any anatomical site from the central nervous system to gastrointestinal tract. The lung and abdomen are commonly affected sites, however, pulmonary IMT is predominantly located within the parenchyma rather than presenting as endobronchial lesion. IMTs may occur in any age group, but they are observed most commonly in children and adolescents. Here, we present a case of IMT arising from the left main stem bronchus in a 10-year-old girl.

Introduction

Inflammatory myofibroblastic tumor (IMT) was first described by Brunn in 1939. According to the 2013 World Health Organization (WHO) Classification of soft tissue tumors, IMT has been defined as an intermediate fibroblastic or myofibroblastic tumor.[1] This lesion arises from soft tissue or viscera, which is characterized by the presence of spindle-shaped myofibroblasts, and a chronic inflammatory infiltrate composed of eosinophils, lymphocytes, and plasma cells. IMT can occur throughout the body, including the lung, bladder, spleen, breast, pancreas, liver, spermatic cord, prostate, peripheral nerves, soft tissue, and orbit. The true prevalence of IMT of the lung is difficult to calculate because varying terminology caused a great deal of confusion, but it accounts for 0.04-0.7% of all lung tumors across all age groups. Pulmonary IMT is predominantly located within the parenchyma rather than presenting as endobronchial lesions. Preoperative diagnosis of endobronchial IMT is quite difficult and requires a multi-disciplinary medical approach. Bronchoscopy and CT studies are the main methods to evaluate this rare disease entity. Bronchoscopy allows only a visual evaluation of the tumor surface and subsequent biopsy. Other information about the origin, internal composition, enhancement pattern and extent of the lesion can be easily obtained through contrast-enhanced CT scan. IMT can be suspected preoperatively through some hematologic abnormalities and radiologic findings, but correct diagnosis mainly depends on histopathological findings.[2] Endobronchial IMT in the pediatric population is relatively rare and nearly 136 cases have been reported up to date in the English literature.[3-29] Because of rarity of endobronchial IMT, the experience regarding imaging evaluation, treatment and long-term outcomes need to be further accumulated. Therefore, we present the clinical and radiological features of an additional case.

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Case Report

A 10-year-old girl complaining of a progressive shortness of breath was admitted to our hospital. She repeatedly suffered from pneumonia for the past 3-year. Meanwhile, she also described chest tightness and intermittent dyspnea on exertion exercise. She did not have other systemic symptoms such as pyrexia, abdominal pain, weight loss and night sweat. Physical examination revealed a well-nourished girl without acute distress. Her vital signs were normal, and oxygen saturation on room air was 99%. There was no thyromegaly, jugular venous distention or cervical lymphadenopathy. Rhonchi and wheezing were heard in the left lung field. The cardiac examination and abdominal examination were unremarkable. Erythrocyte sediment reaction and C-reactive protein were elevated with the value of 63mm/1h and 32mg/L respectively. Tuberculin skin test was negative. Chest radiography showed increased opacity over left lung field and mediastinal shift to the left, suggesting the collapse of the left lung. Non-enhanced computed tomography showed typical obstruction of the left main bronchus associated with complete left lung atelectasis. Subsequent contrast-enhanced CT showed a significantly enhanced oval mass measuring 1.0×2.0×2.2 cm within the left main bronchus (Figure 1), which completely obstructed the distal portion of the left main stem bronchus and its branches. There was no evidence of mediastinal infiltration and lymphadenopathy. At the bronchoscopic examination, an ovular vessel-rich mass was noted at the distal end of the left main bronchus and causing a complete occlusion of the lumen (Figure 2). Considering the appearances of contrast-enhanced CT suggesting vessel-rich lesions, endoscopic resection of the tumor was not a candidate.

Radical surgical resection of the mass was proposed to the patient's parents and informed consent was granted. Under general anesthesia, the patient underwent total resection of the tumor and the left main bronchus and bronchoplasty through a left posterolateral 5th intercostal space. The resected neoplasm was gray-yellow, solid and gritty. Microscopic findings visualized a cellular lesion characterized by abundant spindle-shaped cells and inflammatory cells (HE×200) (Figure 3). Immunohistochemically, the tumor was positive for desmin, smooth muscle actin and anaplastic lymphoma kinase (ALK), and negative for CD117, CD34, S-100. The tumor had a low Ki-67 proliferative index. Based on histopathological findings and immunohistochemical analysis, a diagnosis of endobronchial IMT was made. The postoperative period was uneventful and the patient was discharged on the 10th postoperative day. The child was growing well with no sign of relapse on the 6th month follow-up. A check-up bronchoscopy was reported to be normal and follow-up CT showed complete resolution of the left lung atelectasis (Figure 4).

Discussion

IMT was first observed in lung and described by Brunn in 1939, and was named by Umiker *et al.* in 1954 owing to its propensity to clinically and radiologically mimic a malignant process.[30] IMT has ever been described by various terms because of its variable cellular components, which include plasma cell granuloma, inflammatory pseudotumor, xanthogranuloma, inflammatory fibrosarcoma, and pseudosarcomatous myofibroblastic proliferation. However, these names are unified as inflammatory myofibroblastic tumor. It can almost be found in every site of the body from the central nervous system to gastrointestinal tract, but the lung and abdomen are commonly affected loca-

tion. IMT can occur at any age and both sexes are equally affected. A large series study by Coffin *et al.* reviewed 84 cases with IMT involving various sites, the age of these patients ranges from 3 months to 46 years.[31] In the pediatric patients with primary pulmonary tumors, IMT constitutes approximately 50% of benign intrapulmonary tumor. However, pulmonary IMT is predominantly located within the parenchyma rather than presenting as endobronchial lesion.[3] But endobronchial IMT in the pediatric population is not rare with more than 136 cases reported in the English literature up to date,[3-29] and 10 cases was listed in the table for the available result of ALK analysis (Table 1).[3-10]

Among 6 children, ALK translocation/overexpression was definite. The positive rate of ALK in children with endobronchial IMT is similar to that in all IMT patients.

IMT is poorly understood about its etiology. Trauma, surgery, infections *i.e.* herpes and Epstein-Barr virus, radiotherapy, steroid use and autoimmune reactions have been suggested as etiological factors.[32] By several authors, it was postulated that pulmonary inflammatory pseudotumors occur as a result of unchecked immunologic response to a viral or foreign antigen-antibody reaction.[33,34] But in endobronchial IMTs, pneumonia is more likely to be a common obstructive pulmonary outcome rather than a cause of it.[20] Currently, IMT is mostly considered as a neoplasm of intermediate malignant potential as evidenced by the fact that nearly 50-70% of the cases carry rearrangements of *ALK* gene.[35] *ALK* gene, located on the short arm of chromosome 2 at 2p23, encodes a tyrosin kinase receptor.[36] Its expression is normally restricted to the brain, particularly in the developing nervous system. ALK is involved in the pathogenesis of several tumors, and anaplastic large cell lymphoma is the most famous one. This is also seen in at least a part of IMTs. The ALK status has a role in a number of differential diagnoses. In fact, the majority of the lesions that enter the differential diagnosis with IMT are ALK-negative.[38,39] *ALK* gene could be a potential target molecule, and specific targeted therapy, such as tyrosine kinase inhibition, has been used in selected inflammatory myofibroblastic tumors with encouraging results, as noted by Butrynsky.[39] Though more study needed, the response of IMT to tyrosine kinase inhibition may be another evidence for the influence of ALK to this group of diseases.

The clinical presentations of pulmonary IMT can be variable ranging from asymptomatic to variable symptoms. Most presented symptoms are cough, hemoptysis, chest pain and dyspnea, and fever. After the surgical resection, the systemic symptoms of IMT may resolve and tumor recurrence may be found easily by a return of clinical abnormalities.[2]

Radiologic findings of pulmonary IMT are variable and unspecific. The most common radiological presentation is a solitary peripheral well-circumscribed lung mass, with variable size between 1.5 cm and 14 cm according to a series of 28 cases reported by Kim *et al.*[40] Endobronchial polypoid forms arising in the bronchus are the rarest but have also been reported, and chest radiography only reveals non-specific finding such as pulmonary atelectasis or obstructive pneumonia. Non-enhanced CT can be helpful in identify intralesional calcifications, which are shown more frequently in pediatric cases. Dynamic contrast-enhanced CT can show the origin, internal component, enhancement pattern and extent of the lesion. Regarding the dynamic enhancement features, Takayama *et al.*[41] speculate that delayed enhancement could be attributed to abundant fibrous tissues such as myofibroblasts, which were the main structural material of the tumor.

The treatment of choice for IMT remains controversial, and appropriate management should be based on the site of tumor and the condition of the patient. The common option of therapeutics includes surgical resection, corticosteroids and non-steroidal anti-inflammatory drugs (NSAID). Although surgical intervention in child is challenging, the surgical resection is very important in complete removal and good prognosis. For those patients who are unsuitable for complete surgical resection such as the case of multiple tumors or mass infiltrating adjacent organs, other modalities can be considered. There are also sporadic reports of rapid and sustained resolution with corticosteroid monotherapy and NSAIDs.[42,43] There are also sporadic reports of success with laser, but some authors point that it can result in recurrent relapse of IMT.[12]

The prognosis of IMT is usually good, but it depends on tumor size (less than or equal to 3 cm) and complete resection. The overall 3-year

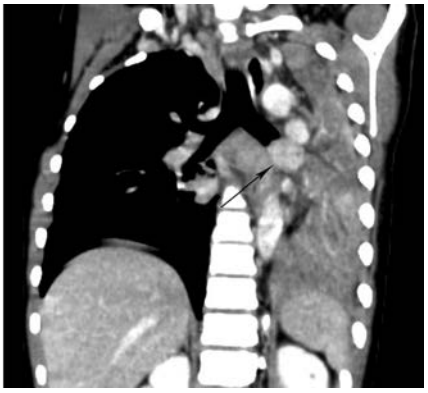

Figure 1. Contrast-enhanced reformatted coronal image showed a significantly enhanced oval mass situating within the left main bronchus, which completely obstructed the left main stem bronchus.

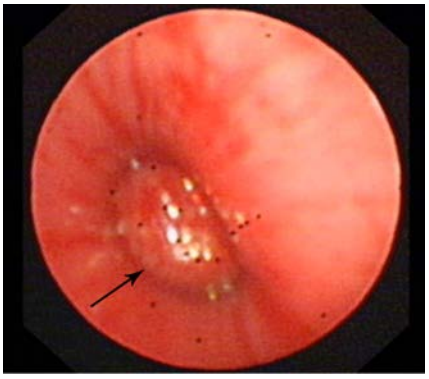

Figure 2. Bronchoscopic examination revealed an ovular neoplasm with rich vessels.

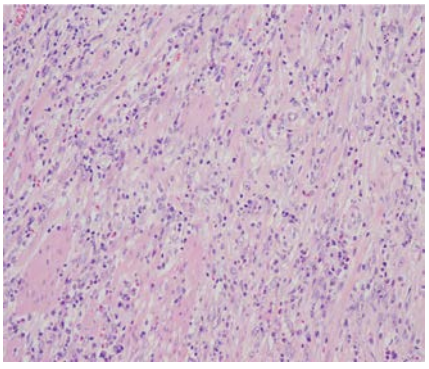

Figure 3. Microscopic examination show a cellular lesion characterized by myofibroblast-like spindle cells admixed with abundant acute or chronic inflammatory cells (HE×200).

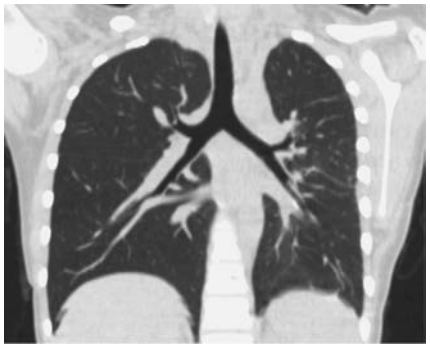

Figure 4. Follow-up computed tomography showed the norm of the left lung on postoperative 12 months.

Table 1. Cases of children with endobronchial inflammatory myofibroblastic tumor and available results of anaplastic lymphoma kinase staining.

Study	Age (y)	Gender	Localization	Size (mm)	Follow-up period (months)	ALK translocation/over-expression
Uchida *et al.*[4]	9	M	RMB	14	12	Positive
Fujino *et al.*[5]	10	F	RB	-	6	Positive
Dhouib *et al.*[6]	11	M	LMB	18×12×17	3	Positive
Karnak *et al.*[3]	9	F	LMB	-	3	Negative
Singh *et al.*[7]	12	M	RUL	9	-	Positive
Brodlie *et al.*[8]	15	F	LMB	-	36	Positive
Brodlie *et al.*[8]	11	M	Trachea	-	18	Negative
Sacco *et al.*[9]	6	F	RUL	-	16	Negative
İçmeli *et al.*[10]	16	F	RUL	40	-	Negative
Present study	10	F	LMB	20×20×12	6	Positive

F, female; M, male; LMB, left main bronchus; RMB, right main bronchus; RB, right bronchus; RUL, right upper lobe; RML, right middle lobe.

survival rate is about 82% and the overall 5-year survival rate is about 74%.[44] Local recurrence rate of pulmonary IMT after resection was between 6.6% and 13%, occurring predominantly in those cases with incomplete resection. Rare distant metastases have also been reported due to multifocal characteristic of this disease entity rather than metastatic spread. Close follow-up radiological studies are strongly recommended. Bronchoscopy should also be planned even if postoperative radiologic images are normal. We are confident that complete resection was achieved in our case, follow-up bronchoscopy and CT showed no evidence of tumor. Although rare, endobronchial IMT should be known as a possible cause of atelectasis in children. Imaging findings together with appropriate management in our patient will further accumulate clinical experiences of IMT.

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