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CASE REPORT

A rare aetiology of respiratory failure in a 10-year-old boy: inflammatory myofibroblastic tumour

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SUMMARY

Primary neoplasms of the respiratory tract are rarely encountered in the paediatric population. Inflammatory myofibroblastic tumour (IMT) is a rare soft tissue mesenchymal tumour but a distinct disease entity accounting for less than 1% of all primary lung tumours. We report a case of a 10-year-old boy who presented with respiratory failure and left lung collapse. On flexible fiberoptic bronchoscopy, a pedunculated mass in the lower part of the trachea originating from the left main stem bronchus was identified. The patient subsequently underwent a left-sided pneumonectomy with complete resection of the mass. The histopathological analysis was consistent with IMT. Two years of follow-up and the patient remains well.

BACKGROUND

Primary neoplasms of the respiratory tract are rarely encountered in the paediatric population.[1] Inflammatory myofibroblastic tumour (IMT) is a rare soft tissue mesenchymal tumour but a distinct disease entity accounting for less than 1% of all primary lung tumours.[2] Although it has a higher propensity to affect children and young adults, it can occur at any age group.[3–5] The first case was reported to be in the lung by Brunn[6] but since then, IMT has been identified to affect a wide range of anatomical locations including the liver, spleen, pancreas, bladder, larynx, tongue, breast, retroperitoneum and central nervous system.[3]

Multiple terms have been used to describe IMT in the past including inflammatory pseudotumour, histiocytoma, plasma cell histiocytoma complex, plasma cell granuloma, fibrohistiocytoma, xanthomatous granuloma, spindle cell pseudotumour and inflammatory fibrosarcoma (IFS).[7 8] However, the term IMT was coined around two decades ago owing to its distinctive pathological and molecular features.[7] Although these tumours were initially regarded to be benign and non-neoplastic, it is now widely accepted that these tumours may have a tendency to grow aggressively leading to local invasion to adjacent organs, recurrence and distant metastasis.[5 9]

Because of its rarity and ability to mimic other malignant tumours on gross appearance and clinical and radiological features, IMT can be a diagnostic challenge to a physician. It is hence, imperative for the histopathologists to be aware of this condition. We report a case of a previously healthy 10-year-old boy who was diagnosed to have IMT of the left main bronchus and was successfully treated by pneumonectomy.

CASE PRESENTATION

A 10-year-old boy presented to our emergency room (ER) with a 6-month history of productive cough, difficulty in breathing and a weight loss of 5 kg. Owing to the endemicity of tuberculosis (TB) in our region, he was being treated for pulmonary TB since 3 months by a general practitioner without any clinical or radiological improvement. Medical and family history of the patient was insignificant. There was no history of TB contacts.

On initial examination in the ER, the child was in obvious respiratory distress with a respiratory rate of 30 breaths/min, oxygen saturation of 85% on room air, heart rate of 120/min and blood pressure of 120/78 mm Hg. There was no clubbing or cyanosis. The respiratory system examination revealed an asymmetric chest rise, dull percussion note and absent breath sounds on the left side. Rest of the systemic examination was within normal limits.

INVESTIGATIONS

An arterial blood gas was performed which revealed a pH of 7.43, $PaCO_2$ 39.9 mm Hg and a PaO_2 55.9 mm Hg. The chest X-ray showed near-complete opacification of the left hemithorax with a mediastinal shift to the affected side (figure 1). Ultrasound of the chest was then performed which did not show any pleural effusion on either side. Subsequently, CT scan of the chest was ordered which confirmed a left lung collapse with ipsilateral mediastinal shift and no pleural effusion or lymphadenopathy.

A provisional diagnosis of left lung collapse and respiratory failure was made and the child was admitted to the paediatric intensive care unit. He was initially started on broad spectrum antibiotics and kept on non-invasive ventilation. There was a suspicion of an endobronchial lesion-like foreign body or neoplasm. He subsequently underwent a flexible fiberoptic bronchoscopy which revealed a pedunculated mass in the lower part of the trachea originating from the left main stem bronchus almost completely occluding the lumen. The bronchoalveolar lavage was not taken as mass was occluding the proximal airway and patient was unstable. An emergent surgery consult was hence obtained for the resection of the lung mass.

DIFFERENTIAL DIAGNOSIS

The initial differential diagnoses were of left lung pneumonia, foreign body, endobronchial TB and tumour leading to postobstructive atelectasis. However, after visualisation of a pedunculated

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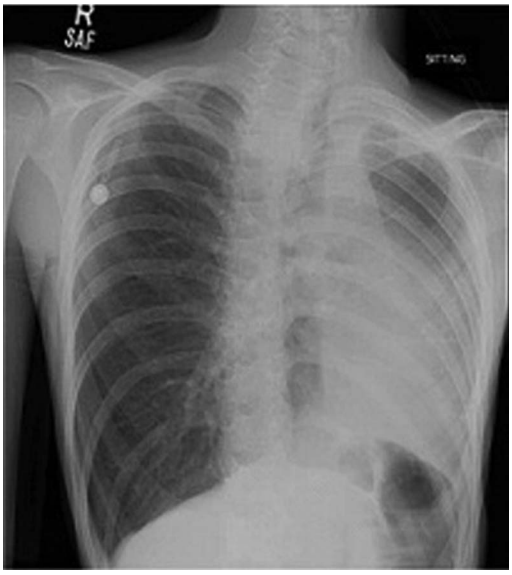

Figure 1 A chest X-ray showing left lung opacification and volume loss.

mass through flexible fiberoptic bronchoscopy, the diagnostic possibilities had narrowed down to a neoplasm and surgery was planned consequently.

TREATMENT

The patient successfully underwent left pneumonectomy with complete resection of the mass. On gross examination, the mass was grey white in colour and homogenous measuring 3×2×1.5 cm. Hisotopathological analysis revealed a spindle cell neoplastic lesion arranged in fascicles admixed with numerous plasma cells and lymphocytes (figure 2). The neoplastic cells had oval nuclei, inconspicuous nucleoli and eosinophilic cytoplasm. Immunohistochemical staining showed positivity for α-smooth muscle actin (ASMA), anaplastic lymphoma kinase (ALK) protein and desmin (figure 3). In contrast, the tumour cells were not reactive to cytokeratin AE1/AE3 and S-100. A diagnosis of IMT was made.

OUTCOME AND FOLLOW-UP

The patient was extubated within 24 h of surgery. He remained well during his stay in the hospital and was discharged home on the fifth postoperative day. At 2 years of follow-up, the patient is doing well without any relapse or complications.

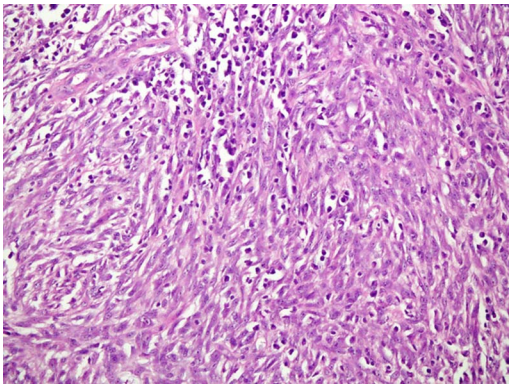

Figure 2 H&E stained section showing intricate admixture of lesional spindle and inflammatory cells (high magnification: ×40).

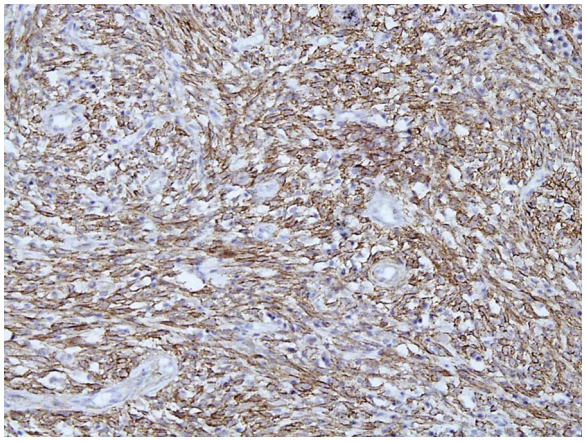

Figure 3 Positive immunohistochemical staining (brown) for anaplastic lymphoma kinase protein in lesional cells (high magnification: ×40).

DISCUSSION

IMT is a rare soft tissue mesenchymal tumour, the aetiology of which still remains unknown. It has been postulated that patients might have a recent respiratory tract infection triggering the inflammatory response which has been found in almost 30% of the cases.[10] On the contrary, some studies suggest that IMT might be a true neoplasm due to a mutation on chromosome 2p23 leading to the over-expression of the ALK protein resulting in increased cell proliferation, initially found in anaplastic large cell lymphomas.[11] Owing to the varying nomenclature, the incidence of IMT has been difficult to calculate; however, it has been estimated to comprise less than 1% of all primary lung tumours.[2] It is more likely to affect the paediatric population and young adults without any gender predilection. The lung is recognised to be the most common organ involved but IMT can virtually affect any organ and site in the body with the abdomen and pelvis being the most common extrapulmonary manifestations.[3–6]

The patients may present with a wide spectrum of symptoms including the focal respiratory symptoms (shortness of breath, chest pain, non-resolving cough, hemoptysis) as well as the non-specific systemic symptoms (fever, chronic fatigue, weight loss) attributed to the raised inflammatory markers such as interleukin 6 in the body.[3–6] In rare cases, patients have been reported to have arthalgia and clubbing of the fingers which got resolved after resection of the tumour.[4] However, patients might also be asymptomatic and the tumour may be found incidentally on imaging or direct visualisation through bronchoscopy.[4] Our patient presented with symptoms of non-resolving cough and severe respiratory distress and was found to have complete atelectasis of the left lung which has been rarely reported before.[10 12]

Owing to its diverse clinical, gross and radiological manifestations, IMT can mimic malignant tumours and can be a diagnostic dilemma for physicians. The CT scan and MRI are useful in localising the lesion in the respiratory tract. Most commonly, a solitary well-circumscribed lesion is found in the periphery ranging between 1.5 and 14 cm.[13] Endobronchial masses, as in our case, are much rarer. In our case, the mass could not be identified on imaging and was visualised on flexible bronchoscopy.

Histopathological analysis remains the cornerstone for diagnosing IMT and exclusion of malignancy. Characteristically, IMT is composed of myofibroblastic spindle cells with a

prominent inflammatory infiltrate in the background comprising plasma cells, lymphocytes, histiocytes, eosinophils and neutrophils. It has been subjected to multiple terminologies depending on the predominant cell type involved while the term pseudotumour denotes its potential to mimic invasive malignant tumours.[3–8] Matsubara *et al*[14] used the term inflammatory pseudotumour and classified it into three histological subtypes: (A) organising pneumonia with resolving alveolar exudates, (B) fibrous histiocytoma with lymphocytic aggregation and (C) lymphoplasmocytic type involving the aggregation of the plasma as well as lymphocyte cells (as in our case). Immunohistochemical staining reveals positivity for ALK protein in almost 50% of the cases (as in our case). Alterations with ALK are more likely to be reported in the pulmonary and abdominal IMTs. Although ALK positivity has been found to be associated with a higher chance of local recurrence, ALK negativity has a poorer outcome associated with a greater risk of distant metastasis.[11]

Initially thought to be a benign lesion, IMT is now considered to have a more aggressive nature having a tendency of local invasion to adjacent organs, recurrence and rarely malignant transformation and metastases.[3] Carillo *et al*[5] and Gallego *et al*[9] have reported cases of IMT of the lung with adrenal gland and maxillary metastases, respectively. The term, IFS has been utilised to classify these tumours with aggressive nature and metastases.[3 9]

Surgical resection remains the diagnostic and therapeutic modality of choice. It has been reported that transthoracic or transbronchial needle biopsy may not be definitive and it may be difficult to differentiate between IMT and other neoplasms including fibrohistiocytic neoplasms, nodular sclerosing Hodgkin lymphoma, primary lung cancer and mediastinal fibrosis.[2] Therapeutically, complete surgical resection, has shown to have excellent prognosis and low rate of recurrence.[3 4 10 13] In cases where resection is not possible, use of lasers, steroids and non-steroidal anti-inflammatory drugs have shown some promise.[15 16] Recently, the potential role of crizotinib, a competitive inhibitor of ALK tyrosine kinase has been highlighted in treating ALK-positive IMTs.[17] This report describes the case of a patient with IMT exhibiting ALK rearrangement, who achieved substantial response to crizotinib despite considerable tumour burden. On the contrary, another patient with ALK negative IMT, failed to show an improvement on crizotinib, hence enforcing the role of ALK-dependent signal transduction in a subgroup of patients with IMT.[17]

Learning points

- Inflammatory myofibroblastic tumour (IMT) is a rare soft tissue tumour that can present as an endobronchial lesion leading to atelectasis and respiratory failure.
- Although IMT was initially regarded to be benign and non-neoplastic, it is now known to have a tendency to grow aggressively leading to local invasion of adjacent organs, recurrence and distant metastasis.
- It is imperative to have a high index of suspicion of malignancy in patients with chronic symptoms and atelectasis. It is also important for the histopathologists to be aware of IMT as a potential condition/disease.
- It is possible that an endobronchial mass may not be visualised on CT scan of the chest. In such cases with prolonged respiratory symptoms, bronchoscopy plays a vital role as an investigative modality.
- Complete surgical resection of the mass remains the treatment of choice.

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Competing interests None.

Patient consent Obtained.

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