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CLINICAL RECORD

Inflammatory myofibroblastic tumours of the respiratory tract: paediatric case series with varying clinical presentations

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Abstract

Objectives: To highlight the clinical importance of inflammatory myofibroblastic tumours of the respiratory tract in children, and to present a case series of three children which illustrates this tumour's variable clinical presentation.

Case history: The series includes: a nine-year-old girl with a diagnosis of juvenile idiopathic arthritis, who presented with finger clubbing and was found to have an inflammatory myofibroblastic tumour in her right upper lobe; a 15-year-old adolescent with a left main stem bronchial inflammatory myofibroblastic tumour, who presented with breathlessness and chest pain; and a 12-year-old girl with a tracheal inflammatory myofibroblastic tumour who presented with stridor. In each case, the tumour was resected surgically.

Conclusion: Inflammatory myofibroblastic tumour are a rare but clinically important and pathologically distinct lesion of the respiratory tract in children. The cases in this series highlight some of the varied clinical presentations of inflammatory myofibroblastic tumours, and illustrate some of this tumour's different anatomical locations within the paediatric respiratory tract.

Key words: Tracheal Neoplasms; Child; Bronchial Neoplasms; Bronchoscopy

Introduction

Historically, the term 'inflammatory pseudotumour' has been used to describe a broad range of pathological lesions which share the common histological appearance of stromal spindle cell proliferation accompanied by a chronic inflammatory infiltrate.[1–3] Such lesions represent a spectrum ranging from inflammatory myofibroblastic tumours to non-neoplastic proliferations associated with infectious or reparative processes.[1] However, inflammatory myofibroblastic tumours are increasingly recognised to be a distinct clinical, pathological and cytogenetic entity.[1] These tumours have traditionally been regarded as benign lesions; however, they are now frequently considered to represent a locally aggressive neoplastic process.[4]

Inflammatory myofibroblastic tumours occur most commonly in children and young adolescents.[1,5] They may occur in a wide range of anatomical locations, although one-third are found in the respiratory tract.[6] The case series presented in this paper illustrates the varied clinical presentations of inflammatory myofibroblastic tumour, and the different anatomical locations in which it may occur within the paediatric respiratory tract. The clinical management and histology of these tumours are also discussed.

Case reports

Case one

A nine-year-old girl was originally referred to a rheumatologist with a two-month history of painful, bilateral knee and ankle swelling.

On presentation, the patient's inflammatory markers were raised, with an erythrocyte sedimentation rate of 94 mm/hour and a C-reactive protein concentration of 40 mg/l. An autoantibody screen was negative, although her antistreptolysin O titre was markedly raised, at 800 units/ml. Systemic examination, other than musculoskeletal, was unremarkable.

A diagnosis of sero-negative juvenile idiopathic arthritis was made, and the patient was commenced on prednisolone and oral methotrexate.

However, at review one month later she was found to have finger clubbing (Figure 1). A chest radiograph was therefore performed, which identified a well demarcated lesion in the right upper lobe (Figure 2). The patient was referred to the regional paediatric respiratory and oncology centre for further assessment.

A computed tomography (CT) scan of the thorax confirmed a solitary, 2.4×2.3 cm lesion in the apical segment of the right upper lobe, with no associated abnormalities or lymphadenopathy. Abdominal ultrasound was unremarkable. Results for aspergillus testing and interferon-γ release assay for tuberculosis were both negative.

Over the next three months, the patient's arthritis responded to treatment. She remained well clinically and her chest lesion did not enlarge on repeated imaging. However, there was diagnostic uncertainty about the precise nature of the lung lesion, the finger clubbing remained and a new skin lesion was noted on her left thigh.

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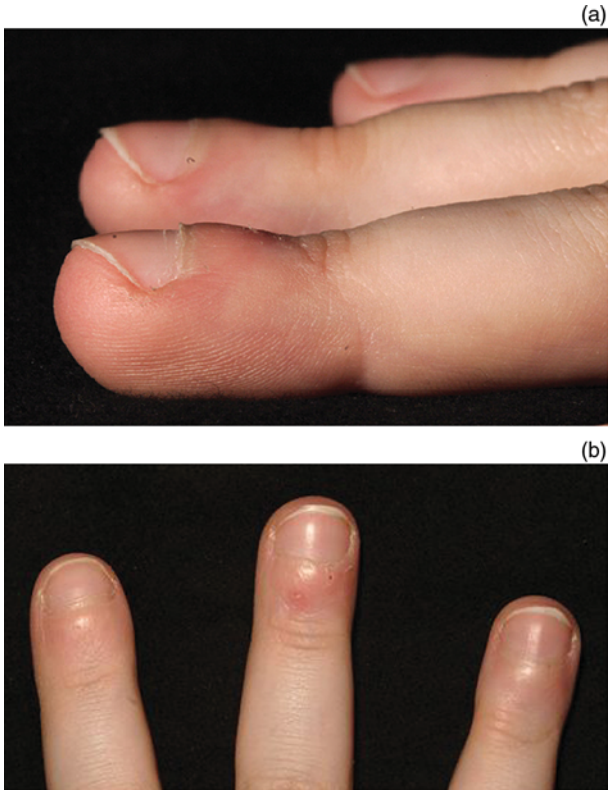

FIG. 1
Finger clubbing seen in case one.

Surgical excision was therefore performed of both the lung and thigh lesions. Histological analysis of the lung lesion revealed complete excision of an inflammatory myofibroblastic tumour, consisting of characteristic spindle cells with an inflammatory infiltrate. Staining for anaplastic lymphoma kinase and human herpes virus eight was negative.

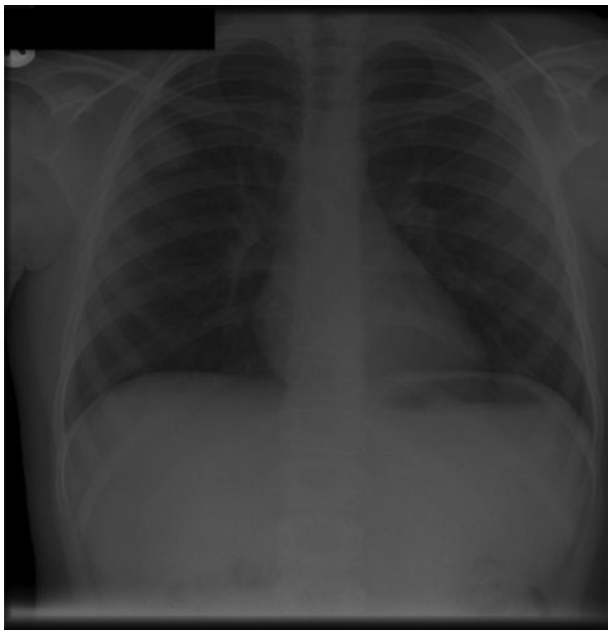

FIG. 2
Posterior-anterior chest radiograph in case one, showing a circular lesion in the right upper lobe.

The thigh lesion was found to be an apparently unrelated cellular dermatofibroma.

By three months post-operatively, the child's finger clubbing had resolved.

At the time of writing, approximately two years after initial presentation, the patient remained healthy, and her arthritis was well controlled on maintenance methotrexate therapy.

Case two

A 15-year-old girl presented acutely to her local paediatric department with chest pain and shortness of breath on minimal exertion. There was a background history of progressive breathlessness and cough over the past six months. During this time, her family doctor had made a diagnosis of possible asthma, although there had been no clinical improvement with a trial of inhaled salbutamol, and she had also received several courses of antibiotics for presumed lower respiratory tract infections.

On examination, there was markedly reduced air entry and a dull percussion note throughout the left side of the patient's chest.

A chest radiograph demonstrated complete 'white out' of the left hemithorax. A CT scan revealed a well demarcated lesion in the left main bronchus, which was initially thought to be an inhaled foreign body. However, at bronchoscopy a fleshy, vascular lesion was identified in the left main stem bronchus, and excised as far as possible.

Histological examination of the lesion revealed an incompletely excised inflammatory myofibroblastic tumour (Figure 3a). Immunohistochemical staining for anaplastic lymphoma kinase was strongly positive (Figure 3b). Cytogenetic analysis showed rearrangement of the anaplastic lymphoma kinase gene on chromosome 2p23.

It was therefore decided that complete surgical excision was necessary. Accordingly, a sleeve resection of the left main stem bronchus was performed.

The patient made an excellent post-operative recovery.

At the time of writing, three years after presentation, there was no sign of local recurrence on CT scans or surveillance bronchoscopies.

Case three

An 11-year-old girl presented to her local paediatric department with a two-week history of stridor. She initially responded to treatment with a budesonide nebuliser, but represented six days later with recurrence of stridor. At this point, she was referred to the regional paediatric ENT department.

A chest radiograph and barium swallow study were both normal. However, bronchoscopy revealed subtotal obstruction of the midtrachea by a large mass. The bulk of the mass was promptly excised at bronchoscopy, establishing a good airway but leaving an irregular surface.

Histological analysis showed the lesion to be an incompletely excised inflammatory myofibroblastic tumour, which did not express anaplastic lymphoma kinase.

A further bronchoscopy, performed one month later, showed approximately 30 per cent obstruction of the tracheal lumen by residual tumour, which was removed by laser with good effect.

A further examination six weeks later showed tracheal granulations, which were again removed by laser.

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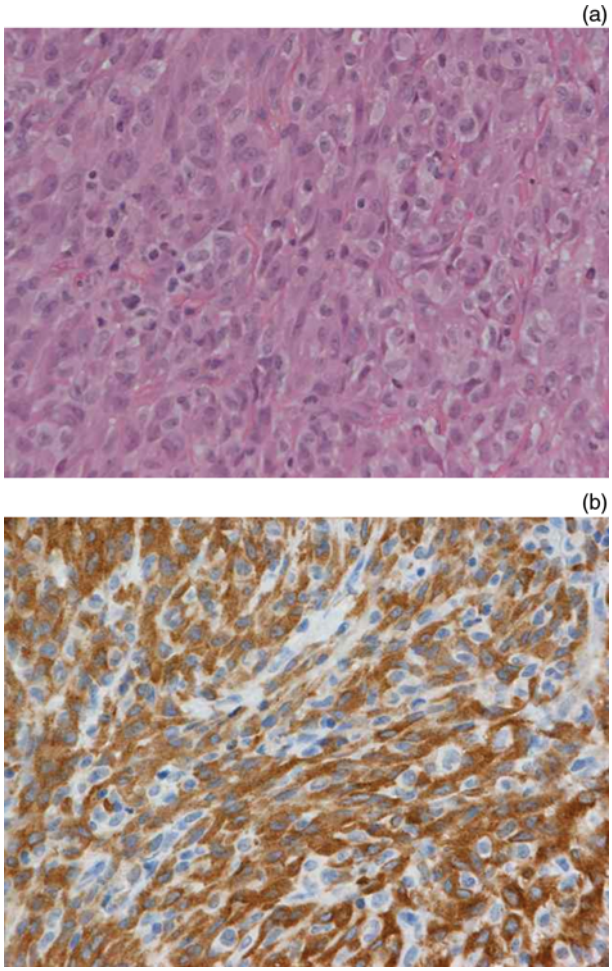

FIG. 3

(a) Haematoxylin and eosin stained section of inflammatory myofibroblastic tumour from case two, showing dense spindle cell proliferation (×400). (b) Positive immunostaining (brown) for anaplastic lymphoma kinase in case two (×400).

The patient remained well clinically over the following 18 months. Subsequent bronchoscopies revealed a satisfactory appearance of the trachea, and no further intervention was needed.

Discussion

Inflammatory myofibroblastic tumours are most frequent in children and young people, and may occur in a wide range of anatomical locations.[1,5] One-third are found in the respiratory tract; the most prevalent non-pulmonary sites include the abdomen, pelvis and retroperitoneum.[6,7] Inflammatory myofibroblastic tumours of the trachea (as described in our third case) are rare and only a limited number have been reported in the medical literature.[8]

Pulmonary inflammatory myofibroblastic tumours may present with respiratory symptoms due to airway obstruction or with focal chest signs; alternatively, they may not be associated with any discernible clinical features.[9] A non-specific syndrome of chronic malaise, fever and weight loss associated with raised inflammatory markers is also a recognised presentation, as illustrated by case one. Classically, such systemic symptoms resolve following surgical resection, and may be associated with increased serum levels of the cytokine interleukin-6.[1,10] Pulmonary inflammatory myofibroblastic tumours may also be identified incidentally as a mass on imaging of the thorax, or directly observed at bronchoscopy.[9,11]

The three cases presented in this report demonstrate the varied ways in which inflammatory myofibroblastic tumours may present clinically. Interestingly, presentation with finger clubbing and joint problems has been documented previously. Pichler *et al.* reported a case of a 12-year-old girl with arthralgia and finger clubbing in whom a chest radiograph revealed a lung tumour.[12] The tumour was resected and found to be an inflammatory myofibroblastic tumour; following resection, the patient's arthralgia disappeared.

In view of the characteristic intense inflammatory infiltrate found histologically in inflammatory myofibroblastic tumours, and the clinical incidence of systemic symptoms, a potential infective aetiology has been proposed.[13] However, evidence to support this hypothesis, from molecular analysis of true inflammatory myofibroblastic tumours for Epstein–Barr virus and human herpes virus eight, is weak.[1] Alterations in the anaplastic lymphoma kinase locus are well described in cases of inflammatory myofibroblastic tumour, and immunohistochemical testing for anaplastic lymphoma kinase is positive in around 50 per cent, as in case two.[1,8] It has been suggested that anaplastic lymphoma kinase abnormalities occur most frequently in cases of pulmonary and abdominal inflammatory myofibroblastic tumour which present in the first decade of life; such tumours are associated with a higher frequency of recurrence.[14]

The treatment of respiratory tract inflammatory myofibroblastic tumours is primarily surgical. In terms of prognosis, the major problem is local recurrence, with a much lower risk of distant metastasis (in less than 5 per cent).[1,5] Provided that excision of a solitary lesion is complete, recurrence is infrequent. However, if complete excision is technically difficult, due to the anatomical site (as seen in case three) or the multinodular nature of the lesion, local recurrence is much more common.

- **Inflammatory myofibroblastic tumours are rare but clinically important lesions occurring in the respiratory tract of children**
- **These tumours are characterised histologically by stromal spindle cell proliferation accompanied by a chronic inflammatory infiltrate**
- **Clinical presentation is variable**
- **The tumours may be locally invasive**
- **Complete surgical resection is the treatment of choice**
- **Long-term follow up is indicated**

Interventional bronchoscopy is an important treatment modality for endolumenal lesions in children, as demonstrated by case two, in which initial mechanical debulking was performed, and case three, in which definitive treatment was achieved in combination with laser treatment. Obvious advantages of interventional bronchoscopy include its minimally invasive nature, compared with open surgery, and its ability to maximise preservation of normal lung tissue.[11] However, interventional bronchoscopy may potentially lead to problems with obtaining sufficient tissue for

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histological diagnosis and assessing resection margins.[9,11] In cases with more extensive tumour involvement, or at sites of anatomical complexity in the bronchial tree, open surgical resection and bronchial reconstruction may be required. Hoseok and colleagues recently described the case of a four-year-old boy with an inflammatory myofibroblastic tumour at the carina which extended into the left main bronchus, requiring surgical resection and carinal reconstruction.[15]

In cases in which complete resection is not possible, or in cases of recurrence, corticosteroid or non-steroidal anti-inflammatory treatment, or local laser therapy, have been used.[11,16] An 'atypical' steroid response has recently been reported in a six-year-old girl with paratracheal and endobronchial masses.[17] Inflammatory myofibroblastic tumour was diagnosed histologically, and the paratracheal mass enlarged dramatically during prednisolone treatment. However, the response of inflammatory myofibroblastic tumour to adjuvant chemotherapy or radiotherapy has not been well established. Long-term follow up remains important in view of the fact that late metastasis and recurrence, although rare, have been reported.[18]

Conclusion

Inflammatory myofibroblastic tumours are rare but clinically important and pathologically distinct lesions of the respiratory tract in children. The cases described in this report highlight some of the varied clinical presentations of inflammatory myofibroblastic tumours, and illustrate the different anatomical locations in which they may occur in the paediatric respiratory tract.

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