CASE REPORT

A diagnostic dilemma in a case of pulmonary inflammatory myofibroblastic tumour

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SUMMARY

An 18-year-old man presented to the local hospital in Malta, with dyspnoea, cough, mild haemoptysis, chest pain and night sweats. CT revealed a right hilar mass. Pleural tap, bronchoscopy and open lung biopsy were inconclusive. Biopsies obtained at repeat bronchoscopy and endobronchial ultrasound (EBUS) revealed a likely diagnosis of inflammatory myofibroblastic tumour (IMT). The patient subsequently underwent right pneumonectomy, and histology revealed the presence of two further nodules apart from the main tumour. Follow-up with positron emission tomography (PET)/CT showed the development of a right basal paracardial lesion due to recurrence and the presence of lymph node, pleural and skeletal disease. Despite radiotherapy to the recurrent nodule and chemotherapy, there was skeletal disease progression. Treatment with an anaplastic lymphoma kinase inhibitor, ceritinib, resulted in very good metabolic response. This case report highlights the importance of keeping IMT in mind when the diagnosis of lung tumours is difficult, as delayed diagnosis may lead to worsened prognosis.

BACKGROUND

Inflammatory myofibroblastic tumour (IMT) is rare and difficult to diagnose.

CASE PRESENTATION

An 18-year-old asthmatic man, a non-smoker, with a history of hypospadias and appendicectomy, presented with exertional dyspnoea, cough, mild haemoptysis, pleuritic chest pain and night sweats.

He had been born at 31 weeks gestation following intrauterine growth retardation, and his recovery in intensive care had been complicated by acute respiratory distress syndrome requiring inotropes and continuous positive airway pressure.

He had history of neither recent travel nor contact with tuberculosis.

A chest X-ray (CXR) revealed a well-defined right lower lobe consolidation or mass, with a small right-sided pleural effusion.

The patient was treated with intravenous antibiotics. Pleural fluid aspiration revealed an exudate with numerous mesothelial, but no malignant cells.

CT scan showed a 3×4 cm conglomerate of necrotic lymph nodes in the right hilum compressing the right upper lobe bronchus with mild compression of the intermediate bronchus. There was extensive irregular infiltration in the right lower lobe, a moderate right-sided pleural effusion and a small consolidation in the left lung base.

The abdominal organs were normal, with several borderline right iliac fossa lymph nodes.

At bronchoscopy, there was extrabronchial impingement obstructing the orifice of the right upper lobe and bronchus intermedius, and there was a lot of pus. Bronchoalveolar lavage and sputum analysis were negative for acid-fast bacilli, and cytology revealed no malignant cells.

Positron emission tomography (PET) using 18F-fluorodeoxyglucose integrated with non-contrast low dose CT (PET/CT) showed increased uptake in the right hilar mass and in the left lower lobe corresponding to the area of consolidation.

The patient was scheduled for open lung biopsy. Right thoracotomy was performed and a right hilar mass identified—wrapped in bronchial vessels—and biopsied. Histology showed pulmonary tissue on a background of stroma with smooth muscle, fibrous tissue and abundant lymphocytes, plasma cells and histiocytes. There was no evidence of malignancy.

Despite extensive discussion at pathological meetings, the pathological process remained unclear.

The patient was referred to a UK centre, where he underwent bronchoscopy and endobronchial ultrasound. There was extrinsic narrowing of the right main bronchus. A large heterogeneous mass in the position of station 10R, and a small node at station 4R, were identified. Biopsies were positive for anaplastic lymphoma kinase (ALK) 1, desmin and SMA (patchy), and negative for CD34 and cytokeratin. This immunoprofile was consistent with an IMT. Organising pneumonia and sarcoma were the other differential diagnoses.

A trial of oral steroids was given in view of the inflammatory process identified, with no resultant improvement in the lung mass, and the patient was subsequently scheduled for a right pneumonectomy in the UK.

Meanwhile, he presented to a hospital in Malta, with chest pain and copious frank haemoptysis. CXR showed increased size of the right hilar mass associated with postobstructive consolidation in the right lung and right tracheal shift.

CT was repeated, and revealed significant progression of disease with the right lung nearly completely collapsed with mediastinal shift to the right, and increased size of the hilar mass.

The patient was admitted, treated with intravenous antibiotics, and since the haemoptysis did not resolve, a trial of the antifibrinolytic agent, tranexamic acid, was given. The haemoptysis subsequently resolved.

The patient was transferred to a UK centre where rigid bronchoscopy documented the tumour

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to be visible up to the carina. An intrapericardial sleeve right pneumonectomy with subsequent anastomosis of the left main bronchus into the distal trachea was performed. The perioperative concerns were of two possible small satellite foci within the right lung, adjacent to the primary tumour, and tumour extension into the subcarinal space, although at the time this was not thought to constitute metastatic disease.

Macroscopically, the right lung showed a white irregular tumour located between the upper and lower lobes, partially involving the middle lobe, and measuring 60×55×50 mm; 1 mm away from the tumour described, there was a second nodule in the pleura, reaching the surface, and measuring 11×10×4 mm.

Microscopically, there was a non-encapsulated spindle cell tumour with a storiform configuration. Cellular density was variable, low in collagenised areas and higher at the periphery. There was neither necrosis nor inflammation in the tumour. Mitotic rate was up to 3/10 high-power fields but there were no atypical figures. The other two nodules described shared the same histological appearances. The bronchial and vascular resection margins were free of tumour. Immunohistochemistry showed positive staining for ALK and SMA. S100, CD34, MNF116 and desmin were negative. Proliferation index Ki-67 was approximately 40%. This was consistent with inflammatory myofibroblastic tumour with direct extension into the lymph nodes.

Owing to the complexity of this specimen, and the difficulty to establish posterior resection margins, the case was to be considered as R1 for treatment and follow-up purposes.

DIFFERENTIAL DIAGNOSIS

Histology obtained from the second bronchoscopy led to three possible differential diagnoses—myofibroblastic tumour, organising pneumonia and sarcoma.

TREATMENT

Follow-up PET/CT 2 months later showed increased uptake in the right hilar region. There was also increased uptake along most of the pleura on the right, thought to likely be representing inflammation.

On CT, a solid enhanced 22×18 mm lesion in the right basal paracardial region due to recurrence was seen. The patient underwent radiotherapy to the recurrent nodule, however, repeat PET/CT after completion of radiotherapy showed significant disease progression, with an increased uptake in the known right lung nodule, with new lymph node, pleural and probable skeletal disease.

The patient was started on chemotherapy with six cycles of doxorubicin.

A further PET after chemotherapy showed mixed inhomogeneous response to treatment in the right basal pericardial nodule and mediastinal nodes, however, with evidence of skeletal disease progression. The patient was subsequently started on zoledronic acid, however, PET then showed further disease progression with increased intensity and extent of uptake in the skeletal lesions (right humerus and right sacroiliac joint), and increased uptake in the upper zone of the right lung, with new lesions in mediastinal nodes, liver and pelvis. Since there was ALK positivity on histology, an ALK inhibitor, ceritinib, was started.

OUTCOME AND FOLLOW-UP

After 1 month of ceritinib, there was very good clinical response with improved appetite and weight gain, and the patient reported an improved sense of well-being. There was also

radiological response with PET showing very good, albeit incomplete, metabolic response to therapy. The mediastinal nodes, and lesions in the liver, pelvis and right sacroiliac joint, no longer showed increased uptake on PET, and there was modest uptake in the proximal right humerus, in the upper zone of the right lung and in the right pleura.

DISCUSSION

IMT is rare and difficult to diagnose, and it is not uncommon for diagnosis to be delayed. IMT can occur anywhere, but most often involves the lung and orbit.¹ Most patients are young, under 40 years of age.²

In a reported case of lung IMT, the first two transthoracic biopsies were non-diagnostic.³ IMTs consist of inflammatory and mesenchymal cells,^{2 4} so histological diagnosis is difficult. Misdiagnoses have also been reported.⁵

IMT is mostly innocuous, however, it can be locally invasive.⁵ There may be sarcomatous transformation,^{1 6} and it may behave aggressively, as in this case.

Steroids have a limited role in the treatment of lung IMT, and surgical resection remains the treatment of choice.^{1 4 6}

In completely resected lesions, the 5-year survival rates are >90%,⁷ but long-term survival is <50% with lesions >3 cm not amenable to complete resection.⁶

The incidence of distant metastasis is rare, occurring in <5% of IMT cases. IMTs arising in the lung are those most commonly reported to have metastatic disease.⁸

IMTs are often ALK positive,^{9 10} and ALK inhibitors have been reported as achieving partial response in these tumours.^{11 12}

Learning points

- ▶ Inflammatory myofibroblastic tumour (IMT) is rare and diagnosis can be difficult, so it should be suspected early, especially in young patients with lung masses and inflammation on histology.
- ▶ First choice treatment is surgical resection.
- ▶ If IMTs are anaplastic lymphoma kinase (ALK) positive, ALK inhibitors may be considered.
- ▶ Although prognosis is fair, it is better with early diagnosis and treatment.
- ▶ IMT can behave aggressively despite the seemingly benign histology.

Competing interests None declared.

Patient consent Obtained.

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