

An Asymptomatic Young Lady with Multiple Inflammatory Myofibroblastic Tumours

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Abstract

Introduction: We report a case of inflammatory myofibroblastic tumour with positive PET-CT involving the lung, hilar lymph node, liver and spleen in an asymptomatic young girl. Diagnosis was made four years after the initial presentation.

Treatment: Conservative treatment.

Outcome: Patient remained asymptomatic for 4 years.

Conclusions: Multiple inflammatory myofibroblastic tumour may remain asymptomatic despite multiple organs involvement.

Introduction

Inflammatory Myofibroblastic Tumour (IMT) is also known as plasma cell granuloma, inflammatory pseudo tumour, xanthogranuloma and fibrous histiocytoma. It commonly involves the lung [1]. Other rare sites are liver, spleen, bladder, breast, salivary gland, skull base, orbit, thyroid, spine, lymph node and kidney. Involvement of multiple sites is rare. We report a case of inflammatory myofibroblastic tumour with positive PET-CT involving the lung, hilar lymph node, liver and spleen in an asymptomatic young girl. Diagnosis was made four years after the initial presentation.

Case Report

A 22-year-old Malay lady who is a non-smoker and has childhood asthma first presented in February 2006, with symptoms of acute exacerbation of bronchial asthma secondary to upper respiratory tract infection. There was no haemoptysis, chest pain, prolonged fever, loss of weight or appetite. Physical examination was unremarkable except for diffuse rhonchi in the lungs. Besides elevated lactate dehydrogenase (882 U/L) and leukocytosis ($15 \times 10^9/L$), other blood investigations were normal. Chest radiograph showed two large well-defined nodules each in the right upper zone and left lower zone. There was no chest radiograph prior to this admission. CEA, CA125 and α -FP were normal. She was lost to follow-up until May 2007 when she was seen in clinic again.

She had neither worsened asthma nor constitutional symptoms. CT thorax showed two lung nodules in the right upper lobe (2.3×1.7 cm) and left lower lobe (2.7×2.7 cm) (Figure 1a). CT abdomen showed a nodule in segment IVa of the liver (1.5×1.5 cm) and focal calcifications in the spleen. Bronchoscopy revealed a necrotic nodule over the anterior segment of the right upper lobe bronchus and nodular lesions over the right secondary carina. Endobronchial biopsy was reported as chronic inflammation. Bronchoalveolar lavage was negative for bacteria culture, cytology and acid fast bacilli. CT guided biopsy of the left lung nodules was reported as hamartoma. She was seen three monthly to monitor the size of the lesions.

In Dec 2009, chest radiograph showed a new nodule in the right lung. A repeated CT thorax showed a new nodule in the middle lobe (2.1×2.6 cm) (Figure 1a). The other lung nodules remained the same. CT abdomen showed new peripherally enhancing nodules with central necrosis in segment VIII of the liver (2.5×3.0 cm) and both upper

(2.1×2.0 cm) and lower (1.4×1.5 cm) poles of the spleen (Figures 1b). The segment IVa liver nodule remained the same. At that time, she remained well with no constitutional symptoms. Her asthma was well controlled with symbicort (budesonide/formoterol 160/4.5 mcg) 1 puff bd. Blood investigations showed LDH of 675 U/L, haemoglobin of 9.6 g/dL, WBC of $10.8 \times 10^9/L$ and platelets of $536 \times 10^9/L$. Liver and renal functions were normal. CT guided lung biopsy of the right middle lobe

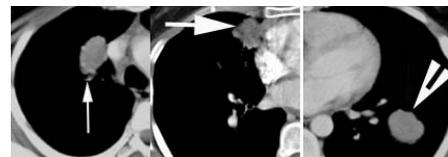


Figure 1a: Axial post contrast CT thorax showing the nodules in the right upper lobe (thin arrow), middle lobe (thick arrow) and left lower lobe (arrow head).

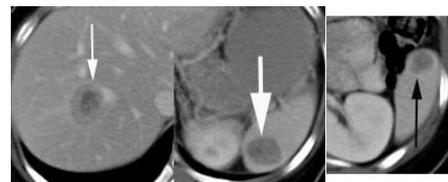


Figure 1b: Axial post contrast CT abdomen showing the nodules in segment VIII of liver (thin white arrow), upper pole of spleen (thick white arrow) and lower pole of spleen (black arrow).

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nodule was reported as synovial sarcoma. PET-CT showed foci of FDG hyper-metabolism over the right upper lobe nodule (SUV max 3.2), right middle lobe nodule (SUV max 7.9), apical segment of left lower lobe nodule (SUV max 3.5), left hilar lymph node (SUV max: 3), liver in segment IV (SUV max 5.4) and segment VIII (SUV max 5.4) and 2 foci in the spleen with SUV max of 5.4 (Figure 2a and 2b).

Subsequently, she had CT- guided biopsy of the liver nodule at segment VIII. The histology showed a benign myofibroblastic tumour. Due to the discrepancy in the histology reported and the fact that the patient was symptomatically well, a senior pathologist was called to review all previous histologies. All the previous lung biopsies and the liver biopsy gave a similar pattern of growth. They were composed of monotonous spindle shaped cells that were arranged in short fascicles with bland nuclei and lacked mitosis (Figure 3). They possessed abundant elongated eosinophilic cytoplasm and some amount of collagen bundles within the background. It was more suggestive of an inflammatory myofibroblastic tumour when intermingled lymphoplasmacytic cells appeared, which were more pronounced in the liver biopsy (Figure 4). This was further supported by the immunohistochemistry that was only positive with Vimentin and smooth muscle Actin but not with other markers such as bcl-2 and CD99. She refused any intervention. CT scan of the thorax and abdomen was repeated six months later, which showed no significant

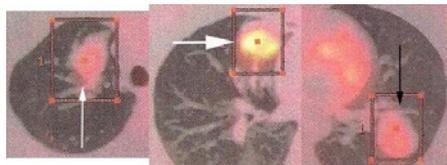


Figure 2a: PET-CT scan showed foci of FDG hyper-metabolism over the right upper lobe (thin white arrow), middle lobe (thick white arrow) and left lower lobe (black arrow) lung nodules.

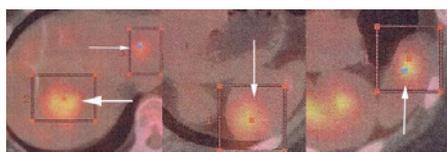


Figure 2b: PET-CT scan showed foci of FDG hyper-metabolism over the segment IVa and VIII of liver (horizontal arrows) and spleen (vertical arrows).

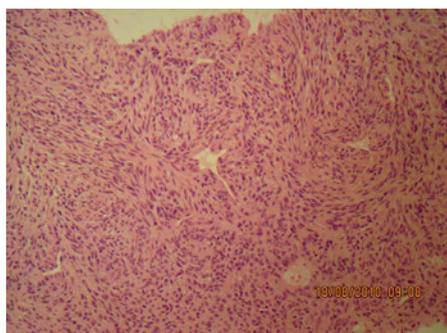


Figure 3: Micrograph of lung biopsy with tumour appearance showing fascicles of monotonous spindle-shaped cells. (Magnification x 400).

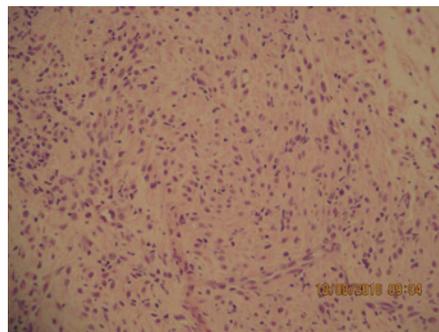


Figure 4: Micrograph of the liver biopsy showing monotonous spindle-shaped cells with uniform bland nuclei and sprinkling of lymphoplasmacytic cells as shown with arrow (Magnification x 200).

changes in the lung, liver and spleen nodules. No new lesion was seen. She remained well at the time of manuscript submission.

Discussion

IMT is a rare tumour which is commonly found in the lung. Multiple lesions in different organs are rare. Our patient had at least four organs involved. It can occur in any age group but commonly seen in younger patients [1]. There is no gender or ethnic preponderance. Most of the patients are asymptomatic and the symptom depends on organ involvement. IMT of the lung can present with cough, shortness of breath, chest pain or haemoptysis. IMT of the liver can present with non-specific symptoms like fever, arthralgia, myalgia, jaundice or abdominal pain [2]. Other rare presentations are weight loss and swelling of eyelid [3].

CT scan features of IMT are very variable and nonspecific but important in the exact characterization of these nodules. The typical appearances in the lung are solitary, peripheral, sharply circumscribed, lobulated mass with preference to the lower lobes [4]. The lung nodules usually appear heterogenous and enhanced post contrast [5]. Calcifications usually occur more commonly in children. CT features of hepatic and splenic IMT are described as hypodense masses with variable patterns of enhancement. These include non enhancement, homogenous enhancement, heterogenous enhancement or early peripheral enhancement with central non enhancement [5]. As seen in our patient, the segment IVa lesion showed homogenous enhancement, segment VIII lesion showed peripheral enhancement with central necrosis and the splenic lesions showed heterogenous enhancement.

IMT is known as a cause of false positive FDG PET scans [6-8]. There are several reports of hepatic and splenic inflammatory myofibroblastic tumours with positive FDG PET scan. The mechanism of FDG accumulation in hepatic and splenic inflammatory myofibroblastic tumour is attributed to the presence of inflammatory cells within the tumour. In our patient, all the nodules in the lung, liver and spleen showed a SUV max of more than 3.0.

Most of the diagnoses were made after surgical resection. In a mesenchymal lesion, diagnosis made via tissue biopsy is limited by the small portion of tissue sample obtained. Furthermore, a different part of the tumour may give a different appearance and mask the actual diagnosis. In a surgically resected lesion, adequate sampling appropriate to the tumour size is obtained to get a proper diagnosis. The patient's earlier biopsy simulated normal smooth muscle tissue and only the presence of inflammatory cells in the background made

hamartoma a possible diagnosis. Negative bcl 2 and CD99 did not support the diagnosis of synovial sarcoma. The liver biopsy was typical of IMT.

There is significant controversy and confusion regarding the pathogenesis and histogenesis of these uncommon tumours or tumour-like masses. This is due to the varying degrees of inflammatory cell infiltration noted on pathologic examination and the observation that the disease process, although usually following a benign course, is sometimes invasive. The most consistent pathologic feature of these lesions is a background proliferation of spindle cells associated with a variable dense polymorphic infiltrate of mononuclear inflammatory cells. The immunohistochemical and ultrastructural studies of the spindle cells show features of fibroblasts and myofibroblasts in various proportions. Focal invasion, vascular invasion and nuclear pleomorphism are all suggestive of more malignant behaviour and a worse prognosis. The inflammatory cells infiltrate such as lymphocytes, plasma cells, histiocytes and occasional eosinophils may have individual cell predominance or mixtures of them. The aetiology of IMT remains unknown with variable theories including an inflammatory reaction to an infection or to an underlying low grade malignancy. Several infectious agents have been linked to the development of IMT e.g. *Eikenella corrodens* and Epstein Barr.

Resection is the treatment of choice for solitary IMT. However, our patient had multiple lesions which made resection impossible. Furthermore, she was completely asymptomatic and the lesions remained largely unchanged over four years. Koea JB et al. [1] reported six cases of IMT of the liver with or without splenic involvement, four of them resolved spontaneously and another two resolved with oral steroids. Goldsmith PJ et al. [2] reviewed 215 patients with IMT of the liver; of these 60 of them had good outcomes. Forty patients were reported to have either spontaneous resolution or regression of lesions.

However, there were five mortalities related to the disease. But among the 75 patients who underwent resection, six died of post-operative complications. They concluded that there was no difference in patients who underwent resection or treated conservatively. Our patient was not keen to take any immunosuppressive agent and decided to come for repeated radiological investigation to monitor the size and number of the lesions. In conclusion, patients with inflammatory myofibroblastic tumours may remain asymptomatic even when multiple organs are involved.

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