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CASE REPORT

Cardiac Metastasis: A Rare Involvement of Primitive Neuroectodermal Tumour of the Lung

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Abstract A 15 year-old adolescent was referred with 2 month history of worsening of breathlessness and haemoptysis. He also reported constitutional symptoms of fever, poor appetite and weight loss. The chest roentgenogram showed a massive right pleural effusion with apparent cardiomegaly. The cardiac silhouette over the right heart border was obliterated and the mediastinum was widened. Computed tomogram of the thorax showed a bulky heterogeneous mass in the right lung with extension to the heart. Subsequent CT guided lung biopsy revealed Primitive Neuroectodermal tumour (PNET). Here, we illustrate the clinical course of an aggressive pulmonary PNET with lethal cardiac metastasis.

Keywords PNET · Cardiac Metastasis · Ewing's Sarcoma · Extraosseous Ewing's Sarcoma

Introduction

Primitive Neuroectodermal tumours (PNETs) arise from mutation of the pluripotent neural crest cells caused by a balanced reciprocal translocation t (11:22) (q24; q12). This sarcoma is the second most common tumour in the first two decades of life [1]. It typically occurs in the bone and soft tissue but other locations have been reported. PNET rarely presents as an organ based neoplasm. Primary lung PNETs rarely involved the heart. Thus far only two documented report of PNET involving the heart had been reported in English medical literature [1, 2]. We report a case of Pulmonary PNETs with pericardial involvement.

Case Report

The patient is a 15-year-old student who was referred for progressive dyspnoea and haemoptysis. His health had been deteriorating for the past 2 months. He also reported constitutional symptoms of intermittent fever, anorexia and weight loss. Due to his poor health, he had been absence from school and was not able to play his favourite football game. He also reported poor effort tolerance for 1 week prior to admission. He had no history of childhood malignancy and there was no first-degree relatives diagnosed with cancer.

Physical examination revealed a cachexic looking young man. He was in respiratory distress and needed oxygen therapy. The fingers were not clubbed. His conjunctiva was pink. He was not jaundiced. The trachea was central. The jugular venous pressure was elevated with prominent "X" descent. The blood pressure was 104/60 mmHg and the pulse rate was 98 beats/minute. The heart sounds were not muffled but the apex beat was displaced. The chest examination was consistent with a massive right pleural effusion as evidenced by stony dullness and diminished breath sound. Other systemic examinations were unremarkable.

The blood investigations showed normal blood count, serum electrolytes, glucose and creatinine. The serum

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Lactate dehydrogenase was raised at 913 u/L. The liver function test was mildly impaired, with mixed cholestatic and hepatic features. Serum tumour markers for AFP, CEA, CA-125 and CA 19-9 were not elevated. The electrocardiogram showed low voltage QRS complexes with electrical alternan, suggestive of massive pericardial effusion. The chest roentgenogram showed a massive right pleural effusion with apparent cardiomegaly. The cardiac silhouette over the right heart border was obliterated and the mediastinum was widened. (Fig. 1)The 2-D transthoracic echocardiography showed a massive pericardial effusion with a mass compressing on the left atrium. The left ventricular function was normal. Pericardiocentesis was performed and drained about 1.5 L of hemorrhagic defibrinated fluid which contained erythrocytes and neutrophils on cytological examination. The computed tomography of the thorax reported a bulky heterogeneously enhancing mass occupying most of the posterior right lower thoracic cavity. It measured about 15×13 cm in diameter. The mass was seen in continuity with the pericardial lining of the right heart border and extends into the pericardium compressing the right atrium (Fig. 2). Technetium Bone Scan showed hot spot on the right anterior 9th rib and diaphysis of the right humerus.

CT guided biopsy was performed. The histological diagnosis was primitive neuroectodermal tumour. The hallmark was the presence of malignant small round blue cell with rosette formation which is pathonogmonic of this tumour. The malignant cells were stained intensely positive for CD 99 and neuron specific enolase (Fig. 3a and b). Chromosomal analysis was not performed on the biopsy tissue.

Following the tissue diagnosis, the patient was staged to be high risk. He was commenced on EURO 99 Ewing

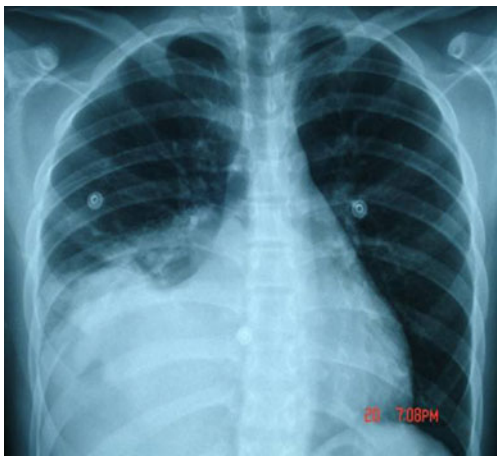

Fig. 1 Is the postero-anterior view of the chest x-ray which revealed a massive right pleural effusion with mass like lesion obliterating the right cardiac silhouette. There is apparent cardiomegaly

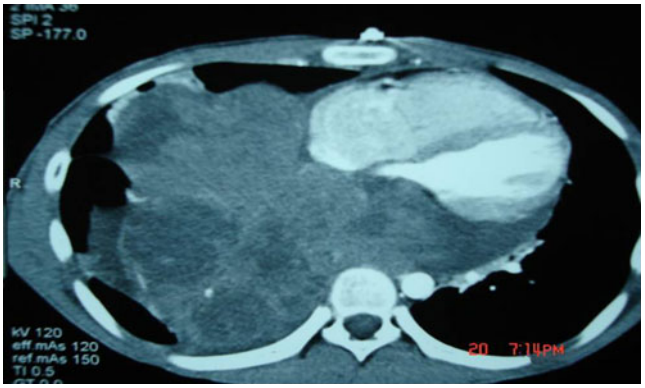

Fig. 2 Showed the CT thorax of the patient with a huge heterogenous mass in the right lung appearing in continuous with the pericardium. The mass was compressing the left atrium with obliteration and deforming the right atrium cavity. The mass was measuring 15×13 cm in diameter

Protocol which consisted vincristine, ifosfamide, doxorubicin, and etoposide. He was planned to complete a total of six cycles of chemotherapy followed by surgical debulking operation. Due to the close proximity of the tumour to the heart, the surgical option was not amenable. Subsequently, the tumour had grown rapidly without further response to the chemotherapeutic agents. This resulted in re-accumulation of the pericardial effusion and bulky thoracic mass effect. The patient health continued to deteriorate and finally succumbed to his illness 1 year later.

Discussion

Human primitive neuroectodermal tumour is a spectrum of the Ewing's sarcoma family of tumour (ESFT) [3]. Askin et al. was the first to describe this tumour in 1979 which they described as malignant small cell tumour of the thoracopulmonary region in childhood [4]. They occur frequently in the bone and soft tissue. This tumour has a predilection in children and young adult. It is extremely rare in our clinical practice. The most common site of origin is at the pelvic bone, femur, humerus and ribs. The historically term extraosseous Ewing's sarcoma is even rarer. They are histological and biologically similar to the osseous Ewing's sarcoma.

Primitive neuroectodermal tumours (PNETs) are extremely aggressive and usually lethal. In our patient, the tumour grew rapidly despite initial successful reduction by four chemotherapeutic agents. PNETs is typically a painful and aggressive tumour that may invade the chest wall, lung, mediastinum and the heart. By far, pulmonary carcinoma with metastasis to the heart is commoner and constitutes about a third of all metastatic cardiac tumours [5]. PNETs

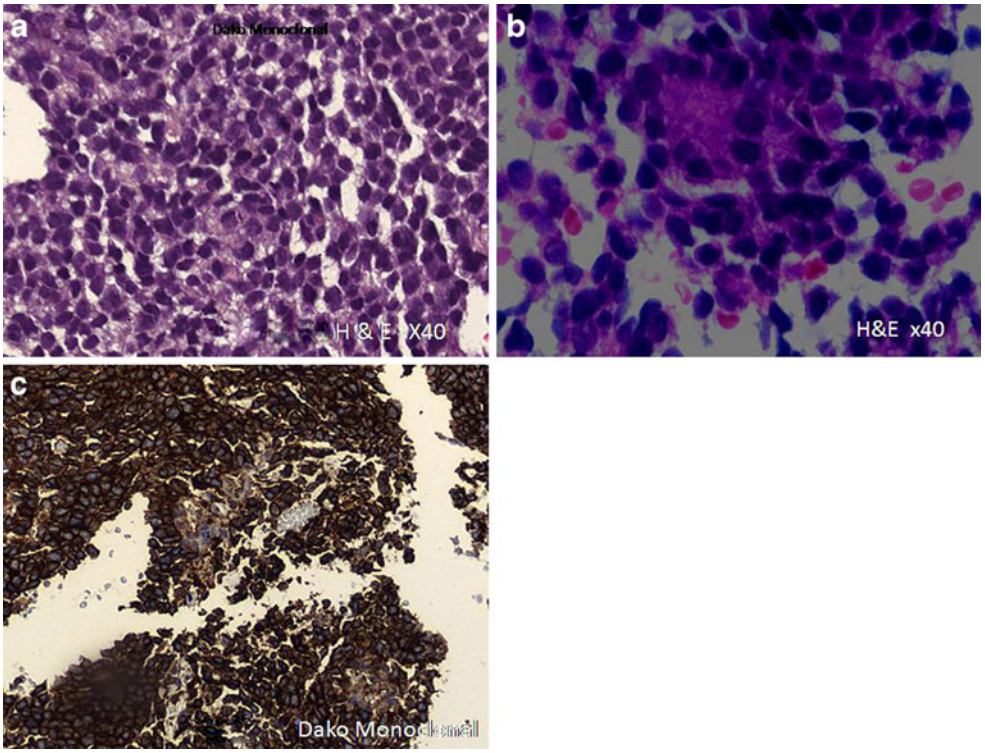

Fig. 3 **a** Showed the histological characteristic of PNETs with small round blue cells. **b** showed the Homer-Wright rosette formation which only present in about 10% of cases. **c** Is the Dako monoclonal immunohistochemistry which stained positive for CD 99

involving the lung with direct metastasis to the cardiac are extremely rare. To our knowledge, cardiac metastasis has only been reported twice [1, 2].

PNETs tumour is a distinctive form of ESFT. In our patient, it is differentiated by the presence of small round blue cell with neuroectodermic differentiation. The presence of Homer-Wright rosettes formation and CD 99 immunopositivity confirmed the diagnosis. CD 99 positivity is identified in nearly all patients with ESFT and constitutes an important immunostaining in diagnosing this tumour. However, Homer-Wright rosettes are found in only 10% of patients. This distinction is important as it carries a significant poorer prognosis in PNETs. The patient was also classified in the high risk group according to the EURO-Ewing-99 protocol. Other poor prognostic features in our patient include the presence of cardiac metastases and the extremely large tumour size (size >8 cm or volume >100 mL). The presence of the chromosomal aberration also carries a poor prognosis but it was not performed in this patient. In our patient, despite the absence of bone marrow metastasis, the overall prognosis remained poor at 10%–20% [6].

The patient was commenced on six cycles of chemotherapy which consist of the standard agents; vincristine, ifosfamide, doxorubicin, and etoposide. Despite regression of the tumour following the treatment, it was not amenable for curative surgery due to the close proximity to the heart. The tumour had grown quite rapidly again and occupied almost the whole thorax with re-accumulation of the pericardial effusion leading to the demise of the patient. Though, some authors have reported successful experimental treatment of metastatic PNET of the kidney with cytokine and autologous stem cell transplant in adjunct to chemotherapy and irradiation, these were not feasible for our patient [7].

In conclusion, primitive Neuroectodermal tumour is aggressive and usually lethal as happened to our patient. Though rare, it should be considered as a differential diagnosis in the young with thoracic mass. The diagnosis is rather difficult and relies on positivity to immunohistochemistry and cytogenetic analysis. The overall prognosis is extremely poor in patient with distant metastasis especially with bone marrow or myocardium involvement.

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