PERSISTENCE OF RED CELL APLASIA DESPITE TREATMENT OF MALIGNANT THYMOMA : A CASE REPORT

G K H Teoh, S L Tien

ABSTRACT

Pure cytopenias are well-recognised associations with malignant thymoma. We present a case of pure red-cell aplasia (PRCA) and malignant thymoma where the PRCA continued to persist despite computerised tomographic scan evidence of regression following radiotherapy and chemotherapy.

Keywords: *pure red-cell aplasia, thymoma.*

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INTRODUCTION

Persistence of red-cell aplasia (PRCA) is perhaps the best known pure cytopenia that is associated with malignant thymoma. In about 3% of patients with thymomas an associated PRCA can be found. In contrast, more than 50% of patients with PRCA demonstrate a thymoma. To the best of our knowledge, this is the first reported case of PRCA in malignant thymoma in Singapore.

PRCA is thought to have an immunological basis and may precede, coincide with or follow the development of the tumour. Recovery from erythropoiesis occurs, in most but not all cases, at variable time intervals after removal or eradication of the tumour. And rarely, spontaneous remission of PRCA occurs in the presence of the tumour[1].

CASE REPORT

A fifty-eight year old female Chinese hawker presented with persistent cough associated with mucoid sputum of four months' duration, fever, anorexia and significant weight loss. The Karnofsky score was 60%. Scattered fine crepitations were heard over both lung fields. The chest x-ray (CXR) revealed a right hilar mass (Fig 1) and computerised tomographic (CT) scan confirmed an irregular right middle lobe mass with bilateral hilar lymphadenopathy (Fig 2). Sputum specimens were repeatedly negative for acid-fast bacilli (AFB) and malignant cells. Three bronchoscopic examinations with bronchio-alveolar lavage (BAL), bronchial biopsy and transbronchial lung biopsy (TBLB) done over five months also failed to demonstrate the presence of tuberculosis or a tumour. An epithelial tumour, suggestive of a malignant thymoma, was found on the percutaneous lung biopsy. The patient refused an open lung biopsy.

The patient also suffered from recurrent episodes of rapid severe normochromic normocytic anaemia with haemoglobin (Hb) of about 6.0 g/dl not associated with any appreciable bleeding or haemolysis. In all episodes, the total white cell (TW) and platelet (Plt) counts remained normal and the patient

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Fig 1 - Chest x-ray at presentation showing a right hilar mass.

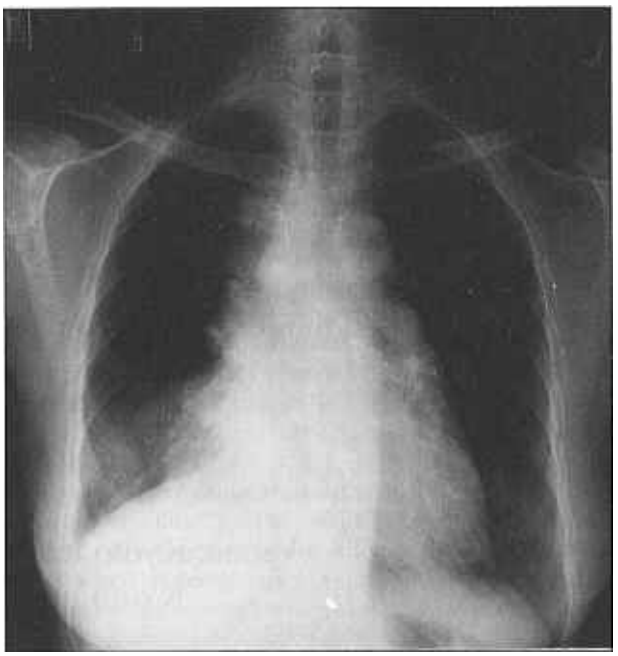
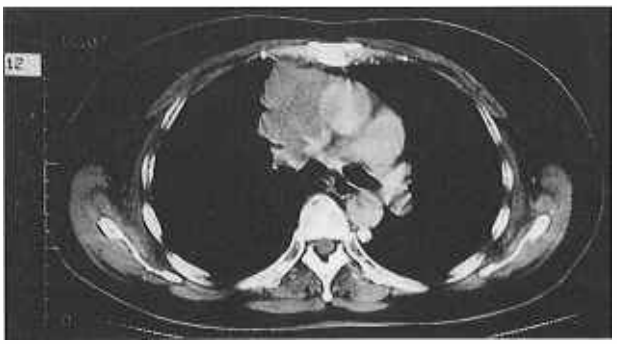


Fig 2 - CT scan thorax at presentation showing an irregular mass in the right middle lobe with bilateral hilar lymphadenopathy.



improved dramatically with red-cell transfusions. More than thirty units of red-cells were eventually transfused. Bone marrow examination showed virtual absence of erythropoiesis, increased granulopoiesis and normal megakaryopoiesis; consistent with pure red-cell aplasia. There was no clinical or electromyographic (EMG) evidence of myasthenia gravis. Anti-skeletal muscle antibodies and a collagen screen were

also negative.

The patient was treated with radiotherapy, corticosteroids and cyclophosphamide for three months with resolution of the mediastinal mass and lymphadenopathy. However, the red-cell aplasia persisted and required frequent transfusions and erythropoietin (EPO). She subsequently developed bronchiectasis and focal emphysema with severe pulmonary restriction from recurrent bronchopneumonia and previous radiotherapy. Eventually, she died from *Pseudomonas aeruginosa* bronchopneumonia and septicaemia. She survived 15 months from the beginning of her illness.

DISCUSSION

Malignant thymomas consist of two basic histological types – epithelial and lymphocytic, and sometimes occur as a mixed variety. Data from the M D Anderson Cancer Centre indicated that lymphocytic thymomas have a better prognosis.[2] However, extensive, invasive tumours[3] and a Karnofsky score of <70%[4] convey a poor prognosis. Our patient had an extensive epithelial tumour and a Karnofsky score of 60%, hence the prognosis was poor.

About 50-70% of thymomas are associated with myasthenia gravis and 5-10% with other immunological states, mostly hypogammaglobulinaemia (4%), PRCA (3%) and systemic lupus erythematosus (SLE)[5]. More than 10% are, however, asymptomatic.[6] The occurrence of myasthenia gravis is no longer considered an adverse factor[7,8] and may convey a better prognosis by allowing earlier detection of the thymoma. Conversely, the association with an immunological state conveys an adverse prognosis as they tend to occur in more advanced and invasive tumours[9]. Furthermore, the associated cytopenias are usually resistant to most forms of therapy. Our patient did not have myasthenia gravis but presented with a fairly large mediastinal mass and PRCA, which are additional poor prognostic factors.

Although long-term survival, up to nineteen years, have been reported in a thymoma with PRCA treated with EPO[10], extremely high doses would have to be administered daily, at a considerable cost to the patient. The doses of EPO that were given to this patient were in comparison very small and might not have influenced her survival.

PRCA is not the only pure cytopenia associated with thymoma; in fact, any individual cell line can be immunologically attacked. In a recent case report by Mathieson, a pure neutrophil aplasia was found in a patient with myasthenia gravis and thymoma.[11] An immunological basis was supported by demonstration of an IgG fraction of serum, taken before immunosuppressive therapy was commenced, that was able to suppress the growth of granulocyte/mononuclear cell progenitors (CFU-GM) both in autologous "remission" marrow as well as allogeneic marrow. Further support of an immunological mechanism was seen in full neutrophil recovery following immunosuppressive therapy which included azathioprine.

Thymomas can also be associated with multilineage cytopenias.[12] In another recent case report, Murase described a patient who demonstrated complement-dependent IgG inhibitor(s) to granulocyte-macrophage and erythroid lineages producing the respective cytopenias.

Although surgery, radiotherapy, cyclophosphamide and corticosteroids have been the main modes of therapy for thymomas, combination chemotherapy has recently been shown to produce reasonable success. Combinations of cisplatin, doxorubicin, cyclophosphamide with or without vincristine have achieved responses in 70-90% of cases with 15-45% complete remissions[13-15]. Finally, total body irradiation may also be used in cases with resistant myasthenia gravis.[16] Our patient refused surgery and was managed with radiotherapy, cyclophosphamide and corticosteroids with eventual resolution of the mass. Her PRCA was, however, resistant to treatment and she developed pulmonary fibrosis and bronchiectasis secondary to radiotherapy and recurrent bronchopneumonia. She died 15 months after presentation from *Pseudomonas aeruginosa* bronchopneumonia and septicaemia while on antibiotics and immunosuppressive therapy.

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