

Case Report

Pure Red Cell Aplasia Following Thymothymectomy: A Case Report

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Abstract

Thymoma, a rare epithelial neoplasm, is the most common anterior-superior mediastinal tumour. Thymoma can occur sporadically or in association with other conditions, such as myasthenia gravis, pure red cell aplasia (PRCA), and hypogammaglobulinemia. Only 5% of thymoma cases develop PRCA; however, 10–50% of patients presenting with PRCA have an associated spindle cell type thymoma. Thymoma complicated by PRCA is associated with a poor outcome. We report the case of a 38-year-old female who presented with chest pain, and was diagnosed with an anterior mediastinal mass. A thymectomy was performed, and histopathological examination revealed mixed thymoma; two months later, the patient developed PRCA. The present case reinforces the need for clinicians to be vigilant with thymoma patients, even following thymectomy.

Keywords: erythropoiesis, mediastinum, pure red cell aplasia, thymoma

Introduction

Thymoma, a rare epithelial neoplasm, is the most common anterior-superior mediastinal tumour. Based on the appearance of neoplastic epithelial cells, the World Health Organization (WHO) has classified thymoma as type A (spindle or oval cells), type B (dendritic or epithelioid cells), and type C (exhibiting combined features of types A and B). Thymoma can occur sporadically or in association with other conditions, such as myasthenia gravis, pure red cell aplasia (PRCA), and hypogammaglobulinemia (1). Only 5% of thymoma cases develop PRCA. However, 10–50% of patients presenting with PRCA have an associated spindle cell type thymoma (2). PRCA is characterised by failure of erythropoiesis, with preserved granulopoiesis and megakaryopoiesis (3). Thymoma complicated by PRCA is associated with a poor outcome, and thymectomy provides a low PRCA remission rate in such patients. Hence, possible onset of PRCA should be anticipated, and close follow-up of these patients is recommended (3,4). The patient in this case initially presented with thymoma and PRCA post-thymectomy.

Case Report

A 38-year-old female who presented with left-sided chest pain and cough of three months duration had a history of thyroidectomy for Hashimoto's thyroiditis five years prior.

Computerized Tomography (CT) scan revealed a large, encapsulated, well-defined, heterogeneously enhancing lesion in the left side of the anterior mediastinum with preserved fat planes. Laboratory investigations showed the following; haemoglobin 9.3 gm%, haematocrit 27.8%, total leucocyte count 10 400/cu mm, and platelet count 319 000/cu mm. Exploratory left thoracotomy disclosed a large anterior mediastinal lobulated mass with cystic and nodular areas. A thymectomy was performed, along with excision of the mass. Pathological examination revealed a nodular tissue mass weighing 232 gm and measuring 11 × 6 × 4 cm. A cut section showed vaguely lobular, tan-grey to white areas, separated by fibrous bands. Microscopy revealed ill-defined, angulated islands, and lobules composed of a two cell component. The predominant, Type B areas consisted of small lymphocytes with scant cytoplasm and coarse chromatin. The other population consisted of lymphocyte poor Type A areas with interlacing fascicles and nests of epithelial cells with vesicular nuclei surrounded by thick, fibrous septum-containing vessels (Figure 1). The capsule was free. Immunohistochemistry revealed that the epithelial cells showed CK positivity, with the lymphoid component being CD3 positive. These features were consistent with thymoma type AB. Two months following surgery, the patient presented with progressively increasing fatigability, exertional breathlessness,

palpitations, giddiness, and repeated episodes of transient syncope. Physical examination revealed severe pallor, bilateral pitting oedema, and facial puffiness. Laboratory investigations showed haemoglobin 2.8 gm/dL, haematocrit 7.8%, normal total leucocyte count, and increased platelet count. Microcytic hypochromic anaemia was diagnosed on a peripheral smear. Bone marrow examination showed marked paucity of erythroid elements, with predominance of myelopoiesis and normal megakaryopoiesis (Figures 2,3). Bone marrow iron stores were markedly increased. These features prompted a diagnosis of PRCA. The patient was treated with blood transfusion and steroids, following which her condition improved and her haemoglobin rose to 5.4 gm/dL. The patient was discharged. One year later, she presented with increased fatigability, exertional breathlessness, pedal oedema, cough, and reduced urinary output. Her haemoglobin was 10.5 gm/dL. The patient was diagnosed to have tricuspid regurgitation and was started on digoxin and sildenafil. She had also developed oral candidiasis and urinary tract infection, for which she was treated appropriately. Due to repeated blood transfusions, the patient had elevated serum ferritin levels, for which she was started on iron chelation therapy. Her condition improved and she was discharged.

Discussion

The presented case of thymoma type AB, with a history of Hashimoto's thyroiditis, developed PRCA two months following thymectomy. Thymoma is associated with various haematological disorders, such as PRCA, erythrocytosis, pancytopenia, megakaryocytopenia, T cell lymphocytosis, acute leukaemia, and multiple myeloma (2). PRCA associated with thymoma has an immunological basis that includes humoral suppression of erythropoiesis by antibodies against erythropoietin and erythroblasts, as well as cell-mediated suppression of erythropoiesis (1). This basis was re-emphasised in the present case, as the patient had a history of Hashimoto's thyroiditis, an autoimmune disease of the thyroid. The most common histological type of thymoma associated with PRCA is spindle cell type (2). In a study by Masaoka et al., all of their 17 cases of PRCA associated with thymoma were spindle cell type and stage 1 (5). Murakawa reported three cases each of spindle cell and round-oval cell morphology. All cases with spindle cell morphology were stage 1. Of the three cases

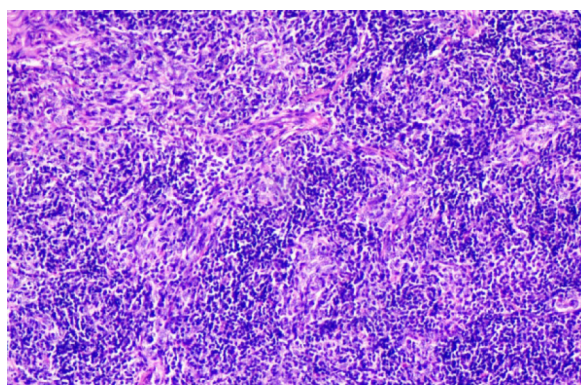


Figure 1: Mixed thymoma. Pre-dominantly type B areas showing small lymphocytes, along with lymphocyte-poor type A areas with interlacing fascicles and nests of epithelial cells (haematoxylin and eosin, 10× magnification).

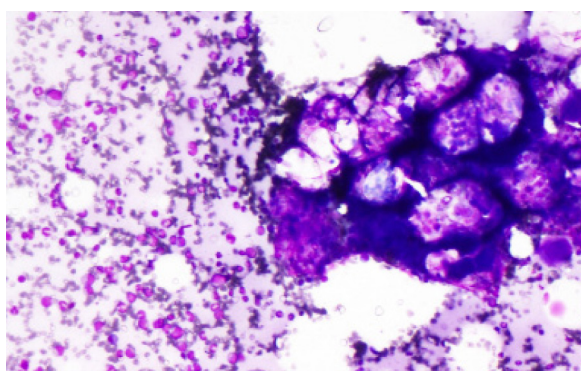


Figure 2: Pure red cell aplasia. Bone marrow aspirate showing cellular marrow particles with paucity of erythroid cells (Leishman's stain, 20× magnification).

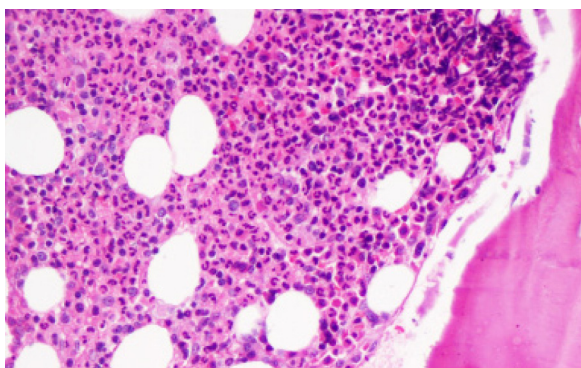


Figure 3: Pure red cell aplasia. Trephine biopsy showing cellular marrow spaces with paucity of erythroid cells haematoxylin and eosin, 20× magnification).

with round-oval cells, two were stage IVa and one was stage III (4). The present case was different in that it was a mixed type of thymoma, showing both spindle and oval cells, and it was encapsulated, hence classified as stage I. The patient developed PRCA two months after the thymectomy. Patients with thymomas complicated by PRCA are known to have a poor outcome, comparable to advanced stage thymomas.

In the study by Murakawa et al., three patients developed PRCA following thymectomy: within one year in two patients and after eight years in one patient. Five of the six patients in the study also received immunosuppressive therapy for PRCA. However, four died due to complications associated with PRCA (4). The present case developed PRCA in spite of the thymectomy, perhaps indicating the presence of residual thymic tissue. PRCA associated with thymoma is known to have a poor prognosis; hence, adequate and early treatment is essential for improving survival rates in such patients. It has been proven that complete surgical resection of all the thymic tissue by extended or maximal thymectomy is essential in the treatment of thymomas associated with autoimmune diseases. This is explained by the close correlation of the presence of thymic tissue and the development of PRCA (4). Additional immunosuppressive medications, such as long-term use of corticosteroids, cyclosporine, and ATG are useful in controlling PRCA associated with thymomas (2,3). Our patient was started on long-term prednisolone, following which she attained remission; however, she developed opportunistic infections, which is a known complication in such patients.

Conclusion

To summarise, the present case is rare in that it was a mixed thymoma associated with PRCA. Nonetheless, the case emphasises the importance of complete removal of all thymic tissue, as well as additional immunosuppressive therapy for maximal treatment of PRCA-associated thymomas. It reinforces the need for clinicians to be vigilant with patients with thymoma, even following thymectomy, as PRCA can develop in these patients. Hence, close follow-up is recommended.

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Conflict of Interest

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Authors' Contributions

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Drafting of the article, collection and assembly of data: BN

Critical revision of the article for the important intellectual content and final approval of the article: ACKR, CM

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