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Management of Thymoma Associated Pure Red Cell Aplasia - Case Seires

Mariappan[1], S. Mughilan[2], Satish Lakshman[3]

[1]Institute of Cardiovascular and Thoracic Surgery, Madras Medical College, Chennai - 600003, India
Email: *mariapsbalaiah[at]gmail.com*

[2]Institute of Cardiovascular and Thoracic Surgery, Madras Medical College, Chennai - 600003, India
Email: *mughijeeva[at]gmail, com*

[3]Institute of Cardiovascular and Thoracic Surgery, Madras Medical College, Chennai - 600003, India
Email: *satishlakshman3[at]gmail.com*

Abstract: ***Pure red cell aplasia (PRCA) is a rare hematological complication associated with thymoma. Remission of PRCA occurs after thymectomy in most of the cases but it can persist or reoccur even after thymectomy in some. This case series present 3 cases of thymoma associated pure red cell aplasia, their diagnosis and treatment course. All three patients underwent surgical excision, two of them showed complete remission of aplasia after surgery and third case, anaemia did not resolve after surgery and was put on medication for same.***

Keywords: Thymoma, Thymectomy, Pure red cell aplasia, Anemia

1. Introduction

Thymomas and thymic carcinomas are the most prevalent types of anterior mediastinum masses. Thymoma - associated PRCA, the presence of the thymoma disrupts normal blood cell production, specifically affecting the production of red blood cells. The exact mechanism by which thymomas cause PRCA is not fully understood, but it is believed to involve autoimmune processes, where the body's immune system mistakenly attacks and destroys its own red blood cell precursors in the bone marrow.

Patients with thymoma - associated PRCA may experience symptoms of anemia, such as fatigue, weakness, and pallor, due to a deficiency of red blood cells. Treatment options typically involve addressing both the thymoma and the anemia.

Thymomas are usually treated with surgery to remove the tumor, and additional treatments such as chemotherapy, radiation therapy, or immunosuppressive therapy may be considered depending on the specific case. Anemia may be managed with blood transfusions and medications to stimulate red blood cell production.

It's important for individuals diagnosed with thymoma - associated PRCA to work closely with their healthcare providers, including hematologists and oncologists, to develop a tailored treatment plan based on the severity of the condition and individual factors.

Histopathologically WHO has classifies thymoma inType A, B1, B2, AB.
Type A composed of bland spindle cells and scattered lymphocytes
Type B1 composed of predominantly lymphocytes with scattered epithelial cells
Type B2 composed of mostly epithelial cells forming clusters
Type AB is a mixture of type A and types B1 or B2.

Many paraneoplastic syndromes are associated with thymoma, one among them is Pure red cell aplasia. Thymoma associated PRCA is a rare scenario. Here we are presenting a case series of three cases with Thymoma associated PRCA.

2. Case Series

Case 1
A 64 year old male presented with symptoms of severe anemia, experiencing pallor, dyspnea, weariness and palpitation during physical activity, which had been worsening recently. His blood investigation showed initial Hb level 5.4 g/dl and red blood cell [RBC] count 1.89 × 10^6/µL.

Peripheral smear showed Normocytic normochromic anemia. Patient had a history of packed red blood cell [PRBC] transfusion. Bone marrow aspiration showed cellular marrow with markedly reduced erythroid precursors with adequate myeloid and megakaryocyte lineage and increased eosinophillic precursors favoring the diagnosis of pure red cell aplasia. Acetyl choline receptor antibodies [AchR] were tested to rule out myasthenia gravis.

CT chest showed well defined anterior mediastinum mass measuring 4.3 [AP] ×4 [Tr] × 4.6 [CS], [Figure 1]. To further confirm CT guided mediastinal mass biopsy was done. The diagnosis of thymoma was made and then the patient was planned for thymectomy. He underwent median sternotomy and thymectomy. All margins of resected mass were free from tumor infestation. Histological examination revealed thymoma type A and pathologic classification P T_1 N_X M_X.

Patient aplasia completely remitted after surgery and he did not require any adjuvant therapy.10 month follow - up of patient shows patient doing fine without medication.

Case 2
An 80 year old female referred to the hospital for progressive fatigue and symptoms of anemia. Her complete blood count revealed Hb - 6.3 g/dl with RBC count 2.21 × 10^6/µl.

Her peripheral blood film showed normocytic normochromic anaemia with reticulocytopenia and absent of erythroblast. CT chest showed anterior mediastinal mass. Thymectomy procedure was performed for this patient. The diagnosis was confirmed by histopathological analysis and it showed thymoma type B1. [Figure 2] Aplasia remitted after the surgical excision. Patient was followed for 6 month after surgery and her hemoglobin level were stable.

Case 3
A 30 year old male referred for treatment of thymoma discovered accidently on Chest X - Ray showed anterior mediastinal mass protruding to left. On blood examination his Hb 3.6 g/dl and reticulocyte count at 6.2 × 10^3/µl low. Other investigations of blood were normal. He had normal B12/Folate/Iron levels. His peripheral blood smear shows normocytic normochromic anemia. Bone marrow trephine biopsy confirmed the diagnosis of pure red cell aplasia. Biopsy showed markedly hypocellular marrow with marked reduction of erythropoeisis. CT chest showed anterior mediastinal mass.

Patient underwent transsternal thymectomy. The diagnosis was confirmed by histopathological analysis. The anemia did not resolve after surgery. Patient was put on cyclosporine 150mg BD, we followed up on this patient for 1 year and his hemoglobin level constantly improved to 11g/dl.

3. Discussion

Thymomas and thymic carcinomas develop in the anterior mediastinum from thymic epithelial cells of Thymus. The thymus is essential for the adaptive immune system's development. [1] Thymomas frequently exhibit histologic heterogeneity, it is difficult to distinguish between benign and malignant thymomas based only on their clinical course; nonetheless, malignant thymomas are significantly more invasive than their benign counterparts. [2]

The link between thymomas and numerous paraneoplastic diseases is well known, with myasthenia gravis (MG) being the most frequent and there are many more syndromes, including PRCA, that have been linked to thymoma. [3]

According to literature the percentage of patient with thymoma goes on to develop PRCA varies, few literature says up to 5%, [4] few of them reported less than 10%. [3]

Thymomas are thought to play a role in the development of Red Cell Aplasia due to their association with autoimmune mechanisms. The thymus gland plays a role in the development and maturation of T - cells, which regulate the immune system. A malfunction in this process can lead to the generation of autoantibodies that attack and destroy red blood cell precursors in the bone marrow, causing Red Cell Aplasia.

Serum thymic factor, which is generated by thymoma, is thought to be the cause of PRCA in thymomas. Serum thymic factor may produce suppressor T cells which inhibit erythroid precursor's results in Red cell aplasia. There are further proposed pathways, including thymic IgG synthesis that produces cytotoxic or inhibitory cytokines that prevent the establishment of erythroid colonies. [3, 5, 6]

Patient of thymoma with red cell aplasia may present with symptoms of anemia, such as fatigue, weakness, and pallor. Other symptoms related to thymoma, such as chest pain, cough, or difficulty breathing, might also be present. [7]

Diagnosis involves a combination of imaging studies such as CT scans to assess the thymoma and blood tests and bone more biopsy to confirm Red Cell Aplasia. Blood profile showing isolated anemia with absent reticulocytes and Bone marrow biopsy showing marked reduction in erythroid precursors is confirmation of pure red cell aplasia [3]

Unfortunately, there are no set treatment protocols since PRCA in conjunction with thymoma is extremely uncommon. The complete surgical resection of the thymoma is often first line of treatment. [7] However, the approach and extent of surgery can vary based on the size, location, and extent of the tumor.

After thymoma removal, some patients have complete remission of PRCA and resume normal hematopoiesis, as seen by the case 1 and 2 described here. According to reports, removing the thymoma results in PRCA remission in 25% to 30% of cases [3, 8], more recent series suggest that this is actually a rare occurrence and that the majority of patients will need additional treatment described here in third case. [9]

In one case study, out of 6 patients with thymoma associated with PRCA, only 2 experienced full remission; interestingly, both had undergone entire thymus and thymoma excision with prolonged thymectomy, whereas the other 4 patients had not. [10]

Jacobs et al. conducted a literature review and discovered 26 instances of PRCA linked to thymoma. Thymectomies were done on 16 of the 26 individuals with thymoma with PRCA. Following surgery, four patients (or 29%) experienced complete remission. following thymectomy, two patients exhibited modest improvement, and they were completely cured following splenectomy, adrenocorticotropic hormone (ACTH), and other procedures. Before any of these 2 procedures, either a thymectomy or a splenectomy, ACTH had little to no impact. [11]

In the case series present here, out of 3 cases, 2 had complete remission of anemia after surgical resection, but the case has been followed for 6 - 8 months, long term follow up is needed to reach the conclusion.

Medical management includes immunosuppressive therapy consist of steroids, cyclosporine, cyclophosphamide, ATG and octreotide. [3, 8, 9], among all cyclosporine considered the best. [lung cancer elseiver 2021] Same treatment was being used in case number 3.

One such case reported by ramesh thangatorai, where the case was inoperable and patient was given Tab. cyclosporine 150 mg BD (5 mg/kg/day), 6 month follow up showed persistant improvement in haemoglobin level [6]

In case number 3 which was followed for 8 months showed constant improvement in blood profile, long term follow up of these patient is required.

Reported cases have shown, complications to PRCA adjunct therapy is most common cause of death among these patient, especially infections secondary to immunosuppressive therapy [7] Hence careful followup of the patient is mandatory.

4. Conclusion

Thymectomy seems to be the best possible treatment for thymoma associated with PRCA. However, not all the documented cases show complete remission of aplasia with surgical resection. Immunomodulatory medication should be tried with steroids or cyclosporin if PRCA continues following thymectomy. It is important to monitor these patients for possibility of infectious consequences.

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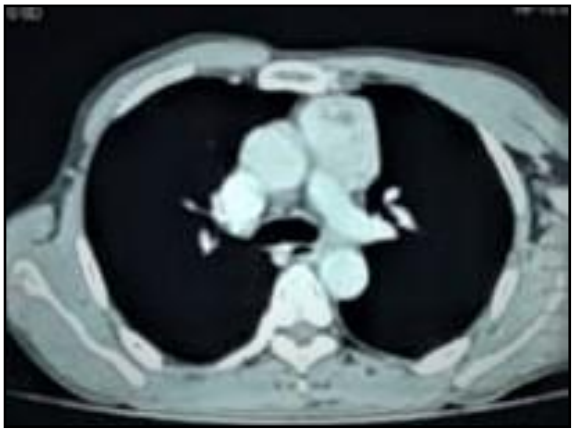

Figure 1: CT chest showing mass in anterior mediastinum

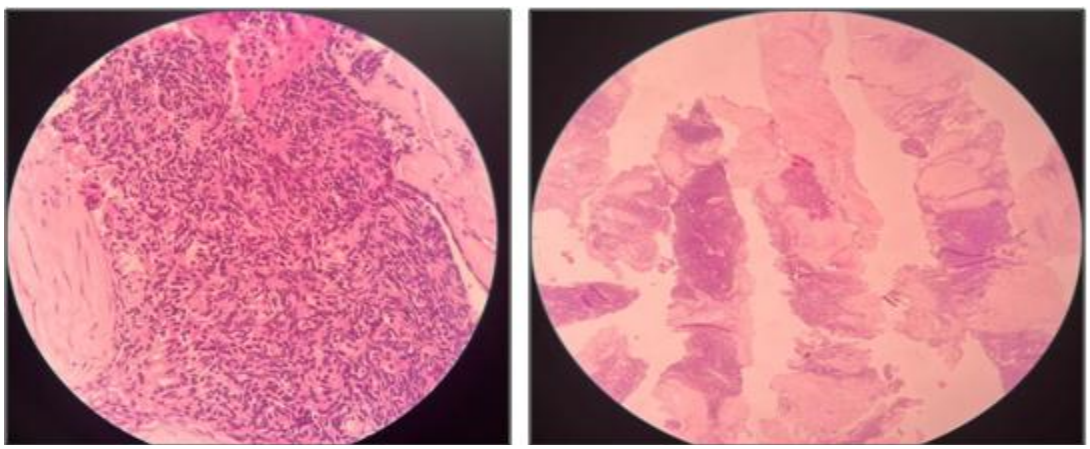

Figure 2: Histopathological examinations shows Thymoma type B1 with predominant lymphocytes

Author Profile

Mariappan is Professor and Director, Institute of Cardiovascular and Thoracic Surgery, Madras Medical College, Chennai - 600003, India
mariapsbalaiah[at]gmail.com

Satish Lakshman, M. B. B. S., M. S., Resident Mch CTVS, Institute of Cardiovascular and Thoracic Surgery, Madras Medical College, Chennai - 600003, India
satishlakshman3[at]gmail.com