Pure Red Cell Aplasia Associated With Thymolipoma in a Patient With Myasthenia Gravis: A Case Report

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ABSTRACT

Introduction Pure red cell aplasia (PRCA) is defined as anemia in the presence of severe reticulocytopenia and absent or markedly decreased erythroid precursors in the marrow. When associated with another disease entity, it is classified as secondary acquired PRCA. A rare entity, thymolipoma, which constitutes 2% to 9% of thymic tumors has been associated with PRCA in some studies. The prevalence of thymolipoma among patients with myasthenia gravis reaches 43.8%. This paper presents the rare presentation of myasthenia gravis associated with thymolipoma and PRCA.

Case We present the case of a 64-year-old female who was diagnosed with myasthenia gravis and has been on maintenance pyridostigmine (Mestinon) for 12 years. She presented with symptoms of anemia and became transfusion requiring. Routine chest CT showed a thymic mass which was confirmed to be a thymolipoma during biopsy. Bone marrow studies confirmed the absence of erythroids, hence the diagnosis of secondary acquired PRCA.

Discussion There have been case reports associating PRCA with thymolipomas. Thymolipomas, which constitute 2% to 9% of thymic tumors are found among patients with myasthenia gravis, but the majority remains asymptomatic despite increasing tumor size. PRCA with associated thymic mass shows improvement of symptoms with tumor removal and immunosuppression. Oral corticosteroids result in a response rate of 39% while cyclosporine results in 77% response. This can be tapered off once response has been achieved.

Conclusion This case report emphasizes the importance of early bone marrow studies among patients with myasthenia gravis presenting with sudden onset anemia.

Keywords pure red cell aplasia, myasthenia gravis, thymolipoma.

INTRODUCTION

Pure red cell aplasia (PRCA) is defined as anemia in the presence of severe reticulocytopenia and absent or markedly decreased erythroid precursors in the marrow. When associated with another disease entity, it is classified as secondary acquired PRCA. [1] A rare entity, thymolipoma, which constitutes 2% to 9% of thymic tumors has been associated with PRCA in some studies.[2,3] A thymolipoma is a benign tumor of the thymus composed of thymic and adipose tissues.[2,3] The prevalence of thymolipoma among patients with myasthenia gravis reached 43.8%.[2-4]

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We present the case of a 64-year-old female who was diagnosed with myasthenia gravis and has been on maintenance pyridostigmine (Mestinon) for 12 years. She presented with symptoms of anemia and became transfusion requiring. Routine chest CT showed a thymic mass which was confirmed to be a thymolipoma during biopsy. Bone marrow studies confirmed the absence of erythroids, hence was diagnosed with secondary acquired PRCA.

There have been three other case reports on thymolipoma associated with red cell aplasia, two of which were treated with immunosuppression, and one case claimed improvement of hemoglobin levels with thymectomy alone.[5-8]

CASE REPORT

Case: This is the case of a 64-year-old female who was diagnosed with myasthenia gravis last 2015 after presenting with dysarthria. She was started on pyridostigmine (Mestinon) and has been apparently well since then. Around 6 weeks prior to admission, she started complaining of exertional dyspnea on leveled ground and loss of appetite. She had complaints of dysphagia and eventual weight loss. She sought a consult after 3 weeks of enduring her symptoms. Her laboratory workup showed anemia of 29 g/L with thrombocytosis of 412,000/uL. Leukocyte count and differentials were within normal range. She was admitted for blood transfusion. Iron studies revealed elevated ferritin levels at 1,530 ng/mL. A CT scan of the chest revealed an incidental finding of thymoma. She was discharged thereafter with improved symptoms.

Follow-up with her attending physician after 3 weeks showed anemia of 77 g/L on repeat CBC with thrombocytosis of 436,000/uL. She was then referred to hematology service. Reticulocytopenia of 0.1% was noted during added work-up.

Diagnosis: In the setting of the patient's persistent anemia, concomitant thymoma and an underlying disease process of myasthenia gravis, PRCA was a primary consideration. A bone marrow biopsy was done, which showed a moderately hypocellular bone marrow (10-15% cellularity) with marked erythroid hypoplasia/aplasia, intact granulopoiesis and adequate megakaryocytes, findings of which are consistent with PRCA.

She underwent video-assisted thoracic surgery (VATS) extended thymectomy with biopsy microsections showing small islands of thymic tissue surrounded by abundant mature adipose tissue consistent with a thymolipoma.

A final diagnosis of secondary acquired PRCA associated with thymolipoma and myasthenia gravis was made.

Cyclosporine 100 mg twice daily was started and the patient was eventually discharged. After 2 months of follow-up, the patient was able to maintain hemoglobin levels at 11.7 g/L and achieved reticulocyte count of 8%.

DISCUSSION

PRCA is defined as anemia in the presence of severe reticulocytopenia and absent or markedly decreased erythroid precursors in the marrow. It can be classified as either congenital, which results from genetic mutations for various ribosomal proteins, or acquired. On the one hand, primary acquired PRCA is autoimmune in nature and results from antibody-mediated mechanisms, while secondary acquired PRCA on the other hand is associated with lymphoproliferative, hematologic malignancies and non-hematologic neoplasms such as thymomas. Reticulocyte percentage is always <1%. Diagnosis can be confirmed by establishing absence or near absence of erythroblasts from an otherwise normal marrow.[1] In this case, our patient presented with new onset anemia and reticulocytopenia. Her background diagnosis of myasthenia gravis for 12 years with a thymic mass on routine imaging increased suspicion of PRCA. Bone marrow studies established a diagnosis of secondary acquired PRCA.

Thymomas are malignant epithelial tumors of the thymus. It is a disorder with the strongest historical association with PRCA. Recent studies suggest that PRCA occurs in <5% of thymoma cases.[1,9] A much rarer entity, thymolipoma, a benign tumor of the thymus composed of thymic and adipose tissues have also been reported to be associated with PRCA in some studies. Thymolipomas constitute 2% to 9% of thymic tumors and an incidence rate of 0.12/100,000 individuals in a year. These are encapsulated and slow growing, which may explain why up to 50% of patients with thymolipomas remain asymptomatic until incidentally discovered in imaging studies.[2,3] The prevalence of thymolipoma among patients with myasthenia gravis reached 43.8%. The

exact pathogenesis is still unknown, but autoimmune stimulation of myoid cells is believed to be a cause. Steroid therapy has also been associated with the development of thymolipoma by causing fatty degeneration of thymomas allowing transformation into thymolipomas.[2-4]

PRCA with an associated thymic mass shows improvement of symptoms with tumor removal.[10] Optimal treatment recommendation for thymolipoma is thymectomy using open surgical techniques or minimally invasive techniques such as video-assisted thoracoscopic surgery (VATS). Once resected, thymolipomas do not recur and have higher rates of stable remission compared to thymoma.[2]

Treatment of secondary acquired PRCA requires management of the underlying disorder, otherwise, immunosuppression is recommended. Traditional immunosuppression makes use of oral corticosteroids (prednisone 1 mg/kg) with a response rate of 39%. Recent data emphasizes the efficacy of cyclosporine in PRCA which results in 77% response. Cyclosporine is a calcineurin inhibitor which inhibits the synthesis of interleukin 2 essential for the self-activation of T-lymphocytes and their differentiation. This drug results in a reversible inhibition of immunocompetent lymphocytes in the G0 and G1 phase of the cell cycle.[11] A starting dose of 6 mg/kg can be used sometimes in association with prednisone 30 mg daily. Trough levels are targeted to be within 150-250 ng/mL. These can be tapered off once response has been achieved.

There have been three other case reports on thymolipoma associated with red cell aplasia. The first report was a 73-year-old man with Klinefelter syndrome, second was an individual with lichen planus and the third was of a 42-year-old patient with chronic lymphocytic leukemia. The first claimed improvement of hemoglobin levels with thymectomy alone while the latter two cases were given immunosuppression. [5-7] After thorough literature search, there were no case reports on patients with myasthenia gravis and thymolipoma presenting with PRCA.

CONCLUSION

This case report emphasizes the importance of early bone marrow studies among patients with myasthenia gravis presenting with sudden onset anemia. Disease entities such as PRCA and thymolipoma should be considered despite its rarity. Incidence rates may not be reflective of the actual number of cases. Diagnostic work-up through bone marrow studies and documentation through case reports are recommended. Treatment options are readily available and response is good with initiation of immunosuppression and tumor removal, hence early therapy is ideal.

ETHICAL CONSIDERATIONS

This report was written in compliance to the following local and international ethical guidelines for research ethics: Declaration of Helsinki 2015, International Conference on Harmonization on Good Clinical Practice (ICH-GCP), Council for International Organizations for Medical Sciences 2016, Good Research Practice (GRP), Philippine National Ethical Guidelines for Health and Health-Related Research of 2017, Philippine Data Privacy Act of 2012 and its Implementing Rules and Regulations (IRR) of 2016.

Conflict of Interest

There was no external funding used in this study. The authors declare that they have no conflict of interest regarding the publication of this paper.

Informed Consent Process

Informed consent was obtained from the patient's son who is a Doctor of Medicine. He has a competent grasp of English language; hence the informed consent form written in Tagalog was no longer used. The contents of the consent form was explained in detail and the patient was allowed ample time to make his decision. Consent was voluntarily signed by the patient's son himself, together with a witness and the principal investigator.

Risks and Benefits

The patient and her family did not directly benefit from participating in this case report. The patient will not be compensated for participating in this report. The information that can be shared with other health care professionals, however, may improve the care that is received by others with the same case in the future. There is no untoward effect expected from participating in this case report.

Data Privacy and Confidentiality

Identifying descriptors were removed from the manuscript to preserve the patient's right to privacy. There is however still a limited risk of losing confidentiality by virtue of the uniqueness of the case. The patient's chart, consent forms and result printouts that contain personal identifying information are stored securely in locked file cabinets when not in use and are handled only by the investigators. All electronic data is stored in private computers that require password access. The data will be kept for three years for verification and publication purposes, and then physical copies of data will be destroyed via paper shredder, while electronic files will be permanently deleted.

Vulnerability

Informed consent was obtained from the patient. She was not forced to provide information for this case report. There is no expected untoward effect from participating in the conduction of this case report.

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