

Acquired amegakaryocytic thrombocytopenic purpura - An underdiagnosed entity

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Received: 26-05-2015

Revised: 12-06-2015

Accepted: 23-06-2015

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ABSTRACT

Acquired Amegakaryocytic Thrombocytopenic Purpura (AATP) is a rare cause of thrombocytopenia presenting over a wide age group with symptoms of bleeding and bone marrow showing isolated absence of megakaryocytes in an otherwise normal marrow. Here, we report a case of AATP in a three year old female child who was then treated with anti thymocyte globulin successfully. We report this case because of it's under diagnosis or misdiagnosis as immune thrombocytopenia (ITP) in most of the cases. We also review the literature regarding the pathogenesis and treatment of this undiagnosed entity.

Key Words: Amegakaryocytic thrombocytopenia, misdiagnosis, anti thymocyte globulin, rare, bone marrow

Introduction

Acquired Amegakaryocytic Thrombocytopenic Purpura (AATP) is a rare cause of thrombocytopenia associated with decreased or absent megakaryocytes in otherwise normal bone marrow.^[1] The incidence and prevalence of this disease is unknown as most of the cases are under diagnosed or misdiagnosed as immune thrombocytopenia (ITP) since it is the most common cause of thrombocytopenia in this age group. Herein, we present a case of AATP in a three year old female child which was first treated as immune thrombocytopenia and later diagnosed and treated for AATP.

Case Report

A three year old female presented with history of fever on and off since one week,

bleeding from nose and redness of eyes since four days. On examination she had multiple petechiae all over the body and sub conjunctival hemorrhage. Per abdomen was normal without organomegaly. A complete blood count (CBC) and a peripheral smear examination were done as a routine investigation. CBC showed Hemoglobin- 10.6 gm%, Total leucocyte count-15,500, total platelet count-7,000. Mean corpuscular Volume (MCV)-73.7 fl, Mean Corpuscular Hemoglobin (MCH)- 23.0pg, Mean corpuscular hemoglobin concentration (MCHC)-31.1%, Differential count showed Neutrophil-75%, Lymphocyte-19.8%, Monocyte-2.1%, Eosinophil-1.7%, Basophil-0.5%. Reticulocyte count-3.00%. The CBC findings were correlated with a direct peripheral smear examination which also showed a

decrease in platelet count with normal size and morphology and absence of clumps. Neutrophils showed toxic granules and vacuolations with shift to left. [Fig. 1] A peripheral smear diagnosis of microcytic hypochromic anemia with thrombocytopenia and evidence of infection was made and bone marrow study was advised. In the mean time the child was started with methyl prednisolone considering a diagnosis of ITP but the child did not show any response with it. So, bone marrow aspiration along with biopsy was done. Bone marrow aspiration showed hypercellular marrow particles with increased cellularity. Erythropoiesis is accelerated with micro normoblastic pattern. Myelopoiesis was accelerated. Megakaryopoiesis was suppressed with absence of megakaryocytes after multiple smear study. Lymphocytes and plasma cell were normal in number. No metastatic deposit or leukemia was identified. [Fig. 2,3] Hence, a diagnosis of acquired amegakaryocytic thrombocytopenic purpura with associated iron deficiency and superadded infection was made and the same was confirmed by biopsy. [Fig. 4]

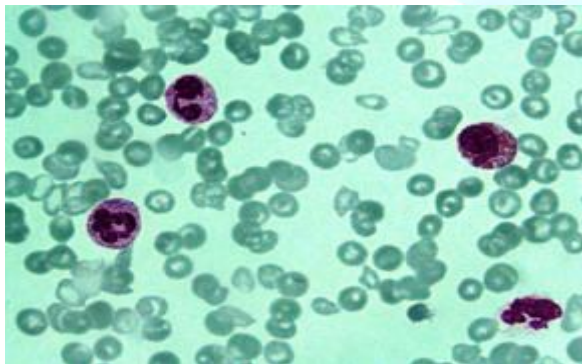


Fig. 1 Peripheral smear showing neutrophilic toxic granules and reduced platelet count. Leishmann Stain (x400X)

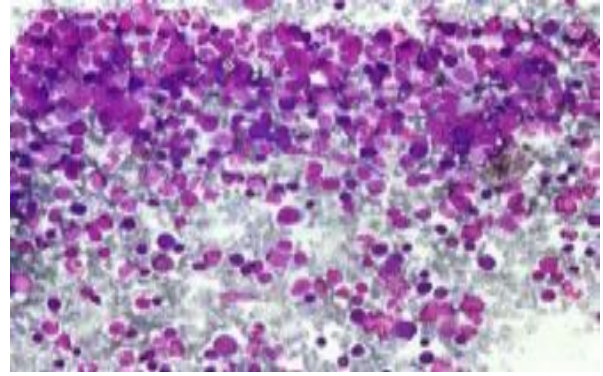


Fig. 2 Bone marrow aspiration showing accelerated erythropoiesis and myelopoiesis and absence of megakaryocytes. Leishmann Stain (x400X)

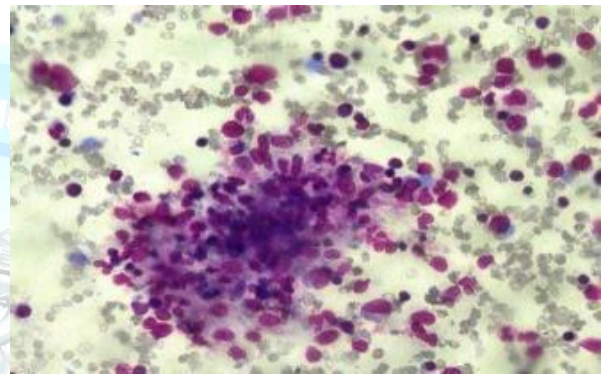


Fig. 3 Absence of megakaryocytes in the hypercellular marrow particle. Leishmann Stain (x400X)

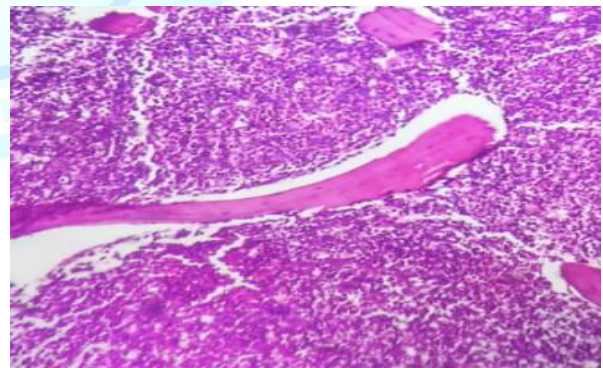


Fig. 4 Bone marrow biopsy showing hypercellular marrow with absence of megakaryocytes. H&E stain (x400X)

The child was given platelet transfusion and a repeat CBC was done which showed an increase in the platelet count. But, platelet count starts falling after every 3-4 days of platelet transfusion. The child was then

planned to be treated with Anti Thymocyte Globulin (ATG) 15mg/Kg/day and showed a very good response with it. Further, the patient was advised for stem cell transplantation for permanent cure and also regular follow up was advised.

Discussion

The pathophysiology of AATP is uncertain. It may be a primary disorder or may be seen in aplastic anemia (AA), pre leukemia, Myelodysplastic Syndrome (MDS) secondary to exposure to environmental agents such as viruses (Cytomegalovirus, Parvovirus B19) and certain toxins such as benzene.^[2] Both humoral and cell mediated immune suppression of megakaryocytopoiesis have been linked to the pathogenesis of this unusual disorder. Hoffman et al. suggested that the defect in AATP occurred in an early progenitor cell of the megakaryocytic lineage.^[3] Gewirtz et al. in 1986 proposed cell mediated suppression of megakaryocytopoiesis by demonstrating in vitro suppression of megakaryocyte colony formation by autologous ancillary marrow cells in two cases of AATP.^[4] Shiozaki et al. further elaborated on the role of humoral antibodies in 2000, when they reported a case of AATP with high levels of antithrombopoietin (TPO) IgG antibodies.^[5] Cytogenetic abnormalities have been shown to occur in association with AATP however, their precise role is not understood.^[6]

This disorder has to be differentiated from Congenital Amegakaryocytic Thrombocytopenic Purpura (CATP) which also presents with thrombocytopenia and absence of megakaryocytes in the bone marrow but this usually presents in the first day of life or usually within 1 month of age.^[7] While

some patients of AATP remain clinically stable, others may progress to aplastic anemia or pre leukemia in due course,^[8] particularly if they present in very young age like in our case. So, careful follow up is needed.

Standard treatment guidelines have not been established for AAT. The drugs that can be used for treatment are corticosteroids, lithium carbonate, androgens, vincristine, immunosuppressive drugs, platelet transfusions and plasma substitution. There have been sporadic reports of use of fresh frozen plasma (FFP) and lithium carbonate in some of these patients.^[8-9] The inducing effect of FFP on thrombopoietin production, probably due to the presence of a thrombopoietin activator or derepressor may be responsible for the beneficial effect.^[9] In occasional patients with subsequent platelet alloimmunization, splenectomy can be effective in reducing transfusion requirement and in maintaining long term clinical remission but that is not the choice in young age like our case. Antithymocyte globulin (ATG) alone, and cyclosporine alone or in combination with ATG, has been shown to be effective in treatment of AATP.^[10] But, there is the risk of further alloimmunization during the time of treatment with ATG.^[11] So, allogeneic bone marrow transplantation would seem to be the next step for a permanent cure, if a suitable matched sibling bone marrow donor can be identified and the patient can tolerate transplant.^[11] Recently, mycophenolate mofetil was used to treat a single case of acquired megakaryocytic aplasia.^[12]

Conclusion

Hence, all cases of thrombocytopenia should be thoroughly evaluated before diagnosing it as immune thrombocytopenia since the disease severity, treatment and prognosis differs with each case. For cases of AATP in young age, stem cell transplantation remains the only option of definitive treatment even when drugs and immunosuppressive agents have been tried in various studies.

References

1. Niparuck P, Atichartakarn V, Chuncharunee S. Successful treatment of acquired amegakaryocytic thrombocytopenic purpura refractory to corticosteroids and intravenous immunoglobulin with antithymocyte globulin and cyclosporine. *Int J Hematol* 2008;88:223–26.
2. Bhattacharyya J, Kumar R, Tyagi S, Kishore J, Mahapatra M, Choudhry VP. Human parvovirus B19-induced acquired pure amegakaryocytic thrombocytopenia. *Br J Haematol* 2005;128(1):128–29.
3. Hoffman R. Acquired pure amegakaryocytic thrombocytopenic purpura. *Semin Hematol* 1991;28(4):303–12.
4. Gewirtz AM, Sacchetti MK, Bien R, Barry WE. Cell-mediated suppression of megakaryocytopoiesis in acquired amegakaryocytic thrombocytopenic purpura. *Blood* 1986;68(3):619–26.
5. Shiozaki H, Miyawaki S, Kuwaki T, Hagiwara T, Kato T, Miyazaki H. Auto antibodies neutralizing thrombopoietin in a patient with amegakaryocytic thrombocytopenic purpura. *Blood* 2000;95(6):2187–88.
6. Xue Y, Zhang R, Guo Y, Gu J, Lin B. Acquired amegakaryocytic thrombocytopenic purpura with a Philadelphia chromosome. *Cancer Genet Cytogenet* 1993;69(1):51–56.
7. Fatma S. Al-Qahtani Congenital Amegakaryocytic Thrombocytopenia: A Brief Review of the Literature. *Clinical Medicine Insights: Pathology* 2010;3:25-30.
8. Hill W, Landgraf R. Successful treatment of amegakaryocytic thrombocytopenic purpura with cyclosporine. *N Engl J Med* 1985; 312:1060-61.
9. Hirsh EH, Vogler WR, McDonald TP, Stein SF. Acquired hypomegakaryocytic thrombocytopenic purpura. Occurrence in a patient with absent thrombopoietic stimulating factor. *Arch Int Med* 1980; 140:721-23.
10. Patel S, Shashidhar B, Kruthika N, Nataraju HV, Vedavathi R, Pradeep C. A Rare Case of Thrombocytopenia - Acquired Amegakaryocytic Aplasia. *IJSS Case Reports & Reviews* 2015;1(11):73.
11. Lonial S, Bilodeau PA, Langston AA, Lewis C, Mossavi-Sai S, Holden JT, et al. Acquired amegakaryocytic thrombocytopenia treated with allogeneic BMT: a case report and review of the literature. *Bone Marrow Transplantation* 1999;24:1337–41.
12. Bulchandani D, Nachnani J, Belt R, Hinton S. Acquired pure megakaryocytic aplasia: report of a single case treated with mycophenolate mofetil. *Am J Hematol* 2007;82:650-1.

Cite this article as: Sindhu R, Behera SK, Nayak J, Mishra DP. Acquired amegakaryocytic thrombocytopenic purpura - An underdiagnosed entity. *Int J Med and Dent Sci* 2015; 4(2):897-900.

**Source of Support: Nil
Conflict of Interest: No**