

# CASE REPORT

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## AN UNUSUAL CASE OF AMEGAKARYOCYTIC THROMBOCYTOPENIA

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**ABSTRACT:** Acquired Amegakaryocytic thrombocytopenia (AAT) is a rare hematological disorder characterized by bleeding and severe thrombocytopenia with marked reduction or absence of megakaryocytes in the bone marrow. Prompt recognition of this condition is essential as the condition does not respond to steroids and immunoglobulins, instead responds better to immunosuppressives like Azathioprine, Rituximab, Cyclosporine, Mycophenolate, Antithymocyte globulin alone or in combination with other drugs. We report such a rare case of AAT with rapid clinical remission by cyclosporine treatment.

**KEYWORDS:** Acquired amegakaryocytic thrombocytopenia, Cyclosporin, Bone marrow biopsy.

**INTRODUCTION:** Thrombocytopenia results from many conditions that cause increased peripheral destruction of platelets like immune thrombocytopenia, drugs, splenic sequestration, or decreased production from variety of causes like viral infections toxins, aplastic anemia, myelofibrosis and bone marrow malignancies. AAT is an unusual hematological disorder characterized by severe thrombocytopenia with marked reduction or absence of megakaryocytes in the bone marrow. AAT does not respond to steroids, as in immune thrombocytopenia but responds well to other immunosuppressives like Antithymocyte globulin alone or in combination with Cyclosporine, Rituximab, Azathioprine, Mycophenolate Mofetil. Here we report a case of AAT with extensive bleeding manifestations that showed dramatic improvement with cyclosporine alone.

**CASE REPORT:** A 20 year old male, agriculturist by occupation, from northern part of karnataka, got admitted to our hospital on 16th June 2014 with complaints of reddish patches under the skin, distributed over the trunk, face and limbs, of 2 months duration. Also he complained of headache, blurring of vision and bleeding in both eyes. The lesions were insidious in onset and progressive.

He did not give history of fever, bleeding gums, hematuria, malena. No h/o joint pain or swelling was present. He gave past h/o jaundice and easy fatiguability 5 months back. He was told to have anemia by local physician, and recovered with blood transfusion and supportive treatment. Documents revealed low platelet counts. Family history and personal history were insignificant. On examination, young male, moderately built & nourished, conscious & well oriented to time, place and person. Pallor was present. Sub conjunctival bleed was present both eyes. Petechial hemorrhages were present in all four limbs. There was ecchymosis over the abdomen and thigh, largest measuring 3 cms over the abdomen. (Figure 1 & 2)

Vitals - Pulse was 90 /min, good volume. Blood pressure was 110/70 mmHg, in right arm and he was afebrile. Cardio vascular and respiratory system examination was normal. Per

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abdominal examination did not reveal any organomegaly. Nervous system examination revealed left lateral rectus palsy. Fundus examination showed vitreous hemorrhage in both eyes. (Fig. 3). Rest of the nervous system examination was normal.

**Investigations Revealed:** Hemoglobin 11gm %, PCV 33.2 %, MCV 92.3 fl, MCHC 33.3 gm/dl. Total WBC count was 5300/cu.mm. Peripheral smear showed normal WBCs with Neutrophils 81%, Lymphocytes 10%, Monocytes 8% Eosinophils 1 % & Basophils 0%. Platelets were not seen in the peripheral smear (fig 4). RBCs were of normocytic normochromic type. Reticulocyte count was 1%. Platelet count was 1000/cumm.

Blood urea was 34.7mg%, Creatinine 0.4mg%, random blood sugar 80mg%. Serum electrolytes. sodium 130meq/lit, potassium 3.7 meq /lit. Serum calcium 9.7 mg %. Serum LDH was 170 u/lit. Urine microscopy was normal. Stool for occult blood was negative. Coagulation profile showed Pro thrombin time of 11.9 sec, INR 0.9, aPTT 12.7 sec. Bleeding time was 13 minutes 30 sec and clotting time 4 min20 sec. Direct and Indirect Coombs test were negative.

Liver function tests showed total bilirubin of 1.0 mg%, direct 0.5mg%, serum proteins 5.8 gm% with Albumin 3.9gm% and Globulin 1.9 gm %. AST was 17 iu/ml and ALT 20 iu /ml. Alkaline phosphatase was 44 iu/lit. Serum iron was 315 microgms/dl. Total iron binding capacity was 360 microgms.

HIV, HBsAg, HCV were negative.

Abdominal ultrasound did not reveal any abnormality. MRI scan of head showed thin rim of sub dural bleed in posterior part of inter cerebral fissure with minimal intraventricular haemorrhage.

A clinical diagnosis of Idiopathic (immune) thrombocytopenia (ITP) was made. Bone marrow was deferred because of severe thrombocytopenia. Patient was started on tab Prednesolone 1 mg/kg daily for 5 days. Multiple platelet transfusions were given with a total of 20 units over a period of one week. As patient's platelet counts did not improve at all, bone marrow aspiration and biopsy was done.

Bone marrow aspiration revealed normal RBC & WBC precursors and absence of Megakaryocytes. (Fig. 5)

Bone marrow biopsy was normocellular with normal Erythroid & Myeloid precursors. No abnormal cells were seen. There was striking absence of megakaryocytes. (Fig. 6)

With these findings, a final diagnosis of ACQUIRED AMEGAKRYOCYTIC THROMBOCYTOPENIA (AAT) was made.

After 15 days there was dramatic improvement in his clinical and hematological condition and he was asymptomatic. However, pallor was present and Hemoglobin was 4gm%. There was no fresh bleeding. Vision was normal. Platelet count was 160,000/cu mm.

**DISCUSSION:** AAT though very rare, should be considered in any case of thrombocytopenia that does not respond to the usual line of treatment, as in our case. Our patient was initially thought to have an immune mediated thrombocytopenia and was appropriately treated for such a disorder. Absence of response to standard immune suppression raised the concerns of other conditions, timely Bone marrow biopsy revealed AAT.

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The Differential Diagnosis of thrombocytopenia includes splenic sequestration, decreased production of platelets due to viral infections, chemotherapy, toxins, irradiation, aplastic anemia, leukemias, myelofibrosis. Other causes are increased destruction of platelets as in ITP, TTP, Autoimmune disorders, drugs, haemolytic Uremic syndrome.<sup>1</sup>

AAT is a poorly understood disease of obscure etiology characterized by severe thrombocytopenia and absent Amegakaryocytes, in the setting of otherwise normal bone marrow.<sup>2</sup> AAT may be associated with other hematological conditions like Myelo Dysplastic Syndrome (MDS), Aplastic anemia (AA), Acute myeloid leukemia, but exact mechanism has not been elucidated. Few authors consider it to be a haemopoietic stem cell disorder, manifesting in a certain period as AAT, which may progress to AA or MDS. There are case reports of AAT associated with SLE and thrombopoietin receptor antibodies, the authors view that AAT may be the result of ineffective thrombopoiesis caused by the auto antibodies leading to suppressed megakaryocyte production.<sup>3</sup> Cytogenic abnormalities (Philadelphia chromosome) have been shown to occur in association with AAT, but their precise role is not yet understood. AAT has also been described in a 91 year old patient as a presenting feature of nonHodgkin's Lymphoma.<sup>4</sup>

It is important to differentiate AAT from other causes of peripheral platelet destruction like ITP. The bone marrow picture of ITP is characterized by hyperplasia of megakaryocytes as against AAT in which there is striking absence or reduction of megakaryocytes. ITP promptly responds to steroids, which is not the case in AAT.

Treatment of AAT also has not been clearly defined. However, there are reports of AAT being treated with cyclosporine as mono therapy or in combination with ATG, Azathioprine, Danazole,<sup>1</sup>

Mycophenolate Mofetil<sup>5</sup> Rituximab<sup>6</sup> with varying degree of success. Cyclosporin takes up to several weeks to exert its clinical effect and may need to be continued for weeks to months. More aggressive approach with myeloablative chemotherapy followed by Allogenic bone marrow transplantation has also been reported to be successful.<sup>7</sup>

Our patient is unique because of bleeding from multiple sites including intracranial and vitreous bleeding and dramatic improvement within two weeks of Cyclosporin therapy alone.

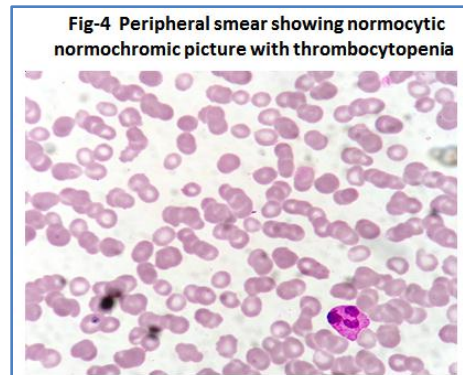
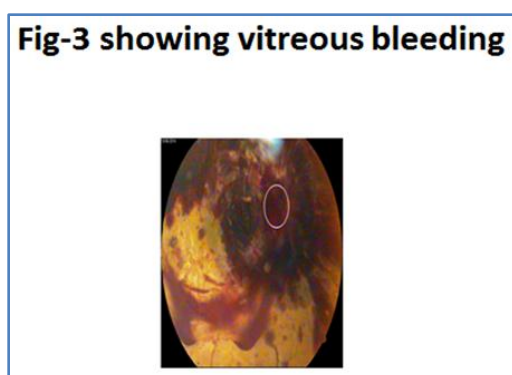
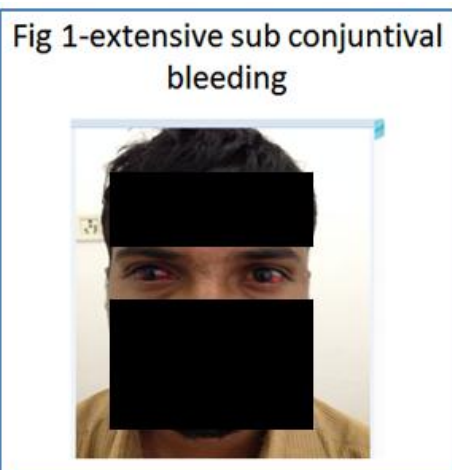
**CONCLUSION:** AAT is a rare poorly understood hematological disorder. Early recognition of this condition is crucial as patients do not respond to the usual line of treatment. In patients with unexplained isolated thrombocytopenia who do not respond to steroids and IV Immunoglobulins, bone marrow biopsy should not be delayed. Cyclosporin therapy is very effective in the treatment of AAT. Patients should be followed regularly as there is a risk of progression to hematological malignancy.

## REFERENCES:

1. Brown GE, Babiker HM, Cantu CL, Yeager AM, Krishnadasan R, "Almost bleeding to death": the conundrum of acquired amegakaryocytic thrombocytopenia. *Case Rep Hematol.* 2014; 2014:806541. doi: 10.1155/2014/806541. Epub 2014 Feb 6.

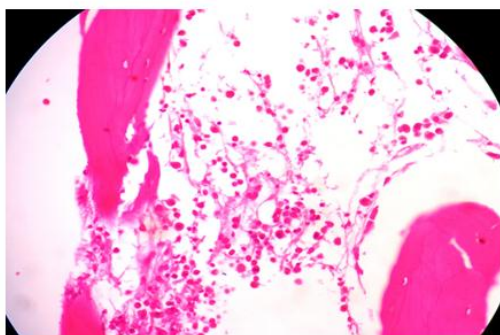
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2. Chaudhary U B, Eberwine S F, Hege K M. Acquired amegakaryocytic thrombocytopenia purpura and eosinophilic fasciitis: a long relapsing and remitting course. *Am J Hematol* 2004 Mar; 75 (3): 146-50.
3. Cela I, Miller I J, Katz RS, Rizman A, Shamma J M. Successful treatment of amegakaryocytic thrombocytopenia with eltrombopag in a patient with systemic lupus erythematosus (SLE). *Clin Adv Hematol Oncol*. 2010 Nov; 8 (11): 806-9.
4. Agarwal N, Spahr JE, Werner TL, Newton DL, Rodgers GM. Acquired amegakaryocytic thrombocytopenic purpura. 2006 Feb; 81 (2): 132-5.
5. Bulchandani D, Nichnani J, Belt R, Hinton S. Acquired pure megakaryocytic aplasia: report of a single case treated with mycophenolate mofetil. *Am J Hematol* 2007 Jul; 82 (7):650-1.
6. Mirzana M, KhaliliS, Hasanpoor A, Shamshiri AR. Anti-CD20 Antibody is Effective in the Patient with Refractory Amegakaryocytic Thrombocytopenia, 25 Months Follow up. *Int J Hematol Oncol Stem Cell Res* 2014; 8 (2): 41-4.
7. S Lonial, P A Bilodeau, AA Langston, C Lewis, S Mossavi- Sai, JT Holden, E K Waller. Acquired amegakaryocytic thrombocytopenia treated with allogeneic BMT: a case report and review of the literature. *Bone Marrow Transplant*. 1999 Dec; 24 (12): 1337-41.

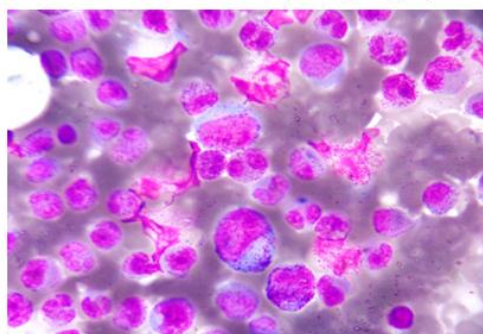


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**FIG 5** Bone marrow biopsy showing all bone marrow elements, but no megakaryocytes



**FIG 6** Bone marrow aspiration. Smear showing all marrow elements except megakaryocytes



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