

Amegekaryocytic Thrombocytopenia: A Rare Initial Presentation of Aplastic Anaemia

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Abstract:

Amegekaryocytic thrombocytopenia is a rare variety of bone marrow aplasia characterized by thrombocytopenia in association with markedly diminished bone marrow megakaryocytes. It can occur as a component of aplastic anaemia or as an isolated form. Here we report a case of a teenage girl presented with bleeding per vagina and generalized weakness which is diagnosed as a case of amegekaryocytic thrombocytopenia by bone marrow examination. It will evolve into aplastic anaemia with the course of the disease.

Key word: Amegekaryocytic thrombocytopenia, Aplastic anaemia

Introduction:

Amegekaryocytic thrombocytopenia is an unusual haematologic disorder. It has got close similarity with idiopathic thrombocytopenic purpura both clinically and in peripheral blood film. Bone marrow examination, particularly trephine biopsy, is essential for its diagnosis. It is characterized by severe thrombocytopenia in the presence of otherwise normal haematopoiesis as opposed to ITP where there is increased or normal megakaryocytes.^{1,2,3}

It may be congenital or acquired.¹ Congenital amegekaryocytic thrombocytopenia is a rare inherited disorder (autosomal recessive type) with or without a variety of congenital anomalies. The majority of patients have a mutation in the gene for the TPO receptor (c-MpL) despite high levels of serum TPO (c-MpL-legand, cytokine). The age of onset has been reported to depend on the severity of the c-MpL function defect. Bleeding is a primary concern; cutaneous, gastrointestinal, pulmonary and intracranial. The diagnosis is usually made by 1 month of age of new born.

The bone marrow problem typically starts with low platelet count. Patient may eventually develop aplastic anaemia when trilinear marrow aplasia occurs. Fanconi's anaemia and thrombocytopenia absent radius syndrome should be ruled out. It can be misdiagnosed as ITP while the later

pancytopenic phase is indistinguishable from aplastic anaemia. Bone marrow/ stem cell transplant is the only thing that ultimately cures this genetic disease.^{4,5}

The acquired variety may develop at any age and cause prolonged thrombocytopenia which may remain stable for many years. On the other hand, it can progress to aplastic anaemia, myelodysplastic syndrome or acute myeloid leukaemia. Majority of the cases are idiopathic. Few may be associated with collagen vascular disease, lymphoid malignancies, infectious agents, drugs or toxins. Major clinical manifestation is bleeding or symptoms related to anaemia in case of significant bleeding.⁶

Due to rarity of this condition, we have reported the case here. In general, the approach is similar to that adopted for aplastic anaemia.¹

Case Summary:

An 18-year-old, teenage, Muslim unmarried girl hailing from Ghatail, Tangail was admitted into medicine unit of Dhaka Medical College & Hospital with complaints of passage of clotted blood per vagina, generalized weakness, easy fatigability and lightheadedness for 1 year and fever and cough for 2 months. There was history of gum bleeding and purpuric spots over whole body 2 months back. For her illness, she consulted with local doctors and was treated with different drugs with little improvements. There was no history of weight loss, TB, bone pain, chest pain, radiation and insecticides exposure. She received two unit of blood transfusion during her hospital stay. On query she had same kind of problem 3 years back. She was treated with hormonal preparation and got two units of blood transfusion before hospital admission. Her parents had consanguine marriage. On physical examination, she had thalassemic facies, severely

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anaemic, mildly icteric, blood pressure - 110/70 mmHg, pulse – 84 bpm, Temp - 100⁰F, bony tenderness - absent, tourniquet test - negative. Systemic examination reveals no abnormality.

Lab studies showed CBC: Hb - 2.4 g/dl, ESR - 50 mm in 1st hour, TC - 13,870/cumm, Platelet - 11,000/cumm, Reticulocyte count: 7.23%. PBF - Hereditary haemolytic anaemia, PBF (reviewed) - microangiopathic haemolytic anaemia. Hb electrophoresis - Beta thalassemia trait. BT, CT, PT, APTT – normal, S. bilirubin - 1.57 mg/dl, SGPT - 52 U/L, S. Albumin - 3.76 mg/dl, Viral markers – negative, S. creatinine - 0.69 mg/dl, Urine R/M/E - pus cell:8-12, RBC: 4-6. Serum LDH: 334 U/L, USG of whole abdomen – normal, CXR – normal.

Finally bone marrow examination revealed - Myeloid Erythroid ratio: decreased, Erythropoiesis: markedly hyperactive shows dimorphic erythropoiesis including megaloid and micronormoblastic erythropoiesis, Granulopoiesis: Depressed but maturing into segmented forms, Megakaryocyte: virtually absent, Lymphoid cell: normal, Plasma cell: normal, Histiocyte : unremarkable, Parasites /ectopic cell: not found. Comment: feature consistent with amegakaryocytic thrombocytopenia

We concluded that this was a case of Amegakaryocytic thrombocytopenia with beta thalassemia trait. Beta thalassemia trait was an incidental finding. Amegakaryocytic thrombocytopenia will gradually florid into aplastic anaemia with the course of the disease. After blood transfusion the patient was discharged with cyclosporine & folic acid and advised for regular follow up. On her follow up she had gradual improvement.

Discussion:

Acquired amegakaryocytic thrombocytopenia is an uncommon disorder characterized by severe thrombocytopenia and selective markedly reduced to absent marrow megakaryocyte. It is a disease of diverse etiologies. It is thought to be an immune mediated disorder (humoral and cell mediated immune suppression occur). Though exact cause is unknown, infections like viruses (CMV, Parvovirus B19); genetic & immune cytotoxicity; exposure to toxins (benzene); drugs may play role. It may be an early sign of more severe progress diseases such as aplastic anaemia or myelodysplasia. This disorder can occur at any age. Patient usually present with thrombocytopenic bleeding such as echymosis, gum bleeding, epistaxia; superficial bleeding like menorrhagia, GI bleeding, intracranial haemorrhage.^{7,8} The diagnosis can be made by measuring serum anti TPO IgG ab & TPO level. Confirmation of the diagnosis is made by

bonemarrow examination.⁶ It is important to exclude ITP, Aplastic anaemia, Myelodysplastic syndrome & SLE at initial presentation mainly because of different management strategies & prognosis.¹ A careful history failed to identify any inciting agent or exposure in our patient. Physical examination was unremarkable except for purpuric lesions of the mucous membrane and skin. Finally bone marrow examination revealed amegakaryocytic thrombocytopenia with depressed granulopoiesis. It indicates our patient will subsequently develop aplastic anaemia with the course of time. Currently there is no standard treatment for acquired amegakaryocytic thrombocytopenia. Treatment is usually supportive in the form of blood and platelet transfusion which should be given according to the physiological demands. Use of antifibrinolytic agents can reduce the need for transfusions. Cyclosporin or Mycophenolate mofetil; antithymocyte globulin or antilymphocyte globulin can be used. However a positive response in patient with amegakaryocytic thrombocytopenia using steroids alone has rarely been reported. Allogenic bone marrow /stem cell transplantation can be done in a refractory disease or with disease progression.¹

Conclusion:

It is important to evaluate all patients with thrombocytopenic purpura for the diagnosis of Acquired amegakaryocytic thrombocytopenia as the management & out come differs significantly from ITP. Diagnosis has often been missed due to its rare prevalence. Patients are mostly misdiagnosed as ITP. However in contrast to ITP, most patients are of middle to old ages and invariably have other abnormalities in the complete blood count such as cytopenia in other cell lineage. Spleen is not usually palpable. Bone marrow examination must be done to confirm diagnosis. All these features should help in mainly an early diagnosis and subsequent appropriate treatment.

Conflict of Interest : None

References:

1. George JN, Aster RH. Thrombocytopenia due to diminished or defective platelet production. In: Beutler H, Lichtman MA, Coller BS, Kipps TJ eds. *Williams Haematology*, McGraws Hill Inc, New York. 1991, 10:1343-1351.
2. Gewirtz AM, Hoffman R. Human megakaryocyte production: Cell biology and clinical consideration. *Haematology-Oncology Clinics of North America*, 1990; 4:43-64.
3. Gorden-Smith E. C, Lewis S. M. Aplastic anaemia and other types of bone marrow failure. In: Hoffbrand AV, Lewis SM

- eds. Postgraduate Haematology, Heinemann Medical Books, London. 1989; 3 (2): 83-120.
4. Fatma s. Al-Qahtani. congenital Amegakaryocytic Thrombocytopenia: A Brief Review of the Literature. *Clinical Medicine Insights: Pathology* 2010, 3:25-30.
 5. Savoia A, Dufour C, Locatelli F, Noris P, Ambaglio C, Rosti V and et al. Congenital amegakaryocytic thrombocytopenia: clinical and biological consequences of five novel mutations. *The Hematology Journal* 2007; 92(09): 1186-1193.
 6. Antonijević N, Terzić T, Jovanović V, Suvajdzija N, Milosević R, Basara N, Elezović I. Acquired amegakaryocytic thrombocytopenia: three case reports and a literature review. *Med Pregl.* 2004; 57 (5-6): 292-7.
 7. Shafayan B, Khodabandeh A, Keyhani M and Bakhshi M. Amegakaryocytic Thrombocytopenic Purpura: A Fifteen Year Experience. *Acta Medica Iranica* 2006; 44(3): 203-207.
 8. Hoffman R, Bruno E, Elwell J, Mazur E, Gewirtz AM, Dekker P and Denes AE. Acquired amegakaryocytic thrombocytopenic purpura: a syndrome of diverse etiologies. *Blood* 1982; 60 (5): 1173-1178.