Rapid progression of acquired amegakaryocytic thrombocytopenia to myelodysplastic syndrome: case report

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ABSTRACT

Acquired amegakaryocytic thrombocytopenia (AAT) is a rare disease characterized by severe thrombocytopenia due to selective reduction or absence of megakaryocytes in the bone marrow. More commonly, patients with AAT have additional hematologic abnormalities such as macrocytosis or dyserythropoiesis, abnormalities which may predict progression to aplastic anemia or myelodysplasia. A 52-year-old female was admitted to hospital with mucosal and gingival bleeding. Megakaryocytes were not seen on the bone marrow aspiration and biopsy. AAT was diagnosed. Although she was treated with immunosuppressive therapy including prednisolone and cyclosporine, her disease progressed to myelodysplastic syndrome. She died at the third month of diagnosis because of cerebral bleeding.

Key Words: Acquired amegakaryocytic thrombocytopenia, Myelodysplastic syndrome.

ÖZET

Akkiz amegakaryositik trombositopeninin miyelodisplastik sendroma hızlı dönüşümü: Olgu sunumu


Anahtar Kelimeler: Kazanılmış amegakaryositik trombositopeni, Miyelodisplastik sendrom.
INTRODUCTION

Acquired amegakaryocytic thrombocytopenia (AAT) is a rare disease characterized by severe thrombocytopenia due to selective reduction or absence of megakaryocytes in the bone marrow[1,2]. It may be a primary disorder or may be seen in aplastic anemia (AA), preleukemia, systemic lupus erythematosus (SLE) and nutritional B12 deficiency[3-8].

Acquired clonal cytogenetic abnormalities also lead to AAT and may indicate an un rare progression to AA or myelodysplastic syndrome (MDS). Under these circumstances, macrocytosis or dyserythropoiesis often accompanies AAT[4]. Especially the differentiation from a unilineage MDS seems to be very difficult[9].

Study trials that evaluated immunosuppressive treatment of AAT with antilymphocyte globulin (ALG) or antithymocyte globulin (ATG) combined with cyclosporine showed effectiveness in patients[10,11].

We describe a case of AAT that evolved into MDS within three months of initial symptoms.

CASE REPORT

A 52-year-old female who presented in March 2004 was admitted to hospital with oral mucosal and gingival bleeding. She had no pain, fever, chills, or melena. She had recurrent mucosal and nasal bleeding for five years. Medical history revealed diabetes mellitus, and no allergies or B-symptoms (fever, weight lose and sweating). Familial history was unremarkable. There was no history of viral infection, alcohol intake, intoxication, deficiency of vitamin B12, connective tissue disease or other autoimmune diseases. On physical examination, upper mucosal and gingival bleeding were observed. She had no hepatosplenomegaly or lymphadenopathy.

Initial complete blood cell count showed: white blood cell (WBC) count 11,300/mm³ with normal differential, hemoglobin 6.3 g/dL, hematocrit 18.3%, and platelets 7,000/µL. Mean corpuscular volume (MCV) was 109.5 fl, mean corpuscular hemoglobin (MCHb) 37.9 pg, and mean corpuscular hemoglobin concentration (MCHC) 34.6%. Mean platelet volume (MPV) was 7.3 fl, and reticulocyte count was 1.2%.

Peripheral blood smear showed macroovalocytosis, poikilocytosis, and moderate anisocytosis, with rare giant platelets. The bone marrow aspiration and biopsy showed normal cellularity and absence of megakaryocytes. Erythroid and myeloid cell lines showed normal maturation and there was no increase in lymphocytes and also no metastatic cells (Figure 1, x40). The bone marrow aspiration and biopsy were performed from different parts but results were unchanged. Bone marrow biopsy imprint with Prussian blue showed minimal iron collections in the interstitium without ring sideroblasts. Levels of serum folate, vitamin B12, iron, total iron-binding capacity and ferritin were normal. In urine examination with Prussian blue, there was no iron excretion. Liver and renal function tests results were normal. Results of thyroid function tests were all within normal limits. Tests for antibodies to the human immuno-deficiency virus (HIV), Epstein-Barr virus (EBV), cytomegalovirus (CMV), parvovirus B19 and serologic tests for hepatitis A, B, C, Salmonella, Brucella, toxoplasmosis, and syphilis were non-reactive. ANA, dsDNA and

![Figure 1](https://example.com/figure1.png)
Coombs, tests were also negative. There was no immunologic destruction of platelets (CCI: 57,000/µL). Cytogenetic examination could not be performed due to financial problems. These findings led us to the diagnosis of AAT.

Initially the patient was treated with methylprednisolone, 1 mg/kg/day, without any improvement in thrombocytopenia. While we proceeded with the prednisolone treatment, reducing it to a maintenance dose of 30 mg/day, after two weeks, treatment with oral cyclosporine was included at a dose of 600 mg/day. Due to the complaints of blurred vision, funduscopy was performed and revealed microhemorrhagia. During the first month, severe thrombocytopenia was still apparent and continuous transfusions of highly concentrated platelets were required. The patient became independent of platelet and red blood cell transfusions so she was discharged with methylprednisolone 32 mg/day and cyclosporine 600 mg/day p.o. One month later, she was readmitted with gingival bleeding and acneiform lesions on her face due to steroid treatment. Platelet count was 10,000/µL in whole blood. Danazol 400 mg/day was initiated, cyclosporine was decreased to 400 mg/day and steroid was stopped, but gingival bleeding persisted and she died the same night of spontaneous intracranial bleeding.

**DISCUSSION**

The disease is slightly predominant in the female population, and although it has been reported in a wide range of ages, most occurrences are in middle-aged or elderly patients. Bone marrow aspiration and biopsy specimens from these patients are relatively unremarkable, with the exception of a marked decrease in or absence of megakaryocytes. Clinically, patients have problems with easy bruising and bleeding and lack splenomegaly. Laboratory evaluation often shows normal red blood cell (RBC) count or mild anemia, elevated MCV, normal WBC count, and thrombocytopenia with normal MPV[1,2]. Our patient had a typical occurrence of AAT, with severe thrombocytopenia (7,000/µL), markedly decreased megakaryocytes, mucosal bleeding, absence of splenomegaly, macrocytosis, and normal platelet volume. Cause of anemia was explained due to sustained mucosal bleeding. While isolated thrombocytopenia after toxic exposure or with an immunogenic cause is relatively common and immunosuppressive treatment is effective, AAT remains a rare disease in the field of hematologic disorders. But even AAT seems to be, as postulated, more “a syndrome of diverse etiologies” than a singular disease entity[12]. The pathogenesis of amegakaryocytic thrombocytopenic purpura (ATP) may involve a defect in the early progenitor cell of the megakaryocytic lineage as seen by the deficient number of megakaryocytic colonies that can be grown from the bone marrow aspirates of these patients and by the absence of small platelet glycoprotein bearing mononuclear cells which are progenitors of megakaryocytes[13,14]. Serum from such patients is reported to contain appropriately enhanced megakaryocyte colony stimulating activity (CFU-M) in some, whereas it contains humoral inhibitor against CFU-M in others[13,14]. Rapid disease progressions are not uncommon and amegakaryocytosis may impress as an early stage of AA or MDS. Especially the differentiation from an unilineage MDS seems very difficult, though new cytogenetic methods and defined pattern may support the accuracy of discrimination in the future[9].

In our patient the cellularity of bone marrow was not decreased and erythroid cell line was hypercellular. This was secondary to the compensation of anemia. Thus, AA was excluded in our diagnosis due to the age discordance and unilineage MDS. We could not demonstrate a cytogenetic abnormality to confirm the diagnosis because no cytogenetic confirmation could be performed. In the literature, study trials that have evaluated immunosuppressive treatment of AAT with ALG or ATG, corticosteroids, cyclosporine, and
danazol have shown effectiveness in patients\(^{[9,10,12,14-16]}\). Unfortunately in this patient, there was no response despite the treatment with corticosteroids, cyclosporine and danazol.

This case emphasizes the difficulties in the diagnosis of AAT and suggest that MDS AA can ensure in time in these patients and patients should be followed-up in this respect.

**REFERENCES**


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