Case report

A case of acquired amegakaryocytic thrombocytopenic purpura

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Abstract

Acquired amegakaryocytic thrombocytopenic purpura (AATP) is characterized by decreased or absent megakaryocytes in an otherwise normal bone marrow and is a rare cause of thrombocytopenia. We report a case of a 39-year-old woman, who was admitted to a tertiary care hospital for platelet transfusions. She gave history of severe recurrent epistaxis, pupura, bleeding gums and menorrhagia for the past four years, for which she had been investigated in various medical centers. She was eventually diagnosed as having acquired amegakaryocytic thrombocytopenia; her bone marrow study revealed a normocellular marrow with absent megakaryocytes and no abnormal cells; and she was advised an allogeneic peripheral blood stem cell transplant. We report this rare cause of thrombocytopenia in view of its potential interest to physiologists and we also review the literature regarding its pathogenesis and treatment.

Keywords: acquired amegakaryocytic thrombocytopenic purpura, megakaryocytes, platelets, thrombocytopenia

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Introduction

Acquired amegakaryocytic thrombocytopenic purpura (AATP) is a rare cause of thrombocytopenia that is characterized by decreased or absent megakaryocytes in an otherwise normal bone marrow.[1] This case report briefly highlights the difficulty in diagnosis, the pathogenic mechanisms involved and the potential treatment options of AATP.

Case Report

A 39-year-old woman, who was admitted to a tertiary care hospital for platelet transfusions, gave a past history of severe recurrent epistaxis, pupura, bleeding gums and menorrhagia over the last four years, for which she was being treated at various medical centers with repeated platelet transfusions. She gave history of a progressive increase in the number and severity of bleeding episodes over the four

years. Physical examination did not reveal any active bleeding manifestations or hepatosplenomegaly or lymphadenopathy.

Her past history and investigation reports revealed that she had been evaluated for pancytopenia as she initially had severe thrombocytopenia (2000-5000/cu.mm) and decreased counts in all other cell lines also. Thereafter, she was treated as idiopathic thrompocytopenic purpura (ITP) with steroids and the thrombopoietin receptor agonist eltrombopag. Her condition did not improve and she continued to be dependent on platelet transfusions. Subsequent bone marrow studies did not show any increase in megakaryocytes in response to eltrombopag and although gradually the white cell count improved, the platelet count continued to remain low.

During the four year period prior to admission, repeated bone marrow aspiration at various centers had revealed varying pictures including that of a hypocellular marrow raising the suspicion of hypoplastic myelodysplastic syndromes. At another instance the bone marrow was reported as showing prominent hemophagocytosis and the possibility of secondary hemophagocytic lymphohistiocytosis (HLH) was even transiently considered for which she was prescribed cyclosporine and danazol.

The most recent bone marrow biopsy done at another tertiary referral hospital showed a normocellular marrow with absent megakaryocytes and no abnormal cells. Platelets remained low at 11,000/cu.mm. Haemoglobin was 10.8 gm/dl, packed cell volume was 32.6%, red blood cell count was 3.29 millions/cu.mm, reticulocyte count was 2.73%, total white blood cell count was 10,900/cu.mm, differential leucocyte count was within normal limits and blood borne virus screen was negative. A revised diagnosis of acquired amegakaryocytic thrombocytopenia was made in the referral center, in view of the latest reports and the evolving symptoms of the patient. HLA-DR and DQ typing was done for the patient to plan for allogeneic peripheral blood stem cell transplant (PBSCT). A human leucocyte antigen-matched sibling (HLA-matched sibling) was identified as a potential peripheral blood stem cell donor. The patient has discontinued eltrombopag, danazol, cyclosporine and steroids. She remains stable without major complaints other than an occasional pupuric rash that subsides on platelet transfusions as she awaits the allogeneic peripheral blood stem cell transplant.

Discussion

We report this case of acquired amegakaryocytic thrombocytopenia (AATP) in view of its potential interest to physiologists and we also review the literature regarding the pathogenesis and treatment of this rare cause of thrombocytopenia. Basically, either hypoplasia/suppression of megakaryocytes or a thrombopoietic process that is ineffective despite the mass of precursors being normal or a problem in the mechanisms that control thrombopoiesis could cause a deficiency in platelet production.[1] Acquired amegakaryocytic thrombocytopenic purpura (AATP) is characterized by decreased or absent megakaryocytes in an otherwise normal bone marrow and is a rare cause of thrombocytopenia.[1] Both cell-mediated suppression and the role of humoural immunity are implicated in the pathogenesis of AATP although the exact pathogenesis is uncertain; increases in T-activated suppressor cells, an increase anti-thrombopoietin (TPO) IgG antibodies, and even defects in regulation of thrombopoiesis by cytokines are associated with AATP, although the exact cause cannot usually be determined in patients.[1]

Generally, when faced with a case of acquired thrombocytopenia, the differential diagnosis includes splenic sequestration, viral infections, chemotherapy, toxins, aplastic anaemia, myelofibrosis or leukemia among other causes.[2] Idiopathic thrombocytopenic purpura (ITP) is one of the most common causes of

thrombocytopenia and in this case too, like in the case reported by Brown *et al.,* the diagnosis of ITP was initially considered, probably keeping in mind the patient's age and gender (it is common in females under 65 years) and the clinical presentation, until the poor response to treatment prompted the consideration of other etiologies.[2]

The exact prevalence of amegakaryocytic thrombocytopenia is unknown, and literature is mostly limited to isolated case reports.[3] It is however accepted that the prevalence of AATP could be higher than what is reported owing to fact that it is an underdiagnosed entity or it is misdiagnosed as immune thrombocytopenia.[1] Harjai *et al.* had reported a probable case of amegakaryocytic thrombocytopenia In India in 1992,[4] and Patel *et al.* and Betdur *et al.,* from Karnataka, have each reported a rare case of AATP in the last two years.[5,6]

Treatment of acquired amegakaryocytic thrombocytopenic purpura with intravenous immunoglobulins, prednisone, vincristine and cyclophosphamide has not been found to be effective.[1] Treatment with myeloablative agents like busulfan and cyclophosphamide followed by an allogeneic bone marrow transplant from a fully HLA-matched sibling has proven to be effective.[1,7] Treatment with antithymocyte globulin with or without rituximab, azathioprine and cyclosporine has also been found to be effective.[1,2] Thrombopoietic drugs too show promising results.[1]

Cela *et al.* report success with eltrombopag which is a second generation thrombopoietin receptor (TPOR) agonist, while treating a woman with systemic lupus erythematosus (SLE) who developed amegakaryocytic thrombocytopenia.[8] Lown *et al.* point out that by the time most patients are diagnosed, they have probably already received steroids for a probable diagnosis of ITP, and that TPOR agonists would be valuable in those patients who do not respond to steroids.[3] However, such cases should be carefully followed as clonal evolution or progression to acute myeloid leukemia could occur when using TPO mimetics like eltrombopag or romiplostim.[9]

Lonial *et al.* report a patient with AATP who eventually was treated with myeloablative chemotherapy followed by allogeneic bone marrow transplant and who responded well.[7] This patient too was initially thought to have an immune mediated thrombocytopenia, and was appropriately treated.[7] But later, the lack of response to immunosuppression and the progression to a condition in which there were no megakaryocytes in the bone marrow, made them consider myelodysplasia and aplastic anemia, similar to the case we report.[7] Agarwal *et al.* report a case that responded to treatment with cyclosporine but not to Interleukin-11 (IL-11) and advise that allogeneic bone-marrow (stem-cell) transplant should be considered for young patients with refractory disease or with disease progression, if they have matched siblings.[10] The patient reported in our study would fall into this category.

Conclusion

This case report highlights the difficulties in diagnosing acquired amegakaryocytic thrombocytopenic purpura (AATP), its pathogenesis and the various treatment options available to treat it. Though AATP appears to be relatively rare, it still needs to be considered in the differential diagnosis of thrombocytopenia.

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Conflicts of interest: Nil

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