Severe Anemia in a Patient with Warm Autoantibody, Dyserythropoiesis, and X-linked Thrombocytopenia

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INTRODUCTION

Megakaryopoiesis is a complex process involving a large number of molecules including transcription factors, cytokines, cell surface receptors, signaling molecules, cytoskeletal proteins and cell cycle regulators. Inherited thrombocytopenia due to diminished formation of megakaryocytes or arrest of thrombopoiesis by megakaryocytes can occur due to mutation in any of the genes coding for these molecules [1]. We report a case of severe anemia in a 22-year-old man with congenital thrombocytopenia with a family history suggestive of X-linked inheritance. The case is unique in its presentation of severe anemia with presence of warm and cold autoantibodies.

CLINICAL DATA

This 22-year-old man presented with weakness, pallor and jaundice. Significant past history includes two episodes of subarachnoid hemorrhage, one spontaneous, both requiring platelet transfusions. The patient had a maternal half brother with a bleeding diathesis secondary to thrombocytopenia, and twin of the maternal grandfather with a bleeding disorder. Of interest, the maternal grandfather himself, reportedly, has no history of abnormal bleeding. The patient was treated with blood transfusions, steroids and IVIG.

PATHOLOGIC FINDINGS

Laboratory values at admission were: hemoglobin 2.7 g/dL, reticulocyte 1.9 %, platelets 12,000/ul, LDH 319 U/L, and total/indirect bilirubin 9.3/7.5 mg/dL. Further evidence of extravascular hemolysis included spherocytes in peripheral blood (Figure 1) and a positive direct antiglobulin test with IgG. The patient was found to have both cold and warm autoantibodies. Peripheral blood a;so revealed red cell agglutination consistent with a cold agglutinin (Figure 2). A bone marrow exam showed hypercellularity, dyserythropoiesis and increased megakaryocytes (Figures 3, 4).

Peripheral Blood

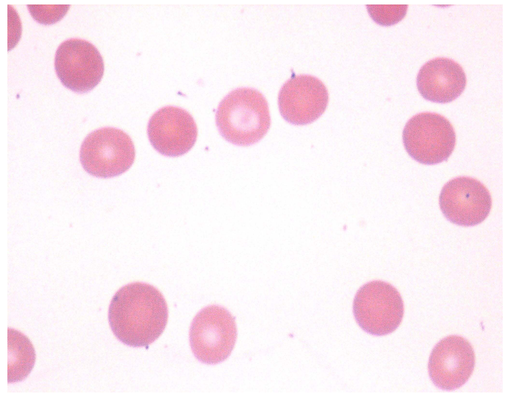

Fig. 1. Peripheral Blood, 100X, shows microspherocytes

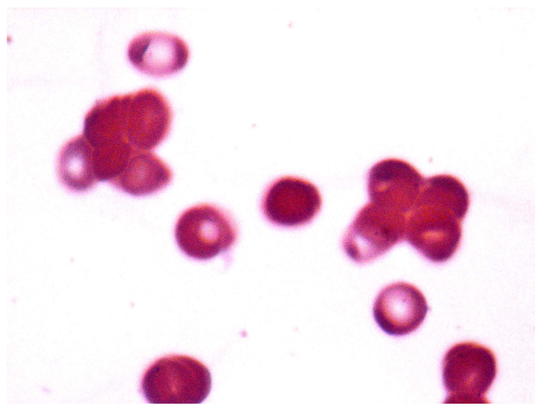

Fig. 2. Peripheral Blood, 100X, shows red cell agglutination

Bone Marrow

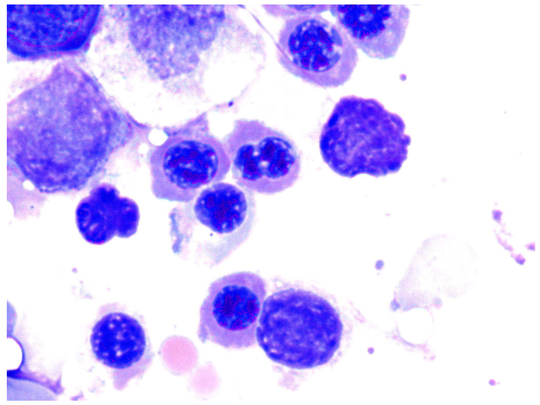

Fig. 3. Bone Marrow Aspirate, 100X, reveals significant dyserythropoiesis

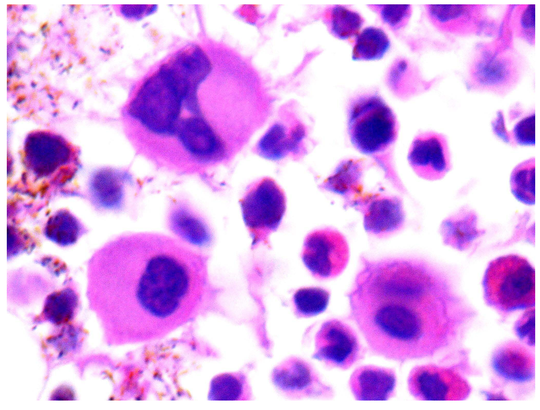

Fig. 4. Bone Marrow Biopsy, 50X, shows increased number of immature megakaryocytes

COMMENT

This case exemplifies congenital thrombocytopenia whose presentation is complicated by erythrocyte autoantibodies (warm and cold) in addition to dyserythropoiesis – showing aberration in the erythrocyte as well as the megakaryocyte lineage development. Instead of a lack of megakaryocytes, an increased number of abnormal megakaryocytes is seen in the bone marrow. The GATA-1 mutation is associated with anemia and dyserythropoiesis and appears to be the most likely etiology of the unusual presentation in this case [2, 3]. GATA-1 transcription factor is critically involved in the development of both the erythroid and the megakaryocyte lineage. Patients with this mutation typically present with X-linked thrombocytopenia, and hypercellular bone marrow with dyserythropoiesis as seen in this case. Mutation study is currently being carried out to confirm GATA-1 mutation in this patient. Warm reactive autoantibodies are encountered in association with various hematologic and autoimmune disorders. In general, DAT is reactive for IgG in all patients with a strength of 2+ or greater, correlating highly with the presence of hemolysis [4]. Erythrocyte autoantibodies occur with an increased incidence in lymphoproliferative disorders and myelodysplastic syndromes [4, 5], but are not yet described in patients with congenital thrombocytopenia.

REFERENCES

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