Isolated CD59 Deficiency Manifesting as DVT

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Abstract
Acquired CD59 deficiency is seen in Paroxysmal Nocturnal Hemoglobinuria (PNH), which is linked to a defect in GPI-anchoring on hematopoietic cells. We are reporting here a case of a patient who presented with unprovoked Deep Venous Thrombosis (DVT) of right external iliac and was found to have isolated CD59 deficiency.

Keywords: Paroxysmal Nocturnal Hemoglobinuria, CD59 Deficiency, Deep venous Thrombosis.

Introduction
Paroxysmal Nocturnal Hemoglobinuria (PNH) is a clonal disorder, known by the triad of intravascular hemolysis, pancytopenia, and tendency to venous thrombosis. In PNH patients, a substantial proportion of erythrocytes become susceptible to lysis by complement system, due to the lack of protective membrane proteins, especially CD59 and CD55. Among them, CD59 deficiency is considered to be most important factorin causing the hyper susceptibility of the RBCs to the activated complements, because CD59 hinders the insertion of C9 polymers into the membrane. The underlying molecular defect is a somatic mutation in the gene required for synthesis of the GPI (Glycosylphosphatidylinositol) molecule, called as the PIG-A gene. This GPI molecule is required to anchor several molecules to the surface membrane of the cells, including CD59 and CD55. Almost each PNH patient has a different PIG- A mutation. These mutations take place de novo in a hemopoietic stem cell, and thus are not inherited. Hence, we see a mosaic of cells in the marrow (mutant and non-mutant cells). In the peripheral blood also, PNH cells and non-PNH (normal) cells, both present. Deep Venous Thrombosis is a well-known life-threatening complication of PNH, although its pathogenesis is not well understood¹. We are reporting here a case of a female patient, who presented with unprovoked Deep Venous Thrombosis (DVT) of right external iliac vein and found to have isolated CD59 deficiency, on flow cytometry.

Case Description
A 30 years old female, who was first diagnosed and treated for Deep Venous Thrombosis (DVT) in...
right common femoral vein, 3 years ago. She had improved with anticoagulant therapy. Right lower limb swelling has re-occurred intermittently, several times since then, usually at a gap of around 7-8 months. When patient presented to us, some residual swelling was still present, associated with visible dilated veins and blackish lesions on right lower limbs. On examination, milder pallor was present, right lower limb was swollen as compared to the left lower limb, multiple purple-bluish lesions of size from 2 cm to 6 cm, were present on right leg, multiple dilated veins were visible on right calf and upper anterior thigh. There were no ulcers, and no calf tenderness. Systemic examination including cardiovascular, respiratory, abdomen, and central nervous system was within normal limits. Her gait was limping toward right side. Duplex ultrasound and CT venography (Fig. 1) were suggestive of chronic partial thrombosis of the right external iliac, common femoral, and superficial femoral veins. Complete blood count was suggestive of mild anemia (Hb = 9.0 gm/dl) with microcytic and hypochromic picture. Total leukocyte count, differential leukocyte count, and platelet count were within normal limits. Serum total bilirubin was 1.2 mg/dl, and serum indirect bilirubin was 0.9 mg/dl. Serum LDH (lactate dehydrogenase) was slightly elevated 373 U/L (<270). Serum haptoglobin was 0.66 gm/L (0.30 - 2.0). Urine for hemoglobin was negative. Renal function tests, liver function tests, lipid profile, thyroid functions tests, Protein C, Protein S, were all within normal limits. Anti-phospholipid antibodies and direct Coombs test were negative. On flow cytometry of peripheral blood, 24% of RBCs showed decreased expression of CD59.

Discussion

Acquired CD59 deficiency is seen in Paroxysmal Nocturnal Hemoglobinuria (PNH), which is linked to a defect in GPI-anchoring on hematopoietic cells. In PNH, all hematopoietic cells are not affected, but there is a mosaic pattern. Some cells have normal expression of GPI-anchored proteins, and some cells have reduced or complete absence of expression of GPI-linked proteins. In addition, in PNH, the defect is in the synthesis of the GPI anchor leading to decreased expression on cell surface, of all those proteins which use GPI-anchoring. In contrast, in congenital CD59 deficiency, only CD59 expression is decreased, and it is decreased not only in hematopoietic cells, but also in all other tissues. It has been shown that CD59 deficiency is the most important factor making PNH cells prone to lysis. In 1990, Ono et al have reported a patient having PNH with normal expression of DAF (Decay Accelerator factor) and normal expression of CD59.
accelerating factor) (CD55) and acetyl cholinesterase on erythrocytes or granulocytes. The same patient was later diagnosed and reported as a case of inherited complete deficiency of 20 kDa HRF (CD59) causing PNH like syndrome.\(^4\)\(^-\)\(^5\). At present, our patient, do not meet the diagnostic criteria of PNH, which requires demonstration of a discrete population of cells, which is CD59 and CD55 negative, on flow cytometry. And in PNH, this population is at least 5% of total red cells, and at least 20% of the total granulocytes. Flow cytometry in this patient has shown that 24% of total RBC population in peripheral blood, have decreased expression of CD59. Though, further workup is required to find out the exact molecular defect causing the CD59 deficiency in this patient, yet the unprovoked thrombosis of the external iliac vein in this patient is probably due to the CD59 deficiency.

**References**


