



OLGU SUNUMU / CASE REPORT

Gray platelet syndrome

Gri trombosit sendromu

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Abstract

Gray platelet syndrome (GPS) is an autosomal recessive disorder characterized by thrombocytopenia and defective platelets that appear pale on light microscope. Patients present with easy bruising, nose bleeds, menorrhagia and prolonged bleeding. There is no specific treatment for GPS and the management includes anticipating risks and preventing bleeding by avoiding drugs that impair platelet function. We present here report of a case who presented with repeated episodes of abnormal bleeding and was found to have GPS.

Key words: Bleeding disorder, gray platelet syndrome, thrombocytopenia

Öz

Gri trombosit (platelet) sendromu (GPS), trombositopeni ve ışık mikroskopunda soluk görünen kusurlu trombositlerle karakterize, otozomal resesif geçişli bir hastalıktır. Hastalarda kolay morarma, burun kanaması, menoraji ve uzun kanamalar görülmektedir. GPS için spesifik bir tedavi bulunmamaktadır dolayısı ile hastalığa karşı, riskleri öngörmek ve kanamanın önlenmesi için trombosit fonksiyonunu bozan ilaçlardan kaçınmak gerekmektedir. Bu olgu sunumunda, tekrarlayan anormal kanama atakları olan ve GPS bulgusu bulunan bir vaka sunulmaktadır.

Anahtar kelimeler: Kanama bozukluğu, gri trombosit sendromu, trombositopeni

INTRODUCTION

Gray platelet syndrome (GPS) is a rare autosomal recessive bleeding disorder characterized by thrombocytopenia and defective platelets that appear pale on light microscope. The platelets are larger in size and are deficient in their characteristic α -granules, which store proteins that promote platelet adhesiveness and wound healing when secreted during an injury. GPS was first described by Raccuglia in a young American boy who presented with petechiae, bruising tendency, and recurrent knee pain presumably from intra-articular bleeding¹. About 50 cases so far have been reported in the literature² but none from Pakistan. We present here report of a case who presented with repeated episodes of abnormal bleeding and was found to have GPS. She and her sister had cardiac defects rarely reported previously in the relevant literature. Due to rarity of the disease, the case was

misdiagnosed and mistreated for years until right identification.

CASE

A 15-year-old female, born of a consanguineous marriage, presented with thirteen years' history of repeated episodes of abnormal bleeding. Her symptoms were discovered at the age of two years when her parents noticed multiple bruises of variable sizes on her arms, legs and hips that persisted for many hours. She was initially evaluated by a pediatrician. Her earlier reports showed a hemoglobin of 10 g/dL (normal 12-16 g/dL), total leucocyte count of $3.6 \times 10^9/L$ (normal $4-11 \times 10^9/L$), a platelet count of $26 \times 10^9/L$ (normal: $150 - 450 \times 10^9/L$) and an erythrocyte sedimentation rate (ESR) of 20 mm at the end of 1st hour (normal: 0-15 mm at the end of 1st hour). Her polymorphs were slightly decreased i.e. 48% (normal: 50-70%)

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and lymphocytes were slightly increased i.e. 42% (normal: 20-40%). Her mean corpuscular volume (MCV) and mean corpuscular hemoglobin concentration (MCHC) were normal. Her peripheral blood film showed giant platelets. Her bone marrow analysis revealed increased megakaryocytes, active erythropoiesis and myelopoiesis and no stainable iron suggestive of a platelet functional defect or peripheral destruction of platelets. Her 2-D echocardiography revealed a mild mitral leaflet prolapse and a mild mitral regurgitation. The patient was, however, treated as a case of Idiopathic Thrombocytopenic Purpura (ITP). She was put on oral medications including prednisolone and remained symptom free for one year.

Over the period of next eleven years she had repeated hospital admissions due to excessive bleeding from gums in the wake of falling milk teeth and recovered only after transfusion of platelets and red cell concentrate each time. She even bled from a vesicular rash in her arm pit and needed platelet transfusion. During the period, she had remained on irregular intake of oral steroids and labeled as suffering from chronic ITP.

At the age of fourteen years, she developed heavy menstrual bleeding on her menarche while still on steroids. She developed cushingoid features but her platelet levels did not improve. In the next year, she had three hospital admissions for heavy menstrual bleeding with gaps of 3 months, 2 months and 1 month respectively and again received transfusions. Thus, she had been transfused with 120 pints of platelets and 10 pints of red cell concentrate.

On physical examination, she was pale and had a pan-systolic murmur. There was no evidence of hepatosplenomegaly. Her hemoglobin was 11.1 g/dL, MCV was 101.1 fL (normal: 76-96 fL) and MCHC was normal. The platelet count was markedly reduced i.e. $6 \times 10^9/L$. Her ESR was 36 at the end of 1st hour and differential leucocyte count was normal. Her bleeding time was prolonged i.e. >30 min (normal: 2-8 min) while prothrombin time and activated partial thromboplastin time were normal. The peripheral blood film revealed large pale (hypogranular) platelets, (Figure-1) suggesting a diagnosis of GPS. The findings on her bone marrow examination were similar to the previous report. (Figure-2) Because her platelet count was too low, the platelet functional studies could not be performed, as the prerequisite for platelet functional studies is a platelet count between $200-400 \times 10^9/L^3$.

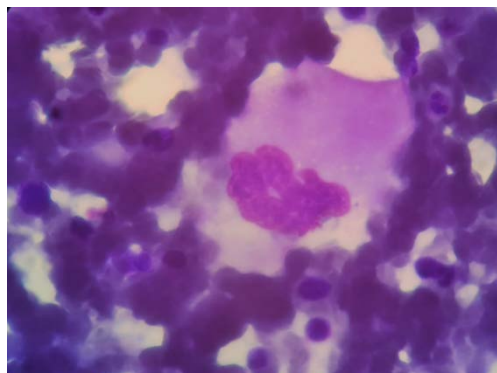


Figure 1. Bone marrow smear with a megakaryocyte

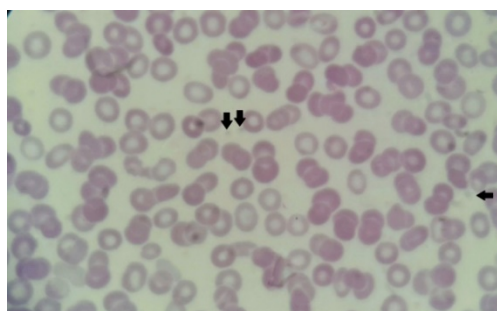


Figure 2. Peripheral blood film with hypogranular platelets

Her younger sister also developed similar complaints of gum bleeding at the age of 3 years and was diagnosed as a case of ITP but till now her platelet function tests have not been done. Her cousin, 8 years of age, was also diagnosed as a case of ITP but was not further investigated. Both relatives had cardiac defects and a low intellect but no active bleeding issues. Their platelet counts remained between $130-200 \times 10^9/L$. After diagnosis, the patient and her parents were counselled about the disease and advised to avoid, where possible, physical trauma and drugs affecting platelet function, improve dental care and take oral contraceptives to reduce menstrual bleeding.

DISCUSSION

GPS is a heterogeneous disorder with more than one molecular cause. The underlying defect is the inability of platelets to store α -granule proteins. The abnormal α -granules appear gray on blood films stained by the May-Grünwald-Giesma stain, hence, the syndrome's name. The haemostatic proteins

contained in the α -granules are not released at the site of vascular injury that results in a bleeding tendency. The platelet count is also reduced. The secretory proteins of α -granules are eventually secreted in the bone marrow when the platelets complete their life and are engulfed by the phagocytes. These proteins include growth factors, which cause myelofibrosis in the marrow^{2,4,5}.

The patients with GPS present with easy bruisability, nose bleeds, menorrhagia and prolonged bleeding. Often, there is a family history of bleeding tendency, particularly following surgery or injury⁶. Spontaneous bleeding is usually mucocutaneous⁷.

The differential diagnosis of GPS includes any cause of mild thrombocytopenia, particularly ITP and other rare thrombocytopathies with large platelets, for example Bernard-Soulier syndrome, May-Hegglin anomaly, Montreal platelet syndrome, Fechtner syndrome, Epstein syndrome, Sebastian syndrome and DiGeorge's syndrome^{8,9}.

The investigations include clotting screening in which the bleeding time is prolonged. The peripheral blood film shows pale (hypogranular) platelets using May-Grünwald-Giesma stain with anisocytosis. The diagnosis can be confirmed by analysis of α -granule proteins, using Western blot, immunological methods or electron microscopy^{2,10}.

There is no specific treatment for GPS. The management includes anticipating risks and preventing bleeding by avoiding drugs that impair platelet function, regular dental care to prevent gingival bleeding and using oral contraceptives to reduce menorrhagia. If bleeding occurs, local measures are used where possible, such as nasal packing for epistaxis. Platelet transfusions may be necessary especially before operation or to treat active hemorrhage. If possible, human leucocyte antigen (HLA)-matched donor platelets should be used in order to reduce alloimmunization. Desmopressin can also be used to improve bleeding time and clotting. Splenectomy does not seem to be

helpful in GPS. Newer therapies such as recombinant activated factor VIIa (rFVIIa) may have a role in some platelet disorders^{11,12}.

Thorough investigation should be carried out when a patient comes with repeated episodes of bleeding tendency. Examination of a blood film is essential, when an automated hematology analyzer shows thrombocytopenia.

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