



# A disease difficult to diagnose: Gardner-Diamond syndrome accompanied by platelet dysfunction

Zeynep Karakaş, Serap Karaman, Burcu Avcı, Ayşegül Ünüvar, Gülyüz Öztürk, Sema Anak, Ömer Devocioğlu  
Division of Pediatric Hematology-Oncology, İstanbul University İstanbul Faculty of Medicine, İstanbul, Turkey

## Abstract

Gardner Diamond syndrome is a rare condition characterized with painful ecchymoses in different parts of the body and cutaneous and mucosal hemorrhages. The etiology is not known fully and psychogenic factors are thought to be involved. Cutaneous lesions and hemorrhages develop mostly following emotional stress and rarely minor traumas and may recur. Although the extremities are involved with the highest rate, the lesions may be observed in any part of the body. Hemostatic tests are generally normal. The majority of the subjects is composed of young women. It is observed more rarely in men and children. In this article, a patient who presented with recurring painful echymoses and bleeding disorder and diagnosed with Gardner Diamond syndrome by intracutaneous injection of autologous blood was presented to emphasize that this syndrome is observed rarely in the childhood and should be considered not only in the differential diagnosis of cutaneous lesions, but also in the differential diagnosis of various system hemorrhages.  
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**Key words:** Child, Gardner Diamond syndrome, platelet dysfunction

## Introduction

Gardner Diamond syndrome (GDS) which is also known as autoerythrocyte sensitization syndrome, psychogenic purpura, painful bruising syndrome is a rare autoimmune vasculopathy which mostly recurs after emotional stress and which is characterized with painful ecchymotic lesions. It was described by Gardner and Diamond in 1995 for the first time in four women who had recurrent ecchymoses after minor traumas (1). It is frequently observed in young adult women. Pediatric cases have also been reported rarely in the literature (2-5). The actual mechanism leading to this syndrome is not known yet. In recent years, it has been reported that antibodies which are produced as a result of increased sensitivity to phosphatidylserine which is a component of the erythrocyte stroma lead to immune complex and complement activation.

In this article, a case of GDS accompanied with platelet dysfunction was presented to draw attention to the possibility of other underlying mechanisms and because it is a rare case.

## Case

A 13-year old female patient presented to our clinic with complaints of headache and painful bruising around the eye, dorsum of the hand and on the feet. In her personal history, it was learned that she had recurrent epistaxis, painful bruising on the body and menorrhagia, her ecchymoses increased with sadness and stress and regressed spontaneously after a while. There was no history of trauma, infection or drug usage. In her familial history, it was reported that her mother had ecchymoses on the skin and they regressed spontaneously. On physical examination, her growth and development was appropriate for age and her vital signs were stable. Her general status was well. She had ecchymoses around the eye, on the dorsum of the

**Address for Correspondence:** Serap Karaman, Division of Pediatric Hematology-Oncology, İstanbul University İstanbul Faculty of Medicine, İstanbul, Turkey. E-mail: drkaramans@yahoo.com

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hands, on the arms and feet which were prominent, round, smooth on the surface, yellow in the middle and painful with palpation (Figure 1-4). No pathological finding was found on otolaryngological examination performed because of recurrent epistaxis. In laboratory tests, complete blood count, biochemical examinations, complete urinalysis, C-reactive protein and erythrocyte sedimentation rate were found to be normal and direct Coomb test was found to be negative. In the coagulation tests, prothrombin time (PT), activated partial thromboplastin time (aPTT), fibrinogen, factor VII, IX, XI, AT, protein C and S, von Willebrand factor (VWF) antigen and activity were found to be normal. On peripheral blood smear, erythrocyte and platelet morphologies were found to be normal and clustering was observed in the platelets. Antinuclear antibody, anti-double stranded DNA, C3, C4, anticardiolipin antibody and lupus anticoagulant were found to be negative. In the platelet aggregometry test, normal aggregation curves were obtained with collagen and ristocetin, near normal aggregation curves were obtained with adenosine diphosphate (ADP) and very low amplitude aggregation curves were obtained with epinephrine. The same findings were present in the mother of the patient. Since increased sensitivity to extravasated erythrocytes was considered, the patient's own erythrocytes were injected intradermally and it was observed that ecchymoses developed (Figure 5, 6).

### Discussion

Gardner Diamond syndrome which is a rare syndrome may progress with recurrent attacks and the intervals between attacks are variable (months or years). Painful ecchymoses may have variable size and usually improve in two weeks (6). They may be observed on the whole body (more frequently on the extremities) (3). In addition to cutaneous lesions, neurological findings including headache, paresthesia and syncope, blurred

vision or diplopia, arthralgia, myalgia, bleedings in the nose, eye, ear and genitourinary system may be observed (6). In our patient, headache, epistaxis and uterine bleeding were also present in addition to cutaneous lesions.

The etiological mechanism leading to the disease is not known fully and severe stress or emotional trauma are thought to trigger the disease. Many psychiatric disorders including mood disorders, anxiety disorder and personality disorder, somatoform and dissociative disorders may be observed (6). In many patients, especially depressive conditions may accompany the picture, but no mortality has been reported. Our patient frequently experienced conflicts with her parents in addition to bursts of anger and skin lesions



Figure 2. Ecchymosis on the dorsum of hand



Figure 1. Ecchymosis around the eye



Figure 3. Ecchymosis on the dorsal part of foot



**Figure 4. Ecchymosis on arms**



**Figure 5. Ecchymoses on forearm half an hour after erythrocyte injection**

and bleedings increased during these periods. Antidepressive treatment was recommended, when a diagnosis of depression was made after psychiatric assessment.

Since women constitute most of the cases, it has been proposed that there is a relation between the hormonal effects of estrogen and GDS. One of the causes of menorrhagia observed in our patient may be this. Although it has been reported that psychological factors are involved in the disease, hematological and immunological abnormalities including abnormal erythrocyte morphology, anticardiolipin antibody positivity, systemic lupus erythematosus, complement deficiency, immune complex nephritis, increased fibrinolytic ac-



**Figure 6. Ecchymoses on forearm 96 hours after erythrocyte infection**

tivity, idiopathic thrombocytopenic purpura have been found in some patients rarely. In the literature, there are only four cases accompanied by platelet dysfunction similar to our case (7-10). Only two of these are pediatric cases (7, 10). In both cases, disruption in platelet aggregation was found with ADP, while response with epinephrine was decreased to a great extent in our patient. In most patients, laboratory findings are normal and the skin test may not be positive in all cases.

It is known that hemorrhagic diathesis together with psychogenic disorders is present in this syndrome, but the cause and frequency of hematological disorders is not known. Serotonin is a neurotransmitter and is involved in cognitive functions including mood, appetite, sleep, learning and memory. Serotonin is also found in platelets. Serotonin which is stored in platelets is involved in platelet aggregation by being released when necessary and in regulation of vascular tonus and coagulation processes. Thus, the risk of bleeding increases, when the amount of serotonin decreases. In our patient, serotonin level in platelets or serum could not be measured, but we think that the level of serotonin was decreased because of the diagnosis of depression. In addition, serotonin level in platelets might have decreased and hemorrhagic diathesis might have increased. In the aggregometry test in which platelet aggregation of our patient was evaluated, lack of aggregation of platelets as a response to epinephrine was evaluated to be "epinephrine unresponsiveness". Epinephrine unresponsiveness may be observed in healthy individuals with a rate of 16-40%, but a decrease in aggregation against ADP is also expected in these individuals. Hemorrhagic diathesis is not observed in this condition which provides a natural protection against thrombosis. However, aggregation with ADP was normal in our patient and bleeding findings were present.

In treatment, antihistaminics, corticosteroids, albumin infusion, immunosuppressive treatment, anticoagulants, antihistaminics, antidepressants, hormones and vitamin C have been tried, but not been found to be very efficient. Nevertheless, the most efficient treatment is psychological treatment. In our patient, the frequency of the lesions was observed to be decreased with antidepressant treatment and psychotherapy.

Conclusively, GDS is a rare disease which is difficult to diagnose. In the differential diagnosis of recurrent ecchymoses and bleedings, this condition should also be considered and the patients should be examined carefully in terms of association of hematological and other diseases.

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