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Case Report Dermatology

Is Gardner-Diamond syndrome related to autoimmunity?

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ABSTRACT

Gardner and Diamond described a clinical picture of painful ecchymosis in the skin and mucous membranes in four female patients and called this entity Gardner-Diamond syndrome (GDS). At present, the exact pathogenesis of the disease is still unknown. In recent years, it has been advocated that antibodies against phosphatidylserine in erythrocyte stroma may cause immune complex and complement activation, leading to this clinical picture. Herein, we found it appropriate to present a case of multiple ecchymotic lesions diagnosed with GDS followed by many autoimmune diseases to draw attention to autoimmune association. As a result of this case presentation and mini-literature review, we think that autoimmunity patients should not be missed in GDS patients.

Keywords: Autoerythrocyte sensitization syndrome; autoimmunity; Gardner-Diamond syndrome; systemic lupus erythematosus.

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In 1955, Gardner and Diamond described a clinical picture of painful ecchymosis in the skin and mucous membranes in four female patients and called this entity Gardner-Diamond syndrome (GDS) [1]. Later, this clinical condition was thought to be a reaction to the patient's own erythrocytes and was also referred to as GDS as well as autoerythrocyte sensitization syndrome [1]. In 1968, Ratnoff and Agle suggested that psychogenic purpura should be renamed the syndrome, referring to the presence of mental factors at the root of the disorder [2]. At present, the exact pathogenesis of the disease is still unknown. In recent years, it has been advocated that antibodies against phosphatidylserine in erythrocyte stroma may cause immune complex and complement activation, leading to this clinical picture [3].

Here, we found it appropriate to present a case of multiple ecchymotic lesions diagnosed with GDS followed by many autoimmune diseases to draw attention to autoimmune association.

CASE REPORT

A 26-year-old female patient presented to the dermatology outpatient clinic with the complaint of recurrent, painful bruises in various parts of the body. It was anamnesis that the lesions suddenly appeared painfully and regressed within 2–3 days. The patient had a history of fatigue, joint pain, and abdominal pain. Complaints have been continuing for 2 years. Her medical history included Hashimoto's disease and irritable bowel syndrome diagnoses. Anti-microsomal and anti-thyroglobulin antibodies were positive for Hashimoto's disease. There was no history of dermatological diseases in her family history.

On the dermatological examination, there were significant painful ecchymotic patches with palpation; 3×4 cm in the abdomen, and multiple prominent ecchymotic patches on legs (Fig. 1A).

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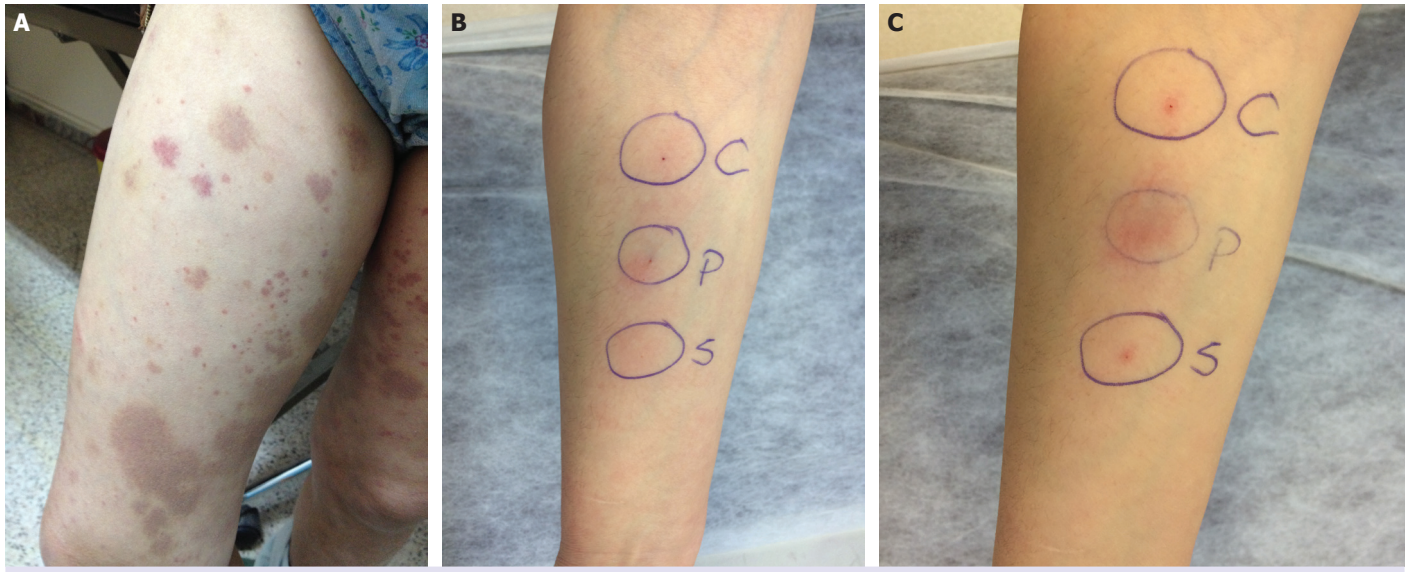

FIGURE 1. **(A)** Multiple prominent ecchymotic patches on legs. **(B)** C (check): Check, only injector, P (patient): 0.1 ml venous blood injected area with plasma separated, S (serum): Serum physiological. **(C)** P (patient): 2×2 cm painful ecchymotic patch in the part where 0.1 ml of venous blood is injected with plasma separated 30 min after injection.

In laboratory examination; C-reactive protein: 2.97 mg/L, erythrocyte sedimentation rate is 12 mm/h, mild hypochromia and anisocytosis in peripheral smear, sufficient, and cluster platelets, 3% eosinophilia, 60% neutrophils, 2% monocytes, and 35% lymphocytes were seen. Prothrombin time, bleeding time, clotting time, prothrombin activity, and activated partial thromboplastin time were within normal limits.

There were prominent dermal capillary vessels, fibrinoid changes in some, neutropolymorphic invasion in perivascular weighted interstitial areas, and extravasated erythrocytes in histopathological examination of the biopsy material taken from the patient's lesions. Papillary dermis was edematous. There was no accumulation on direct immunofluorescence. Histopathological examination was interpreted as vasculopathy.

The case was thought to have GDS due to anamnesis, age, gender, and characteristic skin findings. To confirm the diagnosis, venous blood from peripheral blood was centrifuged and plasma was separated and 0.1 ml was injected intradermally. At the same time, control physiological saline solution 0.1 ml and empty syringe were administered intradermally to the left arm (Fig. 1B). Thirty minutes after the injection, 2×4 cm painful ecchymotic area developed in the patient plasma injected part (Fig. 1C). This ecchymotic lesion regressed within 2–3 days. Skin lesions of the patient were diagnosed as GDS. The patient was treated with mucopolysaccharide polysulfate cream for ecchymotic lesions. No additional psychiatric comorbidity was detected as a result of multiple psychiatric consultations.

The desired antinuclear antibody (ANA) test for joint pain was granular three positive. Rheumatology consultation was requested with a preliminary diagnosis of systemic lupus erythematosus (SLE) to case who presenting with joint pain, oral aphthae, and malar rash. Anti-dsDNA (+), ENA profile (−), ANCA (−), VDRL (−), cryoglobulin (−), cryofibrinogen (−), direct coombs (−), protein electrophoresis, C3, C4, and biochemistry values were normal in the patient who was examined in rheumatology clinic. Desired rheumatoid factor value: 12.5 IU/mL, A cyclic citrullinated peptide antibody value: <0.5 U/mL and was within normal limits and the joint pain was higher in the hip, no pathology was detected in sacroiliac and hand magnetic resonance imaging (MRI). The case was initiated hydroxychloroquine with systemic lupus doubt by rheumatology. The patient's clinical follow-up continues. Informed consent was obtained from the patient for publication of this case report and images.

DISCUSSION

GDS is a clinical entity characterized by recurrent, painful, ecchymotic lesions affecting mostly young women. It is estimated that the true incidence of the disease, which is rare and reported as case reports in the literature, is higher [4].

Ecchymotic lesions are usually found in the arms and legs in GDS, but they can also occur in any part of the body [5]. In our case, recurrent lesions were more prone to appear in the legs.

In addition to skin ecchymoses, bleeding in organs such as respiratory system, digestive system, genitourinary system, ear, and eye have been reported in a limited number of cases [6]. In addition to skin lesions, patients who develop neurological symptoms such as headache, paresthesia, syncope attacks, blurred vision, and double vision are mentioned in the literature. Pain in the abdomen, chest, muscle, and joints can also be seen in patients. Patients often undergo extensive medical research with one or more of these symptoms, applying to more than one specialty (dermatology, hematology, rheumatology, psychiatry, etc.) [7]. In our case, abdominal and joint pain were described during attacks.

Ecchymotic lesions occur spontaneously, especially after emotional stress or mild trauma. Although the association of psychological factors with the disease has been reported, it is controversial whether this condition is primary or secondary to the anxiety and fear of the disease [3, 8]. In our case, no additional psychiatric comorbidity was detected in multiple consultations to psychiatry.

Hematological and immunological abnormalities such as anticardiolipin antibody positivity, SLE, low complement, immune complex nephritis, increased fibrinolytic activity, platelet dysfunction, and idiopathic thrombocytopenic purpura have been detected in some patients in addition to psychiatric comorbidities reported in GDS [9, 10]. The association with these diseases suggests that the disease may be caused by an autoimmune mechanism. It is also supported by the view that antibodies against phosphatidylserine in erythrocyte stroma cause GDS by causing immune complex and complement activation [3, 4, 9, 10]. In our case, ANA, anti-dsDNA, anti-microsomal, and anti-thyroglobulin antibodies were positive. Our patient with a definitive diagnosis of Hashimoto's disease was also being followed up with suspicion of SLE.

In the differential diagnosis of ecchymotic skin lesions in GDS, domestic violence, abuse, artifact dermatitis, idiopathic thrombocytopenic purpura, factor XIII deficiency, Henoch-Schonlein purpura, von Willebrand's disease, Pfeifer-Weber-Christian syndrome, Ehlers-Danlos syndrome, hematologic malignancies, and vasculitic diseases with cutaneous symptoms should be considered [3, 11]. Since the diagnosis of GDS is originally an exclusion diagnosis, it can be reached after a comprehensive history and laboratory study. To support the diagnosis, it is important to develop positivity in intradermal skin test with plasma obtained from the patient's own blood. However, it should not be forgotten that this cannot be observed in all patients [3, 4]. In our case, all the diseases in the differential diagnosis were excluded as a laboratory and the skin test was revealed a significant ecchymosis at the 30th min and the patient was diagnosed as GDS.

Gardner-Diamond syndrome has been reported 20 times more frequently in women than in men in the literature. It is most commonly seen in the 15–40 age range. In the female gender, this age range is the period in which many autoimmune diseases occur. Such female gender predominance in GDS indicates the effect of estrogen and autoimmunity on pathogenesis [3, 4, 9, 10, 12]. In our case, she was a 26-year-old female.

There is still no consensus on the optimal treatment of GDS. The focus is on the psychological component of the disease in the treatment of GDS in the literature. Selective serotonin reuptake inhibitors, tricyclic antidepressants, and psychotherapy are the most commonly used treatment options [5]. In addition, treatments such as antihistamines, corticosteroids, albumin infusion, calcium channel blockers, plasmapheresis, immunosuppressive therapy, anticoagulants, hormones, and Vitamin C have also been reported [5, 7, 13]. All these treatments may help relieve symptoms in patients but have not been shown to prevent GDS attacks. Some supportive treatments may be given to alleviate dermatological symptoms. In our case, mucopolysaccharide polysulfate cream treatment was applied to the lesions. In addition, ANA and anti-dsDNA positivity were started and hydroxychloroquine treatment was started by rheumatology.

CONCLUSION

Herein, we present a case of autoimmune disease and antibody positivity without psychogenic comorbidity to draw attention to autoimmunity in the pathogenesis of autoerythrocyte sensitization syndrome. As a result of this case presentation and mini-literature review, we think that autoimmunity patients should not be missed in GDS patients.

Informed Consent: Written informed consent was obtained from the patient for the publication of the case report and the accompanying images.

Conflict of Interest: No conflict of interest was declared by the authors.

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