Case Report

Recurrent self-healing painful ecchymoses and fever: a case of Gardner-diamond syndrome

Sachanidou M. G.,1 Arampatzis G. D.,1 Zioga A.,2 Gaitanis G.,1,2 Ioannis D. Bassukas1,2*

1Department of Skin and Venereal Diseases, Faculty of Medicine, School of Health Sciences, University of Ioannina, Ioannina, Greece
2Department of Dermatology, 3Department of Pathology Laboratory, University Hospital of Ioannina, Ioannina, Greece

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*Correspondence:  
Dr. Ioannis D. Bassukas,  
E-mail: ibassuka@cc.uoi.gr

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ABSTRACT

Gardner - Diamond syndrome (GDS) is a rare recurrent condition of painful ecchymoses without apparent eliciting factors. We report a 40-year-old woman with GDS without psychiatric comorbidity. She presented with, recurrent episodes of spontaneous, self-limiting corps of painful ecchymotic bruising and fever. Her medical history, physical and psychiatric examinations, a focused imaging work up and bone marrow biopsy were unremarkable; the skin biopsy excluded vasculitis. However, the erythrocyte autosensitization test was positive; a finding that together with history and clinico-laboratory results highly suggests GDS.

Keywords: Erythrocyte autosensitization test, Eryptosis, GDS

INTRODUCTION

Gardner - Diamond syndrome (GDS; synonyms: psychogenic purpura, autoerythrocyte sensitization syndrome, painful bruising syndrome) is seen predominantly in women and comprises painful ecchymoses without apparent eliciting factors.

Psychiatric background and autoreactivity to blood components are well known features of the disease, but the exact cause remains elusive.1,2

The sporadic reporting of GDS is in contrast to the wide geographic distribution and variable underlying background of reported cases, pointing towards a spectrum of conditions that comprise this "by exclusion" diagnosis. Herein, we report a woman with recurrent episodes of spontaneous, painful ecchymotic bruising finally diagnosed with GDS.

CASE REPORT

A 40-year-old woman was admitted to the Dermatology Department for spontaneous, symmetrical, edematous, painful bruises and ecchymotic purpuric lesions of her upper thighs, anterior shins and periorbitally [Figure 1(a)]. Fever (38.9°C) and cough heralded their appearance by three days. With the exception of the facial lesions, the patient reported three similar episodes the previous 16 years. On every occasion, no apparent eliciting factor, including physical trauma or stress could be identified and all episodes subsided within 15 days.

A cholecystectomy performed 3 years earlier did not elicit the clinical syndrome under investigation. Otherwise, medical history and physical examination were unremarkable. The patient was working in the family bakery and no underlying psychiatric signs could be discerned to warrant a specialist evaluation. Extensive
laboratory workout revealed increased white blood cell count (12.40x10^3/μl, neutrophils: 85.4%), C-reactive-protein (13 mg/L, normal<6 mg/L) and erythrocyte sedimentation rate (29 mm/h). Additionally, fibrinogen, factors II and IX were significantly increased (542 mg/dl, 134% and 129% respectively) with normal values in prothrombin time and partial thromboplastin time. Focused laboratory [Widal-Wright, Rose-Bengal and Coombs tests, Interferon Gamma Release Assay (IGRA)] and imaging work up (chest-X-ray, chest and abdominal CT scan, abdominal ultrasound) were unremarkable. A lesional skin biopsy was non-diagnostic; however, vasculitis or granulomatous diseases were ruled out (Figure 2). Under the hypothesis of GDS an intradermal erythrocyte autosensitization test was performed and turned out positive [Figure 1 (c, b)].

With the exception of paracetamol, no therapy was given, and fever subsided by day 12. The skin lesions gradually resolved during the next 15 days, following the well-known clinical course of a bruise. The patient was readmitted to the hospital a month later with a bout of fever (38.5°C) without skin lesions or other findings. This time a bone marrow biopsy was also performed which was unremarkable. She was discharged 3 days later without therapy and remains disease free during a 12-month follow-up.

The long periods of disease remissions, the absence of specific signs or findings, including a non-diagnostic skin biopsy and a positive erythrocyte auto-sensitization test favored the diagnosis GDS, despite the absence of overt psychiatric pathology in this case.

**DISCUSSION**

Erythrocyte autosensitization was a distinctive finding of this patient. A positive erythrocyte autosensitization test is a distinctive, though not characteristic finding of patients with GDS. The pathophysiological mechanism underlying the erythrocyte autosensitization in GDS is not known. Phosphatidylserine a phosphoglyceride of red blood cell membrane is considered to play an important pathogenesis of this condition. This hypothesis is based on the observation that the incubation of normal donor erythrocytes with plasma from GDS patients resulted in redistribution of phosphatidylserine to the erythrocyte surface heralding eryptosis, i.e. the spontaneous erythrocyte cell death. This alteration is proposed to promote the binding of damaged erythrocytes to vascular wall and activate platelets heralding the development of the characteristic ecchymoses of GDS. However, how psychological stress triggers febrile corpus of ecchymoses in GDS cases still remains elusive. Notably, the vast amount of triggers of phosphatidylserine redistribution and eryptosis points towards the existence of distinct subtypes of GDS.

**CONCLUSION**

In conclusion, GDS is a rare, yet exciting clinical condition. Functional studies of erythrocytes in well characterized GDS patients could provide important insights in the mechanisms that underlie eryptosis.
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