When a rheumatologist encounters a Gardner-Diamond syndrome

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Gardner-Diamond syndrome (GDS) or auto-erythrocyte sensitization syndrome is an extremely rare condition occurring prevalently in young women with psychiatric disorders. This syndrome was first described by Frank Gardner and Louis Diamond. It rarely affects children and males.[1,2] The clinical feature that makes it detectable for rheumatologists and dermatologists is the raised purple bump with a diameter of a few millimeters on the skin of the most sloping areas, like in immuno-mediated vasculitis. Moreover, other skin areas may also be affected.[3] The skin pattern mimicking vasculitis may typically progress to extensive ecchymotic lesions in the same areas like purpuric lesions over the next 24 h. The skin of the affected areas is very painful under palpation simulating a neuropathy as in *vasa nervorum* vasculitis. A typical feature of these ecchymotic lesions is their intense deep peri-wound edema which simulates the presence of a hematoma. Indeed, although GDS is a self-limited condition, its variable clinical presentation may mimic a variety of conditions that can make the *diagnosis challenging, as* idiopathic thrombocytopenic purpura, disseminated intravascular coagulation, von Willebrand disease, Henoch-Schönlein purpura, dermal angiitis, systemic lupus erythematosus, and Ehlers-Danlos syndrome.[4,5] The pathogenetic mechanism of GDS remains unclear, but the psychiatric co-morbidity seems confirmed to the extent that a central pathogenetic role may be assumed. Moreover, several cellular abnormalities have also been regarded as potential pathogenetic mechanisms in GDS. In particular, the complex interplay of autoimmune autosensitization to the phosphatidylserine of the erythrocyte membranes, capillary dysfunction and platelet disorders, dysregulation of kinin activity in response to emotional stress seem to play a major role in the development of GDS.[6-9] Phosphatidylserine, a component of the erythrocyte membrane bilayer and the myelin sheath, could represent one of the pathogenetic keys of this syndrome. Its IgE related allergenic role has been confirmed *in vitro*[10] and the possibility of a cross reaction towards this structural component of the nerves could theoretically create a neuropathic mechanism capable of explaining the intense pain of the affected skin areas as well as instability of the venous tone. It is still unclear why erythrocyte and lymphohistiocytic infiltrate characterize the histological pattern of purpuric lesions in GDS.[3] However, we could speculate that alterations of the neuro-immuno-endocrine axis associated with prodromal phases of severe and acute psyco-emotional disturbance in subjects with chronic psychic disorders may play a role in interfering with the regulatory tone and permeability of the vein system due to functional alterations of the kinin-kallicrein system in the endothelial site or to a structural constitutional defect of the endothelial wall. GDS is a diagnosis of exclusion, and there are no specific laboratory tests for this syndrome. Laboratory abnormalities of coagulation, the immune system and inflammation are not common, although they have been reported occasionally.[4-6] The diagnosis is most often made by injecting 0.1 mL of a suspension of autologous washed erythrocytes subcutaneously. It is considered positive, if the ecchymotic lesion occurs at the site of injection, as the antigen is thought to be phosphatidylserine of the red cell membrane.[4] There are no specific therapies in GDS. Corticosteroids and immuno-modulatory drugs are usually ineffective, thus confirming a non-inflammatory causal mechanism.[4-6] Meanwhile, many other therapeutic approaches were tried without success.[4-6] The results obtained with anti-depressant and anxiolytic drugs or with psycho-therapy are controversial for the control of the syndrome, although being necessary for the control of psychic distress. Despite its benign prognosis, a correct diagnosis may help prevent undue patient concerns and prescription of useless and potentially harmful treatments.

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References

1. Kurczynski EM, Cassidy JT, Heyn RM. Autoerythrocyte sensitization; a form of purpura producing painful bruising following autosensitization to red blood cells in certain women. Blood 1955;10:675-90.
2. Ivanov OL, Lvov AN, Michenko AV, et al. Autoerythrocyte sensitization syndrome (Gardner-Diamond syndrome): review of the literature. J Eur Acad Dermatol Venereol JEADV 2009;23:499-504.
3. Jafferany MMD, Bhattacharya GMD. Psychogenic purpura (Gardner-Diamond syndrome). Prim Care Companion CNS Disord 2015;17(1).
4. Edinger LK, Schwartzman RJ. Gardner-Diamond syndrome

associated with complex regional pain syndrome. J Dermatol Case Rep 2013;7:10.
5. Bellot A, Curien R, Derache A, et al. Oral management in a patient with Gardner-Diamond syndrome: a case report. Int J Surg Case Rep 2020;75:367-71.
6. Sridharan M, Ali U, Hook CC, et al. The Mayo Clinic experience with diagnosis and treatment of Gardner-Diamond syndrome. Am J Med Sci 2019;357:411-20.
7. Ratnoff OD. Psychogenic purpura (autoerythrocyte sensitization): an unsolved dilemma. Am J Med 1989;87(3N): 16N-21N.
8. Merlen JF. Ecchymotic patches of the fingers and Gardner-Diamond vascular purpura. Phlebologie 1987;40: 473-87.
9. Strunecka A, Krpejsova L, Palecek J, et al. Transbilayer redistribution of phosphatidylserine in erythrocytes of a patient with autoerythrocyte sensitization syndrome (psychogenic purpura). Folia Haematol (Leipzig, Germany: 1928) 1990; 117:829.
10. Silny W, Marciniak A, Czarnecka-Operacz M, et al. Gardner-Diamond syndrome. Int J Dermatol 2010;49:1178-81.