Benign atrophic papulosis as a paraneoplastic clinical marker

Abstract

Degos' disease is a rare vascular disorder with a cutaneous-limited form - benign atrophic papulosis, and a systemic variant - malignant atrophic papulosis. The aetiology of this condition is unknown. The cutaneous signs – papular skin lesions with central porcelain-white atrophy and surrounding telangiectatic rim – are pathognomonic. Extracutaneous, systemic involvement includes multiple limited infarcts of the gastrointestinal system, central nervous system and other organs. Here, we report a patient with cutaneous manifestation of Degos disease associated with a squamous cell carcinoma of the lung. The patient had no other internal organs involvement. Benign Degos' disease is anecdotally rare, and no other association with neoplastic conditions have been reported, to date. A speculation of the possible common pathogenetic pathways is also presented.

Keywords: *Degos' disease, malignant atrophic papulosis, benign atrophic papulosis, neoplasia*

Introduction

Kohlmeier–Degos' disease or Degos disease, is a rare disorder of thrombo-obliterative vasculopathy (1). Two clinical subtypes have been described according to the underlying systemic involvement: malignant atrophic papulosis (MAP) and the cutaneous-limited form - benign atrophic papulosis (BAP). The malignant form affects skin, gastrointestinal system, and central nervous system, while the benign atrophic papulosis is strictly limited to the skin (2,3). The lesions begin as umbilicated papules and then quickly evolve into characteristic ''porcelain-white'' atrophic scars surrounded by an erythematous telangiectatic border (4).

Herein, we present a case of BAP in a patient with squamous cell carcinoma of the lung. The speculation on the predictive role of skin manifestations as a prodromal paraneoplastic syndrome is suggested.

Case report

A 67-year-old male patient came to our department with erythematous papules, some with central, porcelain-white colored umbilication, surrounded by telangiectatic erythema that affected the trunk and upper extremities. The skin lesions appeared episodically in the last 2 years. Some formed central necrosis and haemorrhagic crusts, leaving atrophic scars. The patient had a history of right lobectomy of a squamous cell carcinoma of the lung dated 6 months ago. No other systemic involvement was detected. Laboratory evaluation revealed low red blood cells 3,59.10^12/l (normal range 4,6 - 6,2.10^12/l), low level of haemoglobin 104.0 g/l (normal range 130 - 180 g/l), an elevated platelets 461.0 10^9/l (normal range 140 - 440.10^9/l) and elevated eosinophils 0,92.10^9/l (normal range 0,04 – 0,54.10^9/l). The coagulation status showed elevated D-dimer 1,79 µg/ml (normal range 0 – 0,5 µg/ml) and high prothrombin time sec – 14,9 sec (normal range 10 – 14 sec). C-reactive protein (CRP) -

7,5 mg/l (normal range 0 – 5.0mg/l) and Lactate dehydrogenase (LDH) – 427.0 U/l (normal range 208 – 378 U/l) were also increased. The immunology work-up demonstrated negative direct immunofluorescence, ANA, anti- Ro and anti- ds DNA antibodies.

The histologic findings showed orthohyperkeratosis, atrophic epidermis, diffuse vacuolar degeneration of the dermo-epidermal junction by a severe lichenoid lympho-histiocytic infiltrate, and obliterated small vessels with adjacent lymphocytic inflammation in deep dermis.

The clinical, laboratory and histopathological constellation suggested cutaneous-limited form of atrophic papulosis. Pentoxyphillin 200 mg twice daily on a continuing everyday basis was introduced to the patient.

Discussion

Degos' disease is a monomorphic polyetiological syndrome, denominated by porcelain-white papules, spontaneously evolving into atrophic scars, usually distributed on the trunk and upper extremities. The disease was first described as a multisystemic disorder of a diffuse popular skin eruption and intestinal infarctions that usually followed a lethal course. Approximately, 200 to 300 cases of atrophic papulosis have been described worldwide. Among them, 15% experienced a long-term survival, remaining strictly limited to the skin. Adults in their 2-5 decade are usually affected with a slight female preponderance (3).

The pathogenesis of Degos disease remains obscure. Three main hypotheses exist, which suggest a coagulation disorder, autoimmune syndrome, and infection. No enough data is accumulated to differentiate specific laboratory constellation, which may further enlighten the exact aetiology (4). Histological findings are also not fully consistent encompassing a spectrum of vascular changes, ranging from pure perivascular inflammation to true lymphocytic vasculitis with thrombotic obliteration (5). Hence, there are also several reports of familial involvement and increased incidence in first-degree relatives, suggests a possible genetic contribution (6, 7). Meanwhile, cases of Degos disease have been reported in various clinical scenarios including following streptococcal infection, during pregnancy, associated with Behçet's disease, lymphocytic vasculitis and lichen sclerosus-like features, and in a patient with acquired immunodeficiency syndrome (8,9).

To date, no association of atrophic papulosis with a neoplastic disorder has been reported. Our patient suffered of periodically evolving crops of atrophic skin papules approximately an year before the detection of his pulmonary cancer (10). Interestingly, upon appropriate chest surgery and adjuvant radiotherapy, he claimed to have less common and less intense relapses of his skin eruption. Therefore, a speculation that tumor-derived growth factors and coagulation mediators which either enhance thrombotic activity or cause endothelial dysfunction in the small- and medium sized vessels of the dermis is suggested (11).

The skin lesions appear initially as small erythematous papules of 2 – 15 mm in diameter. After a few days the centre start to depressed and resolve by leaving an atrophic area of porcelain-white colour (12). This atrophic area may be defined by a border of erythema or may include telangiectasias. The lesions are usually found on the trunk and upper extremities, but other locations such as palms, soles, scalp, and face are infrequently involved (13). MAP is potentially life-threatening form, because affects inner organs such as the gastrointestinal, ocular, pulmonary, cardiovascular and renal systems. The systemic manifestations can be

followed in many cases by serious complications like bowel perforation, peritonitis, thrombosis of the cerebral arteries or massive cerebral hemorrhage, meningitis, encephalitis, radiculopathy, myelitis. Lung involvement can be followed by pleuritis and/or pericarditis (14). This leads to a severe and fatal prognosis with an overall lethal rate of 50% up to the second year of diagnosis. In patients with only skin lesions, but no internal organ involvement, the prognosis is usually better (15, 16)

In early lesions the histological features include superficial and deep perivascular lymphocytic infiltration, with distinct mucin deposition, which resembled lupus erythematosus. The fully developed lesions had more prominent changes in the dermo-epidermal junction, with atrophy of the epidermis and an area of sclerosis in the papillary dermis. The late lesions showed a wedge-shaped necrosis, lymphocytes and less mucin deposition in comparison to the early and fully developed lesions (17).

There is still no effective treatment for Degos' disease because of the lack of knowledge of Degos' pathophysiology. Anticoagulants, antithrombosis treatment and fibrinolysis agents, which support the blood perfusion, have successful results and regression of skin lesions in single cases (18). Eculizumab improves the skin and intestinal lesions, but do not prevent of the development and progression of the disease. In a patient with eculizumab-resistant Degos disease with intestinal and cerebral manifestations subcutaneous Treprostinil is used (1).

Conclusions

We believe to present an anecdotal case of paraneoplastic benign form of Degos' disease, which emphasize the importance of early correct diagnosis and consecutive thorough work-up in all patients with atrophic papulosis. Early finding of organ involvement may prevent complications and following mortality.

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Figures

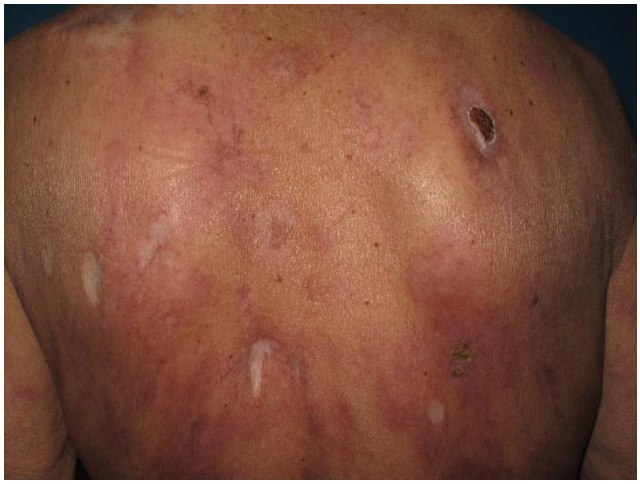

Fig.1 Skin lesions with well-defined, porcelain-white atrophic centre and a surrounding erythematous rim on the trunk

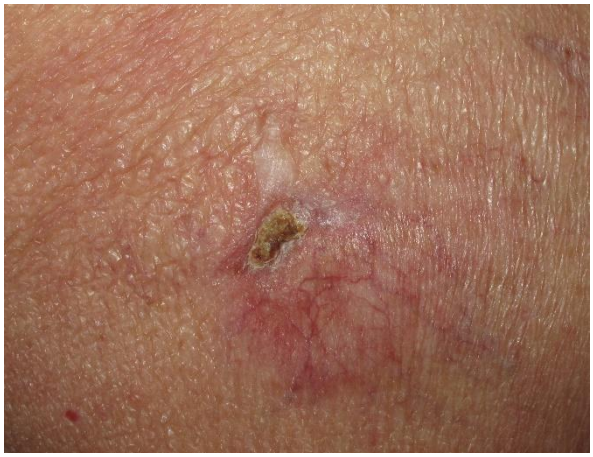

Fig.2 A closer view of atrophic, umbilicated papule covered with haemorrhagic crusts, located on the upper extremity

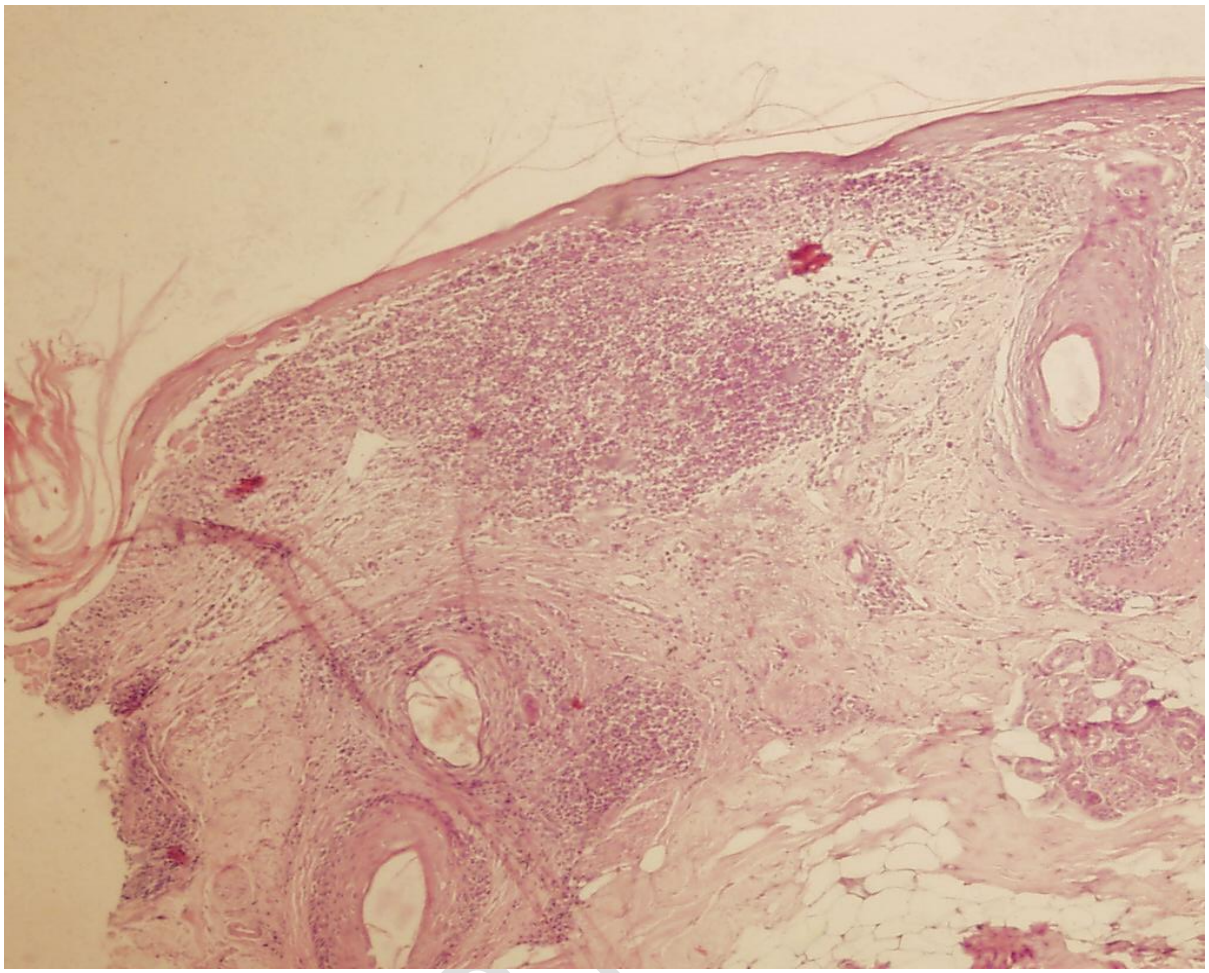

Fig. 3 Orthohyperkeratosis, atrophic epidermis, diffuse vacuolar degeneration of the dermo-epidermal junction by a severe lichenoid lympho-histiocytic infiltrate, and obliterated small vessels with adjacent lymphocytic inflammation in deep dermis (H&E, x 100)