

CASE REPORT

Diabetes mellitus and Degos disease

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Abstract: We present the case of a 75-year-old man who was diagnosed with Degos disease (DD) in the context of type 2 diabetes mellitus. The cutaneous lesions of DD were located at the trunk as well as in the proximal parts of the arms. He presented with positive laboratory test for lupic anticoagulant, but other rheumatologic parameters of interest were within normal limits. The skin biopsy corroborated the diagnosis of DD, and also showed morphologic features traditionally associated to hyaline diabetic microangiopathy. Since the latter has recently been attributed to C5b-9 deposit in the vessel wall, we discuss if both conditions are pathogenetically connected or just coincidental (Fig. 3, Ref. 32). Full Text (Free, PDF) www.bmj.sk. Key words: diabetes mellitus, Degos disease, C5b-9; hyaline vasculopathy, hyaline arteriosclerosis.

Case report

A 75-year-old man came to the consultancy of dermatology clinic complaining of multiple cutaneous lesions that had appeared two years ago. They were temporarily pruriginous, evolving into spontaneously resolving lesions. These disappeared without any scars while new lesions appeared. They were located at the trunk as well as on the proximal parts of the arms (Fig. 1, top). There was no neurological or gastrointestinal symptomatology, and the rest of the examination was anodyne. The patient had been diabetic (type 2; adult type) since three years ago. He also had high blood pressure, but had refused to have any medical treatment until one year ago, when he accepted to receive oral antidiabetics (Repaglinide) and Amlodipine. Additionally, the patient was receiving acetylsalicylic acid (100 mg/day).

Laboratory tests were within normal limits, and serum anti-nuclear antibodies as well as lupus anticoagulant and anticardiolipin antibodies (both IgG and IgM), were negative in the first analysis.

The cutaneous lesions were 6 to 12 mm in diameter, and had a reddish telangiectatic border with a whitish atrophic center (Fig. 1, bottom). Many of them had a thick squamous center that could easily be removed. Mucous membranes were not involved.

Biopsy of one of the lesions from the trunk was performed, and showed a wedge-like zone of dermal acellular necrosis, with bullous change underneath an atrophic epidermis (Fig. 2, top).

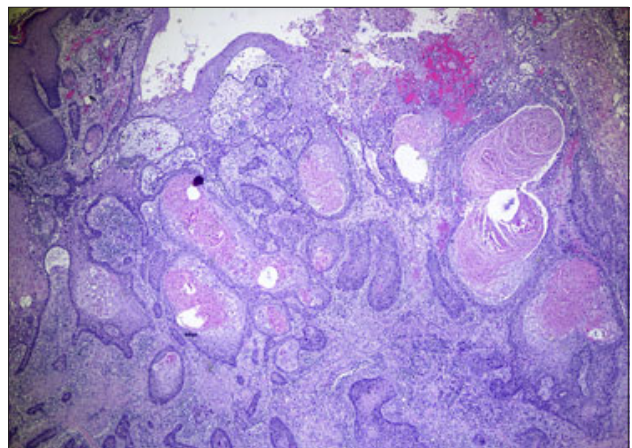
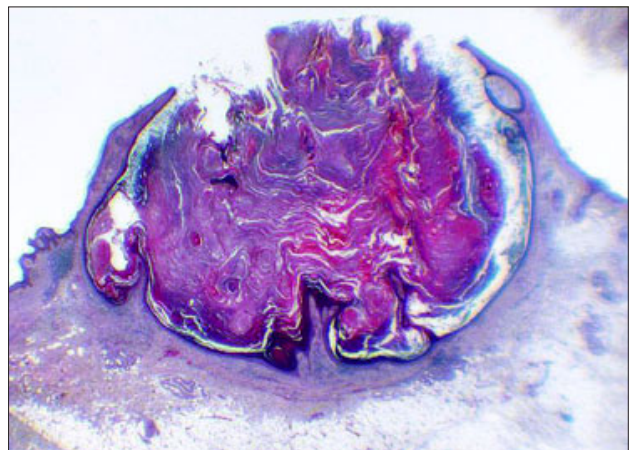


Fig. 1. Top: Lateral view of the patient with multiple papules on trunk and arms. Bottom: Closer view of the lesions, showing an erythematous border, and a central whitish necrotic area.

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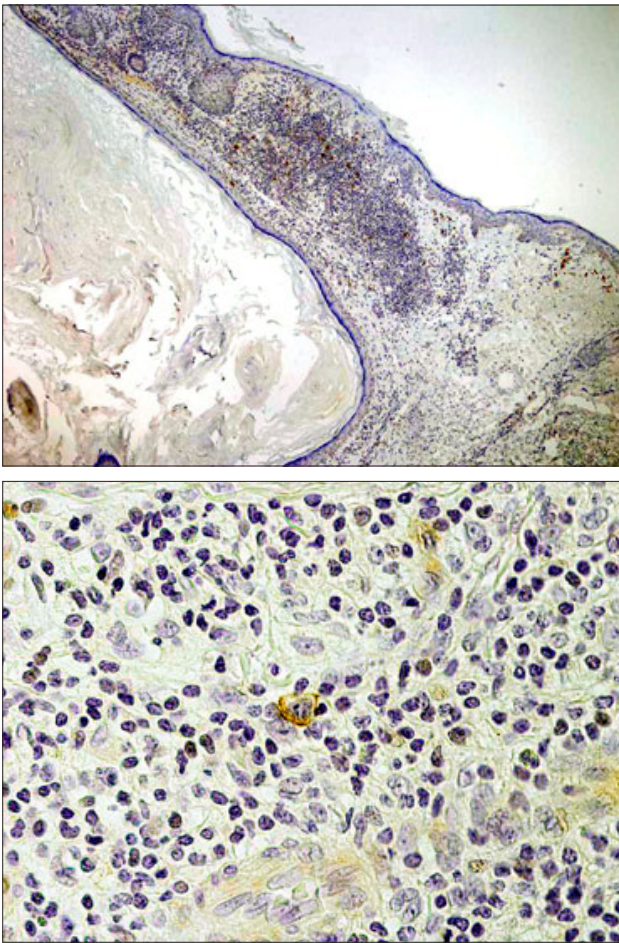


Fig. 2. Top: Panoramic histopathologic view of one of the lesions, showing a V-shaped necrotic dermal area, with bullous change underneath the atrophic epidermis. Bottom: Perivascular inflammatory infiltrate, with fibrinoid material in the wall of the vessel.

There was hyperkeratosis over the atrophic area. The immediate adjacent epidermis showed prominent interface vacuolar change. A superficial and deep perivascular and periadnexal lymphocytic infiltrate was seen with focal reduction of the lumen and deposit of fibrin in the vessel wall (Fig. 2, bottom). An additional finding was the evidence of hyaline thickening in superficial and deep arterioles (Fig. 3, top), with positivity for histochemical stain of Schiff-Peryodic-Acid (Fig. 3, bottom). Congo-Red and immunostaining for Collagen-IV were both negative. Mild perineural lymphocytic infiltrate could also be seen. There was no dermal mucin deposit, even after staining with Alcian-blue.

Lupus anticoagulant determination was repeated four months later and a positive result was obtained this time.

Discussion

The present case raises the question if both conditions (Degos disease plus diabetes) were coincidental or the contrary, pathogenically related.

For Degos disease (DD), three main pathogenic mechanisms have been proposed in the literature: a coagulopathy (1–4), a vasculitis (5–7), or an endothelial-cell disorder (1). All of them have the occlusion of the vessel in common (8). So much so, that some voices have proposed DD as nothing more than a pattern, rather than a specific disease (9).

On the other hand, circulating anti-phospholipid antibodies (APA) have been related to DD in recent literature, and some have claimed that if patients with DD had been tested for anti-phospholipid antibodies (which was not practically possible until the 1980's), many of them would have had high titers (9). Although, this has been true in some reported cases (10–13), it has been far from being a rule (14–18). Even some cases of DD, with morphologic findings which were very suggestive of lupus, did not show antiphospholipid antibodies (18). Nevertheless, the revised criteria for the antiphospholipid syndrome (APS), which were published in 2006, include as a main criterion the presence of antibodies to beta₂-glycoprotein I (9), that should be tested in all cases in which APS has to be excluded (20). This new criteria

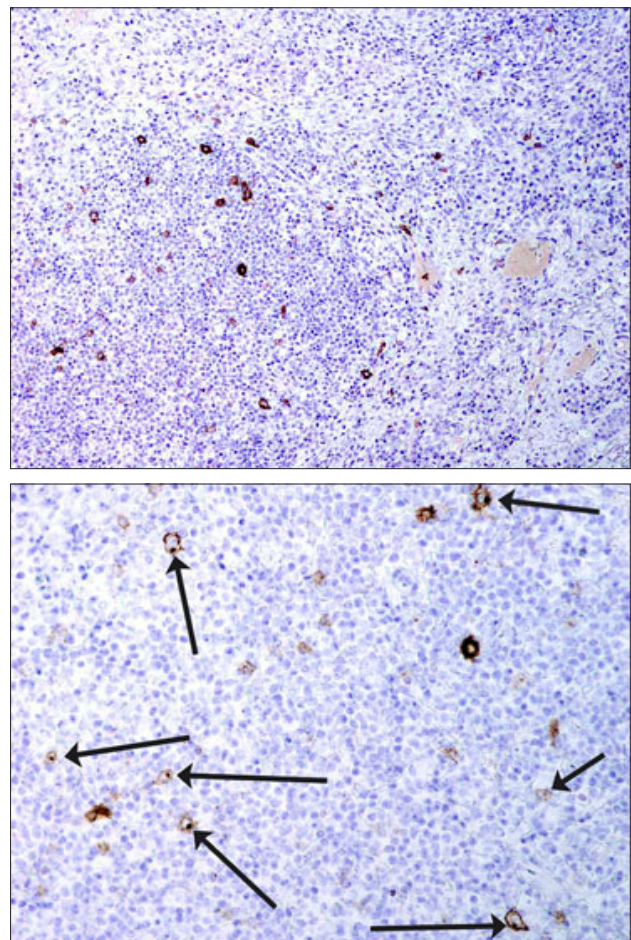


Fig. 3. Top: Hyaline arteriolosclerosis in the dermal vessels from the bioptic sample, which was highly remarked after staining for PAS (Bottom).

will probably help us in the future to clarify if the relation between APS and DD is as close as expected.

On the other hand, in association with diabetes mellitus (DM), cutaneous vascular deposition of C5b-9 has recently been described (21). Although it is alleged that the basis of C5b-9 deposits is not immune in DM, and the authors admit that they have no evidence about C5b-9 as a causal factor in the diabetic microangiopathy, they also mention some studies which suggest a pathogenic role for C5b-9 in the setting of dermatomyositis (22–24).

In the recent literature, some findings seem to indicate that there is a link between APA-mediated thrombosis and complement activation (25), specifically C3 and C5. For instance, some evidence that APA-dependent platelet destruction is mediated by C5b-9 has been found (26). Also, murine models with a deficiency in C5a receptor are protected from thrombophilia induced by APA (27). It seems that in these examples, C5b-9 is the product from the action of the APA rather than a triggering factor of those antibodies, but it does not contradict the fact that in a setting of abundant tissue C5b-9, a high response to low levels of APA could be the outcome. One wonders then, why cases of DD secondary to diabetes are not more often in literature. It can be argued that other hyaline cutaneous vasculopathies, such as some variants of livedo vasculitis (LV), are defined as secondary to diabetes (28), and in fact, some consider DD as nothing more than a type of LV (16). There is also a case in the literature of DD associated with DM (29) in which the most relevant fact was that DD coincided with a spontaneous cure of diabetes. Nevertheless, there are some astonishing points in that report, such as the fact that DD dramatically improved with corticoids (a non-usual event in the behaviour of DD). It was also surprising that there was no diabetic impact on the renal biopsy of their patient, in spite of a 13 year history of diabetes, which needed insulin to be controlled. No vascular widening of the vessels is commented by the authors either, when describing the skin biopsies.

On top of that, there are several reports in which DM is coincidental to APA (30–32), and thrombosis already occurred in these examples when the diagnosis of APS was established.

Again, we wonder if the setting of the complement deposit in the vessel walls could be an exacerbating factor in the action of the APA.

References

1. Black MM, Nishioka K, Levene GM. The role of dermal blood vessels in the pathogenesis of malignant atrophic papulosis (Degos' disease). *Brit J Dermatol* 1973; 88 (3): 213–219.
2. Páramo JA, Rocha E, Cuesta B, Arejola JM, Montejó M, Aguirre J, Prieto J, Rocha Hernando E. Fibrinolysis in Degos' disease. *Thromb Haemost* 1985; 54 (3): 730.
3. Vázquez-Doval FJ, Ruiz de Erenchun F, Paramo JA, Quintanilla E. Malignant atrophic papulosis. A report of two cases with altered fibrinolysis and platelet function. *Clin Exp Dermatol* 1993; 18 (5): 441–444.
4. Katz SK, Mudd LJ, Roenigk HH. Malignant atrophic papulosis (Degos' disease) involving three generations of a family. *J Amer Acad Dermatol* 1997; 37 (3 Pt 1): 480–484.
5. Naylor D, Mullins JF, Gilmore JF. Papulosis atrophicans maligna (Degos' disease): report of the first United States case and review of the literature. *Arch Dermatol* 1969; 81 (Feb): 189–197.
6. Su WPD, Schroeter AL, Lee DA, Hsu T, Muller SA. Clinical and histologic findings in Degos' syndrome (malignant atrophic papulosis). *Cutis* 1985; 35 (2): 131–138.
7. Soter NA, Murphy GF, Mihm MC Jr. Lymphocytes and necrosis of the cutaneous microvasculature in malignant atrophic papulosis: a refined light microscope study. *J Amer Acad Dermatol* 1982; 7 (5): 620–630.
8. High WA, Aranda J, Patel SB, Cockerell CJ, Costner MI. Is Degos disease a clinical and histological end point rather than a specific disease? *J Amer Acad Dermatol* 2004; 50 (6): 895–899.
9. Ball E, Newburger A, Ackerman AB. Degos' disease is a distinctive pattern, chiefly of lupus erythematosus, and not a specific disease. *Dermatopath Pract Conc*. 2001; 7. Available at: <http://>. Accessed October 17, 2007.
10. Farrell AM, Moss J, Costello C, Fearfield LA, Woodrow D, Bunker CB. Benign cutaneous Degos' disease. *Brit J Dermatol* 1998; 139 (4): 708–712.
11. Bogenrieder T, Kuske M, Landthaler M, Stolz W. Benign Degos' disease developing during pregnancy and followed for 10 years. *Acta Derm Venereol* 2002; 82 (4): 284–287.
12. Englert HJ, Hawkes CH, Boey ML, Derue GJ, Loizou S, Harris EN, Gharavi AE, Hull RG, Hughes GR. Degos' disease: association with anticardiolipin antibodies and the lupus anticoagulant. *Brit Med J* 1984; 289 (6445): 576.
13. Mauad T, De Fátima Lopes Calvo Tiberio I, Baba E, Andrade Junior DR, Lichtenstein A, Capelozzi VL, Sotto MN, Saldiva PH. Malignant atrophic papulosis (Degos' disease) with extensive cardiopulmonary involvement. *Histopathology* 1996; 28 (1): 84–86.
14. Zamiri M, Jarrett P, Snow J. Benign Cutaneous Degos disease. *Int J Dermatol* 2005; 44 (8): 654–656.
15. Coskun B, Saral Y, Cicek D, Ozercan R. Benign cutaneous Degos' disease: a case report and review of the literature. *J Dermatol* 2004; 31 (8): 666–670.
16. Requena L, Fariña C, Barat A. Degos disease in a patient with acquired immunodeficiency syndrome. *J Amer Acad Dermatol* 1998; 38 (5 Pt 2): 852–856.
17. D'Avino M, Lo Schiavo A, Baroni A, Buommino E, Ruocco E. Degos' disease: a case with cutaneous lesions only: absence of paramyxovirus by PCR. *Dermatol* 2000; 201 (3): 278–279.
18. Grilli R, Soriano ML, Izquierdo MJ, Fariña MC, Martin L, Manzarbeitia F, Requena L. Panniculitis mimicking lupus erythematosus profundus. *Amer J Dermatopathol* 1999; 21 (4): 365–368.
19. Miyakis S, Lockshin MD, Atsumi T, Branch DW, Brey RL, Cervera R, Derksen RH, DE Groot PG, Koike T, Meroni PL, Reber G, Shoenfeld Y, Tincani A, Vlachoyiannopoulos PG, Krilis SA. International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). *J Thromb Haemost* 2006; 4 (10): 295–306.
20. Lockshin MD. Update on antiphospholipid syndrome. *Bull NYU Hosp Joint Dis* 2006; 64 (1–2): 57–59.
21. Vasil KE, Magro CM. Cutaneous vascular deposition of C5b-9 and its role as a diagnostic adjunct in the setting of diabetes mellitus and porphyria cutanea tarda. *J Amer Acad Dermatol* 2007; 56 (1): 96–104.

22. **Crowson AN, Magro CM.** The role of microvascular injury in the pathogenesis of cutaneous lesions of dermatomyositis. *Hum Pathol* 1996; 27: 15—19.
23. **Magro CM, Crowson AN.** The immunofluorescent profile of dermatomyositis: a comparative study with lupus erythematosus. *J Cutan Pathol* 1997; 24 (9): 543—552.
24. **Vilas AP, Fiuza T.** Classic/amyopathic dermatomyositis. *Acta Med Port* 2000; 13 (5—6): 287—294.
25. **Redecha P, Tilley R, Tencati M, Salmon JE, Kirchhofer D, Mackman N, Girardi G.** Tissue factor: a link between C5a and neutrophil activation in antiphospholipid antibody induced fetal injury. *Blood* 2007; 110 (7): 2423—2431.
26. **Stewart MW, Etches WS, Gordon PA.** Antiphospholipid antibody-dependent C5b-9 formation. *Brit J Haematol* 1997; 96 (3): 451—457.
27. **Romay-Penabad Z, Liu XX, Montiel-Manzano G, Papalardo De Martínez E, Pierangeli SS.** C5a receptor-deficient mice are protected from thrombophilia and endothelial cell activation induced by some antiphospholipid antibodies. *Ann N Y Acad Sci* 2007; 1108 (June): 554—566.
28. **Stevanovic DV.** Atrophic blanche: a sign of dermal blood occlusion. *Arch Dermatol* 1974; 109 (6): 858—862.
29. **Salomon MI, Mandel EH, Gallo G.** Degos' disease associated with a "spontaneous cure" of diabetes. *J Amer Geriatr Soc* 1971; 19 (11): 923—932.
30. **Manzanares JM, Conget I, Rodríguez-Villar C, Tassies D, Fernandez-Fernandez F, Cervera R, Levy I, Gomis R.** Antiphospholipid syndrome in a patient with type I diabetes presenting as retinal artery occlusion. *Diabet Care* 1996; 19 (1): 92—94.
31. **Li HY, Yang W-S, Tai T-Y, Chuang LM.** A diabetic subject with MELAS and antiphospholipid syndrome. *Diabet Care* 2003; 26 (7): 2218—2219.
32. **Kim CS, Kim DM, Park JS, Nam JY, Ahn CW, Cha BS, Lim SK, Kim KR, Lee HC.** A case of primary antiphospholipid syndrome and type 2 diabetes mellitus with large artery thromboses successfully treated by abdominal stent implantation. *Diabet Med* 2004; 21 (11): 1258—1259.

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