

A case of Degos disease successfully treated with corticosteroid combined with cyclophosphamide

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Abstract Degos disease is a rare disorder characterized by systemic vasculitis involving various organs. There is no established, effective treatment for the disorder, and its prognosis is still poor. Combination therapy with corticosteroid and cyclophosphamide is considered effective for vasculitides involving the small arteries such as ANCA-associated vasculitis. We present here a 42-year-old man who developed Degos disease over several months, and was successfully treated using combined treatment with corticosteroid and cyclophosphamide.

Keywords Degos disease · Corticosteroid · Cyclophosphamide

Introduction

Degos disease, or malignant atrophic papulosis, is a rare systemic vaso-occlusive disease of uncertain etiology. There are two distinct forms for Degos disease. The benign form features characteristic eruptions of small reddish papules limited to the skin, while the malignant form is characterized by multiple infarctions in the skin and systemic organs, especially in the gastrointestinal tract and nervous system [1, 2]. Pathologically, Degos disease is characterized by necrotizing vasculitis with endothelial proliferation of the small arteries or arterioles [3]. There is

no established treatment of Degos disease. Some case reports suggest that the prognosis of the malignant form is very poor. It is usually fatal within 2–3 years from the onset of systemic involvement [1].

Notably, patients with ANCA-associated vasculitides (AAV), such as microscopic polyangiitis (MPA), Wegener's granulomatosis (WG), and Churg-Strauss syndrome (CSS), are usually treated with a combination of corticosteroid and/or cyclophosphamide [4–6].

We report a case of Degos disease successfully treated with combined corticosteroid and cyclophosphamide.

Case report

A 42-year-old Japanese man presented with multiple pink papules without pain and itching on the dorsal surface of both hands and inferior limbs. After a few weeks, these papules exhibited umbilication and crusting with blood (Fig. 1a). Around the same time, he developed a high fever and severe abdominal pain with melena. He was admitted to a local hospital in June 2008. Physical examination revealed severe emaciation and abdominal tenderness with guarding. Laboratory examination revealed severe leukocytosis and elevation of serum C-reactive protein (CRP) level. In addition, abdominal computed tomography (CT) revealed segmental thickening of the small intestinal tract wall with ascites (Fig. 2a, b). He was diagnosed with peritonitis, and emergent resection of a portion of the small intestine was performed. Macroscopic examination of the small intestine revealed severe congestion with multiple ulcers (Fig. 3a). Four days after surgery, he suffered melena without abdominal pain again. Abdominal CT study was performed, and revealed a newly developed region of the small intestine which had been considered nearly intact on the last CT

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Fig. 1 **a** Multiple papules exhibiting umbilication and crusting with blood on the dorsal surface of the hand and lower limbs. **b** Ulceration with parakeratosis, abscesses, and altered collagen fibers. (H.E. stain $\times 4$) **c**, **d** Perivascular lymphocytic infiltration in the upper dermis. (H.E. stain $\times 10$, $\times 40$)

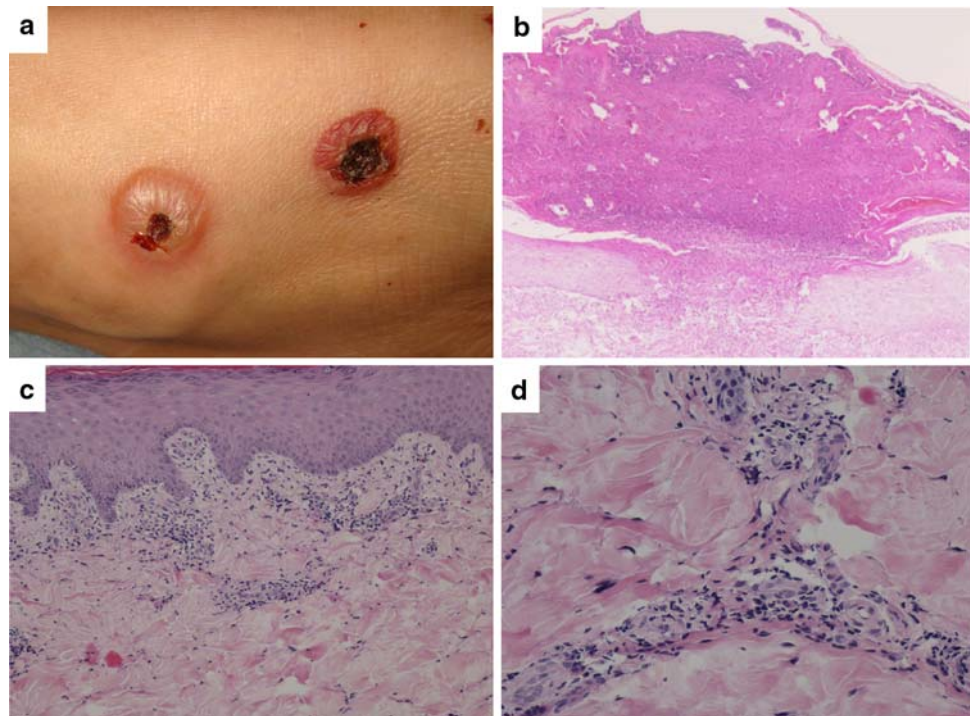
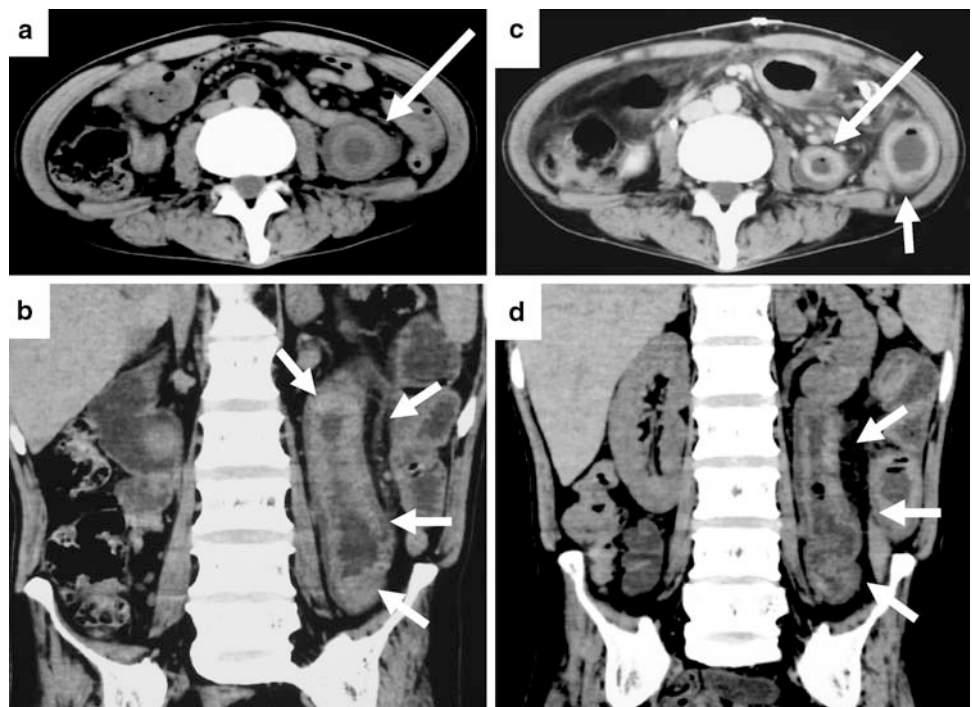


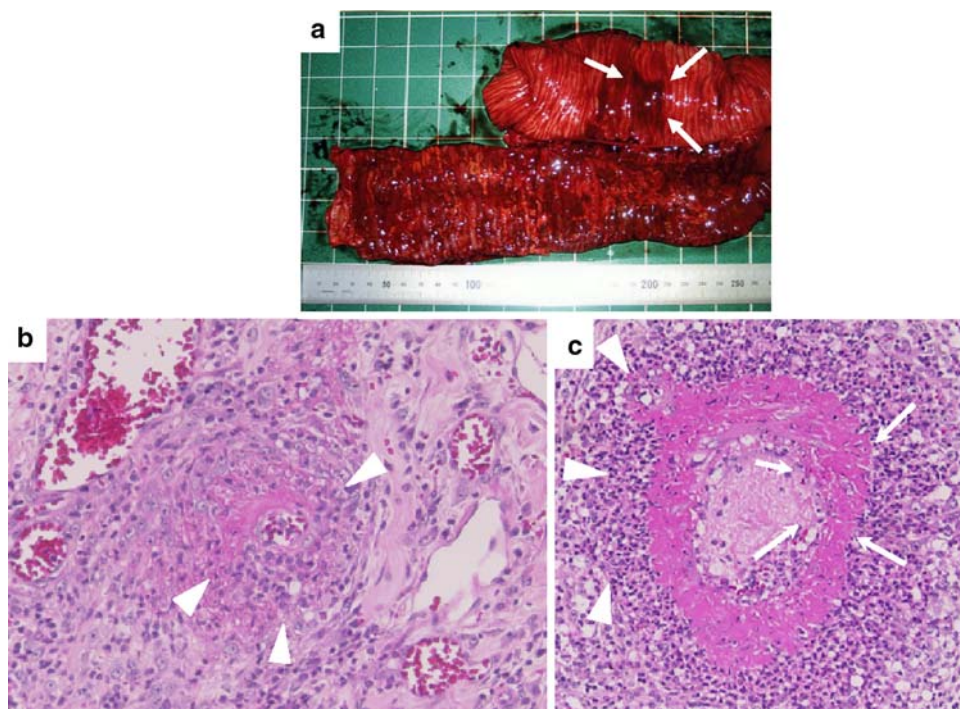
Fig. 2 Abdominal CT findings. **a**, **b** Thickening of small intestinal wall (*arrow*). **c**, **d** Thickening of remaining small intestinal wall on day 4 after surgery (*arrow*)



examination performed at the time of abdominal surgery (Fig. 2c, d). He was transferred to our hospital to determine the etiology of his condition. Pathologic examination of the resected intestinal specimen revealed necrotizing vasculitis of small- to medium-sized arteries with hemorrhage in the submucosa and desquamated epithelium (Fig. 3b, c).

Multiple thrombi were also demonstrated in arterioles. He was on no medications before this event occurred. There was no relevant family history. On admission to our hospital, emaciation and left drop foot were noted, in addition to characteristic papules. Results of laboratory examination were as follows: serum CRP level 3.4 mg/dl (normal range:

Fig. 3 **a** Congested small intestine with ulceration (*arrow*). **b, c** Infiltration by inflammatory cells (*arrowhead*) and fibrinoid degeneration (*arrow*) in the walls of small- to medium-sized arteries. (H.E. stain $\times 40$)



<0.2 mg/dl), total protein (TP) level 4.6 g/dl (normal range: 6.5–8.2 g/dl), albumin 1.6 g/dl (normal range: 3.5–5.5 g/dl), white blood cell count $129.5 \times 10^2/\mu\text{l}$ (normal range: $47\text{--}87 \times 10^2/\mu\text{l}$), red blood cell count $369 \times 10^4/\mu\text{l}$ (normal range: $400\text{--}540 \times 10^4/\mu\text{l}$), hemoglobin 10.0 g/dl (normal range: 13.0–17.0 g/dl), plasma fibrinogen 480 mg/dl (normal range: 200–400 mg/dl), plasma D-dimer 36.5 $\mu\text{g/ml}$ (normal range: <1.0 $\mu\text{g/dl}$), and plasma fibrin degradation products (FDP) 43.5 $\mu\text{g/dl}$ (normal range: <4.0 $\mu\text{g/dl}$). Findings of other biochemical and immunological blood tests and platelet counts were within normal limits. We performed skin biopsy of the pink papules with ulceration on his lower limb. The specimen exhibited ulceration with parakeratosis, abscesses, and altered collagen fibers, along with perivascular lymphocytic infiltration in the upper dermis without mucin (Fig. 1b, c, d). The diagnosis of Degos disease was made based on the characteristic papules, clinical course, and histopathological findings. He received two doses of weekly methylpredisone (m-PSL) pulse therapy and intravenous cyclophosphamide (IVCY) in addition to anticoagulation therapy using heparin (continuous administration) and salpogralate (Fig. 4). By 1 month after initiation of treatment, abdominal manifestations including melena had disappeared, and abdominal CT revealed improvement of thickening of the small intestinal wall and ascites. The neurological manifestations of vasculitis also gradually recovered, and PSL was tapered from 40 mg/day. He is now doing well as an

outpatient. There has been no significant relapse of vasculitis.

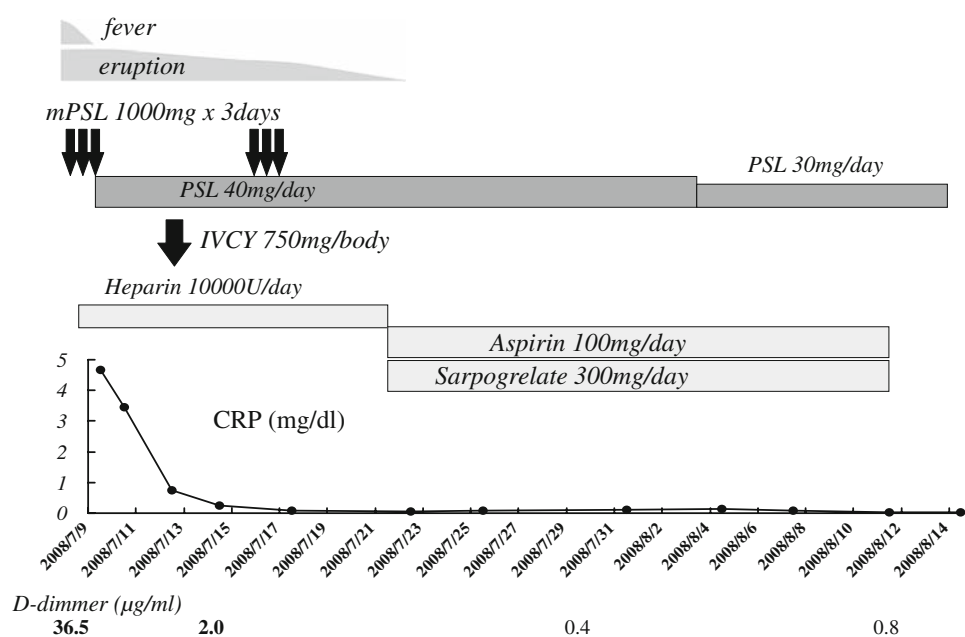
Discussion

Degos disease (malignant atrophic papulosis) was first reported in 1941 by Kohlmeier [7]. One year later (in 1942), Degos et al. described Degos disease [1]. Since the first report, approximately 200 cases of Degos disease have been published.

The etiology of Degos disease is unknown, though suggested causes of it have included infection, genetic predisposition, and autoimmune and coagulation disorders [8]. Some reports discuss the mechanism of vasculitis associated with thrombosis and infarction [8–11]. Heymann suggested reclassification of Degos disease as follows: (1) classical Degos disease with systemic manifestations, further sub-classified as autoimmune, coagulopathy-associated or virally induced; and (2) benign cutaneous Degos disease [12]. The present patient had no evidence of infection. Furthermore, coagulation studies including measurement of anti-cardiolipin antibodies and antithrombin did not reveal abnormal levels. The present patient thus appears to have had Degos disease associated with autoimmune disorder.

Degos disease usually presents in the skin. The initial skin lesions are small, firm erythematous papules or

Fig. 4 Clinical course. He received two doses of weekly methylprednisolone (m-PSL) pulse therapy and intravenous cyclophosphamide (IVCY) in addition to anticoagulation therapy



nodules. These lesions become umbilicated, with their central zone turning matte-white or porcelain-like. Weeks, months, or years after the appearance of skin lesions, patients may develop systemic manifestations [1].

Systemic involvement occur in the gastrointestinal (GI) tract, central nervous system (CNS), eye, heart, kidneys, liver, prostate, gallbladder, and spleen. GI perforation and CNS involvement in particular are associated with a poor prognosis; such patients usually die within several months.

There is no recognized treatment for Degos disease. Anticoagulants such as heparin or fibrinolytic agents are the agents most likely to inhibit the progression of Degos disease. In addition, antiplatelet agents can prevent platelet aggregation prior to thrombus formation. However, these agents are not effective in all cases. Corticosteroids and some immunosuppressants such as methotrexate, azathioprine, and chloroquine have also not been effective for Degos disease [8, 13]. The mortality of Degos disease is high, according to some reports published in the past few years. Zho et al. reported successful treatment using high-dose intravenous immunoglobulin (IVIG) infusion in a patient with Degos disease [14].

We treated our patient with cyclophosphamide combined with corticosteroid, since Degos disease is pathologically a vasculitis. Within 2 weeks, his cutaneous manifestations were improved. At 6 months, the patient has no new skin lesions or gastrointestinal manifestations.

To our knowledge, there is no previous report of successful use of cyclophosphamide combined with corticosteroid therapy for Degos disease. We suggest that this

combined treatment is, in addition to standard therapy with anticoagulant agents, one of the most effective for patients with Degos disease.

References

1. Degos R (1979) Malignant atrophic papulosis. *Br J Dermatol* 100:21–35
2. Zamiri M, Jarrett P, Snow J (2005) Benign cutaneous Degos disease. *Int J Dermatol* 44:654–656
3. McFarkand HR (1978) Papulosis atrophicans maligna (Kohlmeier-Degos disease): a disseminated occlusive vasculopathy. *Ann Neurol* 3:388–392
4. Fauci AS, Haynes BF, Katz P, Wolff SM (1983) Wegener's granulomatosis: prospective clinical and therapeutic experience with 85 patients for 21 years. *Ann Intern Med* 98:76–85
5. Yazici Y (2008) Systemic vasculitis treatment and monitoring update, 2008. *Bull NYU Hosp Jt Dis* 66(3):228–230
6. Lapraik C, Watts R, Bacon P, Carruthers D, Chakravarty K et al (2007) BSR and BHPR guidelines for the management of adult with ANCA associated vasculitis. *Rheumatology (Oxford)* 46(10):1615–1616
7. Kohlmeier W (1941) Multiple Hautnekrosen bei Trombangitis obliterans. *Arch Klin Exp Dermatol* 181:783–792
8. Dubertret L (1999) Malignant atrophic papulosis (Degos' disease). In: Freedberg IM, Eisen AZ, Wolff K, Austen KF, Goldsmith AL, Katz SI, Fitzpatrick TB (eds) *Dermatology in general medicine*, vol 1. McGraw-Hill, New York, pp 1157–1161
9. Ryan TJ (1998) Malignant atrophic papulosis. In: Champion RH, Burton JL, Burns DA, Breathnach SM (eds) *Textbook of dermatology*, vol 3. Blackwell, London, pp 2216–2217
10. Katz SK, Mudd LJ, Roenigk HH (1997) Malignant atrophic papulosis (Degos' disease) involving three generations of family. *J Am Acad Dermatol* 37:480–484

11. Ball E, Newburger A, Ackerman AB (2003) Degos' disease: a distinctive pattern of disease, chiefly of lupus erythematosus, and not a specific disease per se. *Am J Dermatopathol* 25(4):308–320
12. Heymann WR (2009) Degos disease: considerations for reclassification. *J Am Acad Dermatol* 61(3):505–506
13. Howsden SM, Hodge DJ, Herndon JH, Freeman RG (1976) Malignant atrophic papulosis of Degos. Report of a patient who failed response to fibrinolytic therapy. *Arch Dermatol* 112:1582–1588
14. Zhu KJ, Zhou Q, Lin AH, Lu ZM, Cheng H (2007) The use of intravenous immunoglobulin in cutaneous and recurrent perforating intestinal Degos disease (malignant atrophic papulosis). *Br J Dermatol* 157(1):206–207