Lethal systemic Degos disease with prominent cardio-pulmonary involvement

Ali Y. Notash, MD, *Hamed Mazoochy,* MD, *Mostafa Mirshams,* MD, *Azita Nikoo,* MD.

ABSTRACT

يعتبر مرض ديجوس (اعتلال وعائي خبيث) اعتلال وعائي انسدادي نادر الحدوث يميزه وجود آفات الجلد المميزة. تعتبر إصابة أخمص القدم والإبهام والأعضاء التناسلية نادرة. في معظم الحالات، لدى المرض دورة غير مناسبة وإصابات المسالك المعدية المعوية والجهاز العصبي المركزي وبعض الأعضاء الأخرى في بعض الأحيان. تعتبر إصابات جانب غشاء الرئة وحول القلب من الظواهر البسيطة عادة مع طول دورة المرض. تظهر الوفاة في حوالي ٥٠٪ من المرضى نتيجة الى ثقب في الأمعاء أو نزيف في الجهاز العصبي المركزي. نصف هنا حالة رجل يبلغ من العمر ٤٨ عاماً وهو مصاب بمرض ديجوس الجهازي القاتل. تم تجاهل الآفات منتشرة على الجلد مع إصابة أسطح الأخمص والأعضاء التناسلية وفروة الرأس لثلاث سنوات. بينما يظهر المرض في طبيعة خبيثة. تقدم الاضطراب إلى الأعصاب والمعدة والأمعاء والجهاز القلبي الرئوي مما أدى الى الوفاة بعد خمسة أشهر من حدوث الإصابة الجهازية على شكل قصور شديد ومقيد في الجهاز القلبي الرئوي. أظهرت نتيجة تشريح الجثة وجود متغيرات تليفية منتشرة في الغشاء المصلي والأعضاء الداخلية.

Degos disease (DD) is a rare obstructive vasculopathy characterized by distinctive skin lesions. Involvement of the soles, palms and genitalia is rare. In most cases, disease has an unfavorable course and involves gastrointestinal tract, central nervous system and occasionally other organs. Pleural and pericardial involvements are usually minor manifestations with prolonged course. Death occurs in approximately 50% of the patients usually due to intestinal perforation or central nervous system bleeding. We describe a 48-year-old man of lethal systemic DD. Widespread skin lesions with involvement of palmoplantar surfaces, genitalia and scalp were ignored for 3 years, whereas the disease revealed own malignant nature. The disorder progressed to nervous, gastrointestinal and cardiopulmonary system that led to death after 5 months from onset of systemic involvement as severe restrictive cardio-pulmonary insufficiency. Autopsy showed diffuse fibrotic changes in serosal membranes and internal organs.

Saudi Med J 2008; Vol. 29 (1): 133-137

From the Departments of Surgery (Notash, Mazoochy), Sina Hospital, School of Medical Sciences, University of Tehran, Dermatology (Mirshams), and Pathology (Nikoo), Razi Hospital, School of Medical Sciences, University of Tehran, Tehran, Iran.

Received 2nd April 2007. Accepted 2nd July 2007.

Address correspondence and reprint request to: Dr. Hamed Mazoochy, Clinical Researcher, Department of Surgery, Sina Hospital, 11367-46911, Emam Khomeini Ave, PO Box 11365-4151, Tehran, Iran. Tel. +98 (21) 66716545, Fax. +98 (21) 66716545. E-mail: hmazoochy@hotmail.com

Degos disease (DD) also known as malignant atrophic papulosis or lethal cutaneous and gastrointestinal arteriolar thrombosis, is a rare occlusive artriopathy with unknown pathogenesis that involves small caliber vessels of the dermis, gastrointestinal tract, central nervous system and, occasionally other organs. Kohlmeier[1] described the disease for the first time at 1941. Also, Degos et al[2] presented DD as a distinct entity and coined its name. We found approximately 150 reported cases in the literature. It is now well-known that this disorder usually occurs in Caucasian young adults and is more common and severe in males than females. Although most cases are sporadic, familial variant with autosomal dominant pattern were also described. More or less, the first manifestation of DD is skin rash and in approximately 15% of patients, disease remains limited to skin (benign form) whereas in other progresses to systemic involvement (malignant form). Until now no successful medical therapy is known.[3] We present a systemic DD with certainly malignant course, contrary to the classical distribution, skin lesions involved palmoplantar surfaces and genitalia.

Case Report. A 48 year-old Caucasian man presented to the emergency department with 5-day history of generalized abdominal pain, nausea and vomiting which deteriorated and finally developed bloody diarrhea. He never had any previous history of gastrointestinal disorders. He also complained from progressive weakness and impaired sensation in the legs and urge incontinency from one month ago. His medical history was notable for skin lesions persisting for over 3 years, first appeared as pink/reddish rash accompanied by a slight burning sensation then resolved within a few weeks leaving white depressed lesions. These lesions spread from the trunk to extremities. Familial history was unremarkable. On physical examination he was ill, tachycardic and feverish. Skin examination revealed multiple erythematous papules (up to 100 papules, 2-10 mm in diameter) some with necrotic centers, distributed around the trunk, neck, scalp, extremities, genitalia and palmoplantar, sparing the face. The developed papules had a white color atrophic center that was surrounded by raised erythematous telangiectatic rim leaving depressed scar behind (**Figures 1a-1d**). Oral mucosa was not affected. The abdomen was significantly tense with guarding and diffuse tenderness, which suggested surgical acute abdomen. Neurologic examination showed spastic paraparesia with sensory level at fourth thoracic spinal segment, which was suggestive for spinal lesion. Other examination was unremarkable. The patient underwent laparotomy. There was pus collection below the mesocolon on the left side of Treitz ligament. The jejunum contained 2 perforated ulcers (each one were 5 mm in diameter and 5 cm apart). Other parts of gastrointestinal (GI) tract were free of disease. Biopsy was taken from border of ulcers then repaired in 2 layers and peritoneal cavity irrigated with abundant fluid. On the sixth day of admission, he experienced acute neurologic deficit as complete left hemiplegia including the face. Laboratory investigations including complete blood counts, routine chemistry, coagulation

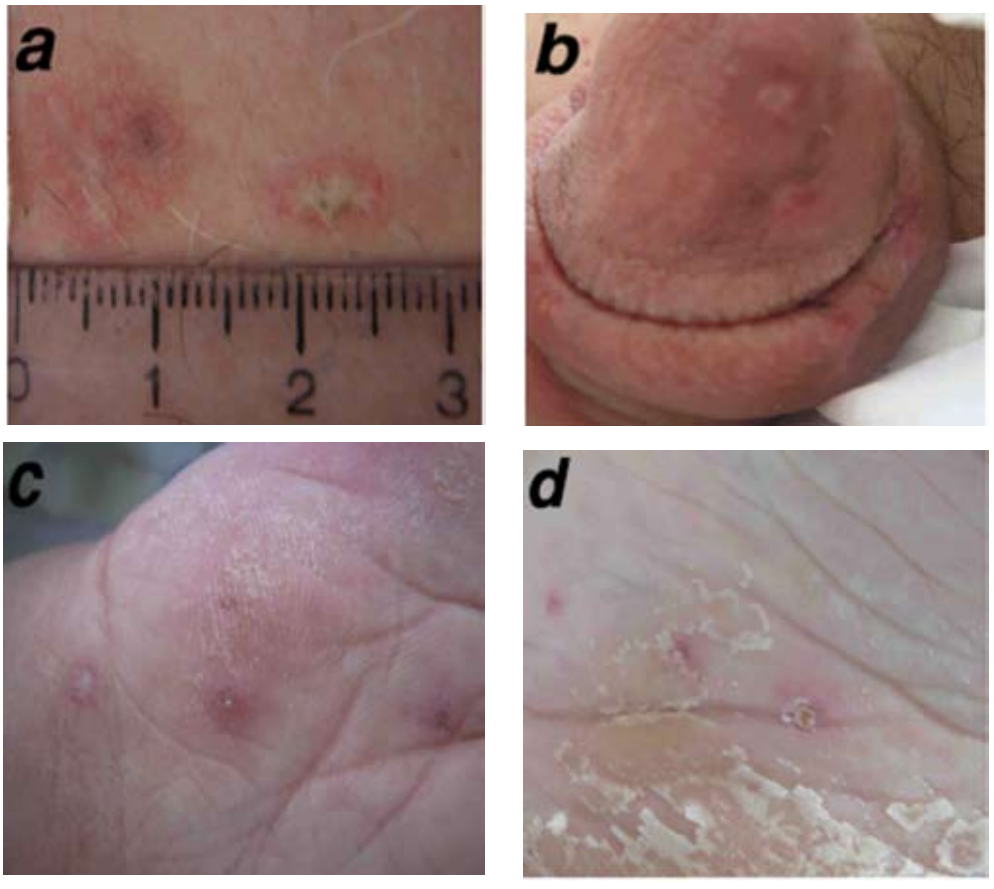

Figure 1 - Typical skin lesions with atrophic porcelain white center surrounded by erythematous and telangiectatic rim on the **a**) trunk **b**) genitalia **c**) palm and **d**) sole

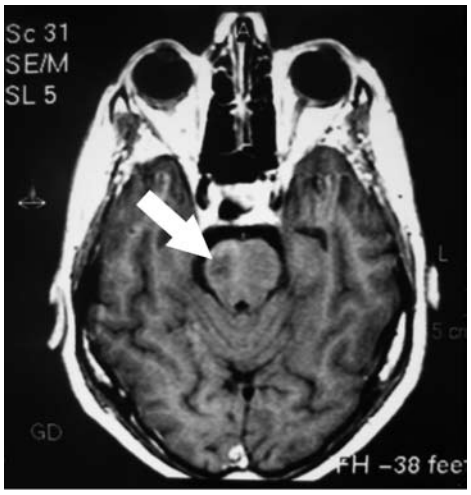

Figure 2 - T_1 weighted brain MRI after intravenous gadolinium infusion from patient showing infarction of the pons on the right side without tissue enhancement.

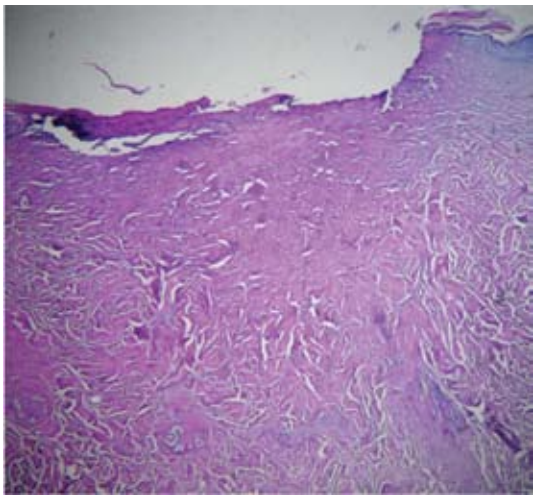

Figure 3 - Histopathological features of an established lesion (hematoxylin and eosin). Low-power view showing atrophy, ulceration and hyperkeratosis in epidermis, besides a wedge-shape ischemic area with fibrosis of the dermis.

profile, venereal disease research laboratory (blood testing for syphilis), antinuclear antibody, circulating anti-neutrophil cytoplasmic antibody, perinuclear anti-neutrophil cytoplasmic antibody, anti-double-stranded DNA, lupus erythematosus cell, rheumatoid factor, antiphospholipid Ab, anticardiolipin Ab, total complement activity, human leukocyte antigen B5, human immunodeficiency virus Ab, hepatitis C virus Ab were negative or within normal reference ranges but hepatitis B surface antigen was positive. PPD was negative. Erythrocyte sedimentation rate and C-reactive protein were slightly increased. Cerebro spinal fluid examination yield normal protein and cell count. Pathologist reported that histopathological features in specimens from skin and jejunal lesions are similar and show dense dermal fibrosis and submucosal collagen deposition respectively. He suggested Scleroderma as possible diagnosis but clinical finding was not compatible. Brain magnetic resonance imaging (MRI) revealed small vessel disease in both cerebral hemispheres with ischemic process in right side of pons without abnormal tissue enhancement (**Figure 2**). Although examination revealed spinal involvement the spinal MRI was normal. Thoracic CT scan demonstrated bilateral mild pleural effusion. We encountered a multisystemic disease that MRI findings supported the vascular basis. Although paraclinic did not determine specific diagnosis, due to strong clinical suspicion to vasculitis and serious patient condition we added prednisolone to his medications (antibiotics with enteropathogenic coverage). Patient's problems persisted and after 4 days, another complaint submerged, manifesting with nausea and vomiting, oral intolerance, accompanied by wound dehiscence and excess leakage of yellow/orange fluid from incision site. Investigation revealed simple small bowel enterocutaneous fistula. Oral feeding was stopped and octreotide was administered. In addition, he developed atrial fibrillation arrhythmias which subsequently controlled by amiodarone. Attempting to make a definitive diagnosis, we requested dermatologic consultation. Dermatologist noticed that cutaneous "porcelain white atrophic scar" with erythematous and telangiectatic rim, strongly characteristic of DD. Elliptical skin biopsy showed epidermal atrophy, ulceration with overlying hyperkeratosis and underlying wedge shape ischemic area with uniformly acellular hypereosinophilic dermis. There was mild perivascular lymphocytic infiltration at the edge of ischemic wedge. Endothelial swelling and obliteration of lumen and fibrin deposition around vessels were also identified (**Figure 3**). Review of peritoneal biopsy showed multifocal polymorphonuclear infiltration and necrosis as well as small vessel thrombosis. On the basis of clinical and histopathological features the diagnosis of DD with multisystemic involvement was made. Thereafter, octreotide and antibiotics were continued, prednisolone was stopped, pentoxifylline in combination with antiplatelet and anticoagulant therapy beside total parenteral nutrition was initiated. Further laboratory tests revealed normal levels of proteins C and S, antithrombin III and hemocystein. Tests for factor 5 leiden was also negative. During the follow up, since no new skin lesions appeared and discharge of fistula limited, he developed progressive dyspnea with multiple episodes of respiratory distress. Repeated chest radiograph showed worsening of

effusion. During 5-month period, patient's condition exacerbated and accompanied with generalized edema, alternation of consciousness and hemodynamic instability requiring mechanical ventilation and also administration of inotropic and vasopressor agents. Ultimately, he expired due to cardio-pulmonary failure. We performed autopsy and the pleura showed severe fibrotic thickening, hemorrhagic fibrinoid exudate with adhesions to the chest wall and compression collapse of both lungs especially in right. Despite severe pericardial fibrosis, heart was slack and large. In abdomen, peritoneal fibrosis, ascites and adhesions were present along the gastrointestinal tract. The bowel contained hemorrhagic fluid. In addition, numerous erosions, ulcers and necrotic areas with perforation in the bowel presented. The liver was strictly fibrotic. Also, with less severity, there was similar pattern in kidneys and vesicle. The cause of death was DD induced severe restrictive cardio-pulmonary insufficiency.

Discussion. Degos disease is a rare disorder characterized by multiple infarctive lesions in the skin and internal organs. Thrombotic occlusion of small and medium size vessels ultimately leads to clinical manifestations. Until now the precise etiology of the thrombosis is not elucidated, however different theories exist, describing DD as coagulopathy, vasculitis or primary disorder of endothelial cells.[4] Caviness Verne et al[5] proposed the hypothesis that a dysregulation of vascular remodeling and increased vascular permeability due to increased VEGF production, as well as a prothrombotic process occurs in DD. Besides, DD has an inconspicuous clinical course. In some patients disease is limited to skin for many years (benign form), in contrast, in most cases it has an unfavorable course and progresses to systemic involvement (malignant form). Until now it is impossible to predict precise prognosis.[4-6] Some authors suggested that Degos is not a distinct disease and proposed it as a morphologic pattern or a variant of lupus erythematosus.[4,7] However, there are strong evidences against this theory (lack of photosensitivity and facial lesions, unresponsiveness to corticosteroids and immunomodulatory agents, invariable fatal course in systemic form and negative DIF findings in DD).[8] Mostly, the first manifestation of DD is skin lesions which can develop at any site; however the face, palms, soles, genitalia and scalp tend to be spared.[3-5] Morphology and less importantly distribution of skin lesions provide keys for early diagnosis. Systemic manifestations usually develop during weeks to years following the onset of skin lesions, or even rarely precede the skin lesions.[3] Gastrointestinal tract, predominantly small bowel, is involved in approximately 50-60% of patients with clinical manifestations ranging from dyspepsia to perforation of viscous and peritonitis (the most catastrophic event in DD).[9,10] Neurologic manifestations occur in approximately 20% of the patients, which vary according to site of involvement. Ocular involvement is present in 13% of patients. Involvement of other organs such as oral cavity, pleura, pericardium, lung, heart, kidney, bladder and pancreas are usually minor manifestations of the disease without clinical significance.[4] There is no specific laboratory test for diagnosis of DD. The histological features are wedge-shaped tissue necrosis and thrombosis of the supplying blood vessels but not evident in all cases.[3] Varieties of therapeutic modalities such as anti-thrombotic, anti-inflamatory and immunomodulatory agents have been suggested, but these are not proven to be effective.[11] The outcome of DD is usually fatal (50-60%) within 2-3 years (range 5 months-14 years) from the onset of systemic involvement. Death most often occurs due to intestinal perforation, peritonitis and sepsis (61%), central nervous system bleeding (18%) and pleural/pericardial involvement (16%).[9] The physicians specially surgeons, gastroenterologists and neurologists should consider DD as a rare cause of common complaints of patients. Typical skin lesions should remind them of this disease. Although central porcelain white scar rimmed by erythema and thelangiectasis is pathogonomic of DD, however, this lesion is not familiar for most physicians. The localization of skin lesions on the palmoplantaris and genitalia is not well known. This report and multiple similar reports[6,9,12] are good reminder that involvement of these sites are not rare in DD. However, pleural and pericardial involvements have been usually reported as incidental findings at autopsy or minor manifestations of prolonged disease. Pierce et al[13] and Mauad et al,[14] described 3 cases with pleural and pericardial involvements as important clinical manifestations of DD. Their patients had relatively prolonged survival (5, 6 and 11 years), whereas in our patient, ran as rapid progressive course. Besides, there are evidences such as present patient regarding the use of immunomodulatory agents and systemic corticosteroids exacerbate gastrointestinal manifestations, therefore physicians should distinguish DD from vasculitis as close mimicker.[11,15] Furthermore, post mortem examination revealed diffuse fibrotic changes in DD. We think that anti-inflammatory agents specially aspirin delay this inevitable process, however further studies necessitate. Ultimately, correct diagnosis of diseases specially in

dermatologic field requires close clinicopathologic correlation. Indeed, we need a dermatopathologist who receive complete clinical description of patient from clinician; also clinician should consider microscopic description and not only end suggestion.

References

1. Köhlmeier W. Multiple Hautnekrosen bei Thrombangiitis obliterans. ***Arch Dermatol*** 1941; 181: 783-792.
2. Degos R., Delort J., Tricot R. . Dermatite papulo-squameuse atrophiante. ***Bull Soc Fr Dermatol Syphiligr*** 1942; 49: 148– 150.
3. Scheinfeld N. Degos' disease. In: Emedicine Dermatology Book. (updated May 4, 2007). Available from URL: http://www.emedicine.com/derm/topic931.htm
4. Ball E, Newburger A, Ackerman AB. Degos' disease: a distinctive pattern of disease, chiefly of lupus erythematosus, and not a specific disease per se. ***Am J Dermatopathol*** 2003; 25: 308-320.
5. Caviness VS Jr, Sagar P, Israel EJ, Mackool BT, Grabowski EF, Frosch MP. Case records of the Massachusetts General Hospital. Case 38-2006. A 5-year-old boy with headache and abdominal pain. ***N Engl J Med*** 2006; 355: 2575-2584. Erratum in: N Engl J Med 2007; 356: 1081.
6. Ojeda Cuchillero RM, Sánchez Regaña M, Umbert Millet P. Benign cutaneous Degos' disease. ***Clin Exp Dermatol*** 2003; 28: 145-147.
7. 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 Am Acad Dermatol*** 2004; 50: 895-899.
8. Scheinfeld N. Degos' disease is probably a distinct entity: a review of clinical and laboratory evidence. ***J Am Acad Dermatol*** 2005; 52: 375-376.
9. Aydogan K, Alkan G, Karadogan Koran S, Adim SB, Kiyici M, Tokgoz N. Painful penile ulceration in a patient with malignant atrophic papulosis. ***J Eur Acad Dermatol Venereol*** 2005; 19: 612-616.
10. González Valverde FM, Menarguez Pina F, Ruiz JA, Gómez Ramos MJ, Mauri Barbera F, Luri Prieto P, et al. Presentation of Degos syndrome as acute small-bowel perforation. ***Arch Surg*** 2003; 138: 57-58.
11. Kocheril SV, Blaivas M, Appleton BE, McCune WJ, Ike RW. Degos' disease mimicking vasculitis. ***Arthritis Rheum*** 2004; 51: 498-500.
12. Thomson KF, Highet AS. Penile ulceration in fatal malignant atrophic papulosis (Degos' disease). ***Br J Dermatol*** 2000; 143: 1320-1322.
13. Pierce RN, Smith GJ. Intrathoracic manifestations of Degos' disease (malignant atrophic papulosis). ***Chest*** 1978; 73: 79-84.
14. Mauad T, De Fatima Lopes Calvo Tiberio I, Baba E, Andrade Junior DR, Lichtenstein A, Capelozzi VL et al. Malignant atrophic papulosis (Degos' disease) with extensive cardiopulmonary involvement. ***Histopathol*** 1996; 28: 84-86.
15. Powell J, Bordea C, Wojnarowska F, Farrell AM, Morris PJ. Benign familial Degos disease worsening during immunosuppression. ***Br J Dermatol*** 1999; 141: 524-527.