doi: 10.1111/j.1365-2230.2007.02497.x

Malignant atrophic papulosis

N. Scheinfeld

Department of Dermatology, St Luke's Roosevelt Hospital Center, New York, NY, USA

Summary

Malignant atrophic papulosis (MAP; also known as Degos' disease) has a purely cutaneous variant and a systemic variant with cutaneous manifestations. Both have similar cutaneous eruptions. MAP manifests as erythematous, pink or red papules (2–15 mm), which evolve into scars with central, porcelain-white atrophic centres. Purely cutaneous MAP is a benign condition that can be life-long. Systemic MAP has a grim prognosis, but is not uniformly fatal. The cause of death is usually intestinal perforation. Death usually occurs within 2–3 years from the onset of systemic involvement. Systemic MAP can involve the nervous, opthalmological, gastrointestinal, cardiothoracic and hepatorenal systems. No specific laboratory test can be used to aid in diagnosing MAP. Histopathologically, a wedge-shaped degeneration of collagen is present with a prominent interface reaction with squamatization of the dermoepidermal junction, melanin incontinence and epidermal atrophy. No treatment has been shown to be effective in the treatment of MAP.

In 1941, Kohlmeier described a case of a disease[1] that Degos recognized as a distinct clinical entity in 1942. The condition that Kohlmeier and Degos described has now been termed malignant atrophic papulosis (MAP) or Degos' disease.[2] MAP occurs both as a benign, purely cutaneous form and as a lethal multiorgan, systemic variant.[3] The recent preponderance of reports of purely cutaneous MAP suggests that this form is more common than previously thought.[4–6]

The cutaneous findings of MAP are the same for both forms of the disease: erythematous, pink or red papules, 2–15 mm in diameter, which evolve into scars with central, porcelain-white atrophic centres. There may be numerous (Fig. 1) or solitary (Fig. 2) papules present in an area. The papules usually have a peripheral telangiectatic rim and may be dome-shaped. In the final stages of evolution of a papule, only a central scar is seen, which occasionally forms a clover-like pattern and is surrounded by telangiectasia resembling the appearance of atrophie blanche.

MAP can affect most body areas, can manifest with an extensive or limited eruption, and can engender alterations in sensation. The eruption occurs more on the proximal than on the distal body areas, and is more widespread on the back than on the abdomen.[7] The average number of papules was 30 in one series, but there may be >600 or <12 papules.[8] Urticaria, ulceropustular and gumma-like nodules have been noted.[7] MAP hardly ever involves the face, the palms or the soles, but commonly involves the penis (Fig. 3).[3] The eruption may be accompanied by a slight burning sensation.

Systemic MAP has an extremely grim prognosis and induces death in virtually all patients. The cause of death is usually intestinal perforation. Death in patients with systemic MAP usually occurs within 2–3 years from the onset of systemic involvement.[3] However, the range of survival time from time of diagnosis varies from <1 year to >12 years. Other causes of death include bowel infarction, cardiopulmonary collapse, and neurological infarction and haemorrhage. In systemic MAP,

Correspondence: Dr Noah Scheinfeld, MD, Department of Dermatology, Suite 11D, Columbia University School of Medicine, St Luke's Roosevelt Hospital Center, 1090 Amsterdam Ave, NYC NY 10025, USA.
E-mail: scheinfeld@earthlink.net

Conflict of interest: none declared.

Accepted for publication 27 March 2007

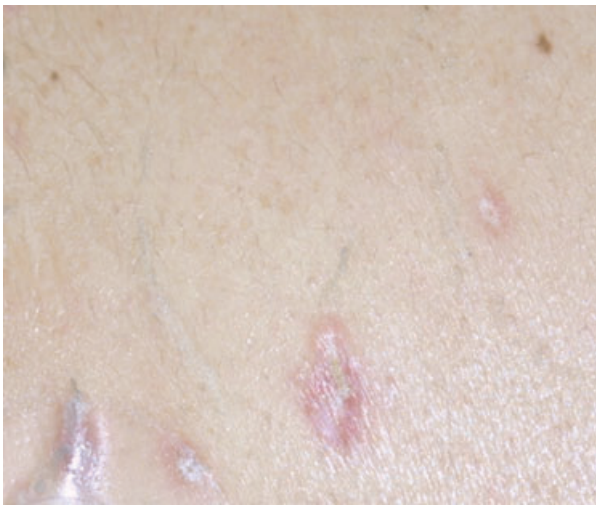

Figure 1 White atropic papules on the abdomen of a patient with systemic MAP.

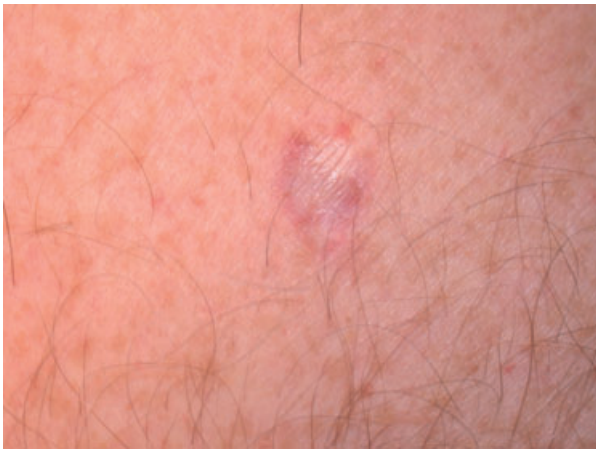

Figure 2 White atropic papule from abdomen of a patient with purely cutaneous MAP.

the systemic features usually develop weeks to years after the onset of skin lesions, or, in rare instances, they may precede the skin lesions. Some authors state that in cases of systemic MAP, skin lesions occur 3 weeks to 3 years before systemic symptoms occur.[8]

The gastrointestinal tract is affected in 50–61% of cases of systemic MAP.[3,7–9] Intestinal perforation is the most severe complication and the most common cause of death. Patients experience abdominal pain. Gastrointestinal bleeding can result in vomiting blood or passing blood with bowel movements. Enterocutaneous fistulae can occur.[3]

The central nervous system is affected in about 20% of cases of systemic MAP.[10] Patients have reported

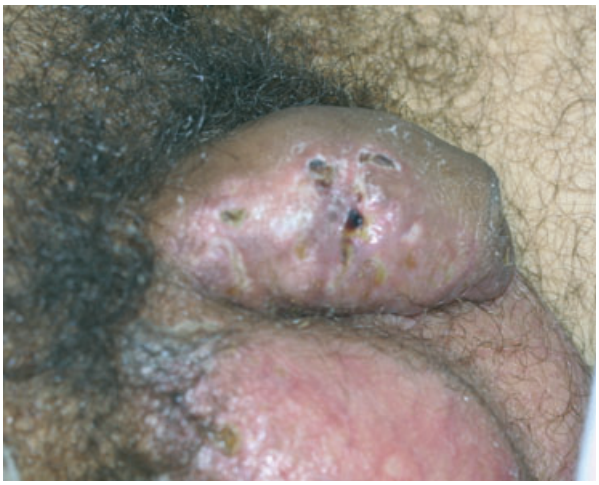

Figure 3 MAP manifesting on the penis.

neurological complaints that include facial and acral paraesthesia, headaches, dizziness, seizures, hemiplegia, aphasia, paraplegia, gaze palsy, strokes, epilepsy or nonspecific neurological symptoms (e.g., memory loss, altered sensation).[3] In 1996, Subbiah[10] described a series of 15 patients at the Mayo Clinic; 10 patients developed neurological manifestations, including fatal haemorrhagic or ischaemic strokes ($n = 5$), disabling polyradiculoneuropathy ($n = 1$), and nonspecific neurological symptoms without objective findings ($n = 4$). Right-hemianopsia, paraparesis (with a sensory level at T12), neurogenic bladder and ascending thoracic myelopathy have been noted.[3]

The eyes, cardiopulmonary system and hepatorenal system can also be involved in systemic MAP. Features of eye involvement include diplopia, ptosis, and visual-field defects. Posterior subcapsular cataracts, visual-field defects, ptosis, third cranial nerve palsies, blepharoptosis, optic atrophy, optical neuritis, papilloedema, and scleral plaques can be present.[11] In 1986, Sibillat noted that ophthalmological symptoms were present in 35 of 105 observations published.[12]

If MAP affects the cardiopulmonary system, patients may experience weakness, shortness of breath, and chest pain.[3] Constrictive pericarditis has occurred in patients with MAP, perhaps induced by pericardial vasculitis, thereby causing an abnormality in the left ventricular wall motion.[3] Pulmonary features include pleuritis and bilateral pleural effusions.[13] In one infant, death resulted from disseminated myocardial infarctions.[7]

Systemic MAP may also involve the liver and the kidneys, and may be associated with vasculitis.[3] Other renal changes include thickening of the afferent

glomerular arterioles and of the capillary basement membrane.

No specific laboratory test can be used to aid in diagnosing MAP. In fact, most test results are normal, with the exception of anaemia secondary to intestinal bleeding. Patients with MAP can have antiphosopholipid antibodies,[14] suggesting that there is a link between MAP and antiphosopholipid syndrome, but this relationship requires further definition and is certainly not found in all patients with MAP. Some reports note increased plasma fibrinogen levels, increased platelet aggregation, and reduced local and systemic fibrinolytic activity.

Notable findings occur in the cells of patients affected by MAP. Virus-like inclusions, observable with an electron microscope, are often present in the endothelial cells and fibroblasts.[3] C3 deposits and the presence of intracytoplasmic cylinders are also often found in the histiocytes. In a series of three patients with MAP, electron microscopy demonstrated an increased number of Weibel–Palade bodies and increased staining of von Willebrand factor in endothelial cells in one patient.[15]

Evaluation of patients with MAP can include examination of the gastrointestinal tract.[3] The first test to perform is a stool guaiac test. More definitive tests include endoscopy of the gastrointestinal tract (i.e., stomach, oesophagus, duodenum, colon, rectum), which may show infarcted lesions or ulcers. Laparoscopy of the intestine may show white plaques with red borders on the serosal surface of the bowel and the peritoneum.

The gross pathology of tissue affected by MAP reveals an occlusive arteriopathy involving small-calibre vessels, which results in tissue infarction. The bland appearance of the vasculopathy in MAP or of endovasculitis on histological examination belies its lethal course if it manifests in the internal organs.

Ackerman has extensively described the histological findings of MAP.[16] Early papules are skin-coloured and can have a superficial and deep perivascular, periadnexal, and perineural chronic inflammatory cell infiltrate associated with interstitial mucin deposition. The overlying epidermis can show a mild vacuolar interface reaction, and, at this early stage, the histological appearances can resemble tumid lupus erythematosus (LE).

Fully developed papules can be raised with umbilicated porcelain-white centres and a surrounding erythematous rim. Usually, wedge-shaped degeneration of collagen is present. A prominent interface reaction with squamatization of the dermoepidermal junction, melanin incontinence, epidermal atrophy, and a developing zone of papillary dermal sclerosis that resembles the early stages of lichen sclerosus et atrophicus in miniature can also be observed at histological examination.[16] These interface reactions are usually confined to the central portion of a punch-biopsy specimen, corresponding to the central, porcelain-white area seen clinically.

Histopathological examination of the skin biopsy specimen can also show hyperkeratosis, epidermal atrophy, dermoepidermal separation, oedema, and necrosis in the papillary dermis.[16] Fibrinoid necrosis and thrombosis can be seen in the papillary dermis and in the vessels below the lesions. Some authors have noted that skin-biopsy specimens show hyperkeratosis, atrophy of the epidermis, and necrobiosis of the collagen layer. Well-developed lesions with epidermal atrophy and hyperkeratosis overlying a wedge-shaped area of cutaneous ischaemia extending into the deep dermis have also been observed. Superficial and deep perivascular lymphocytic infiltrate can be present at the edge of ischaemic areas. Marked endothelial swelling and occasional platelet–fibrin thrombi can be present. The epidermis may show infarctive changes or scattered necrotic keratinocytes. Abundant acid mucopolysaccharides can be present in the dermis, giving the appearance of a dermal mucinosis.[16] Direct immunofluorescence gives conflicting findings, with perivascular fibrin and complement present in various cases.

Because of the small number of cases that have been reported, the epidemiology of MAP requires further definition. It affects all ages and both sexes. A familial variant appears to exist. Katz noted that the disorder usually occurs in young adults, and the male : female ratio is approximately 3 : 1.[17] The natural history of MAP has yet to be defined.

MAP can occur at any age. Lankisch described a 16-year-old white adolescent girl with acute abdominal pain due to visceral involvement of MAP, which required extensive small-bowel resection; the girl eventually died.[9] MAP has been reported in a 7-month-old infant girl in whom no systemic manifestations of the disease could be found; the child showed spontaneous aggregation of platelets and had no fatal complications. In a 17-month-old child, progressive involvement of the fingers and the toes with torpid ulcers and apical necrotic amputations was reported.[18] MAP has occurred in pregnant women[19] and in patients with human immunodeficiency virus.[20]

The differential diagnosis of the cutaneous manifestations of MAP includes atrophie blanche, atrophie blanche-like papules of systemic LE/dermatomyositis, dermal mucinosis, rheumatoid arthritis, guttate lichen sclerosis, guttate morphoea, and scleroderma[3,7,8] These

processes can be distinguished histologically. As MAP can remain confined to the skin for the lifetime of the patient or the disease progress, it is necessary to re-examine periodically any patient with the cutaneous lesions of MAP for any progression of disease. It is likely that cutaneous MAP is underdiagnosed because its eruption is so bland and its complications so minimal.

The differential diagnosis of systemic MAP includes primary ulceration of the small intestine, Crohn's disease, cutaneous–intestinal syndrome with oropharyngeal ulceration and SLE. Systemic MAP as it progresses impairs a patient's ability to function and thus can be distinguished from cutaneous MAP or mimics of cutaneous MAP. As MAP is so rare, other causes of gastrointestinal bleeding and/or neurological impairment are usually suspected before a diagnosis of MAP is entertained. Complicating the diagnosis of MAP is the lack of any definitive test to define it. The histological findings, while highly suggestive of the diagnosis of MAP when read by highly skilled pathologists, can overlap with collagen vascular diseases, particularly those with thrombotic features. Comprehensive blood analysis and examination of tissue pathology specimens is necessary to exclude diseases that mimic MAP. Although most patients die within 1–2 years from the time of diagnosis of systemic MAP, one patient with systemic MAP survived for 12 years. Systemic MAP has a grim prognosis, but cannot be said to be uniformly fatal.

Medical treatment for MAP, whether cutaneous or systemic, remains to be defined. Anti-platelet drugs (e.g. aspirin, dipyridamole) may have a role in the treatment of all variants of MAP. Anti-platelet agents may reduce the number of new lesions in some patients with only skin involvement. However, it may be that reports of successful treatment of purely cutaneous forms of MAP were not a result of the treatment, but rather of the natural history of the disease. There is no standard treatment for systemic MAP. Many treatments have tried without success, including topical corticosteroids, phenformin and ethylestrenol, iodohydroxyquinoline, aspirin and dipyridamole, phenylbutazone, arsenic, sulphonamides, dextran, corticosteroids, heparin, warfarin, niacin, streptomycin, adrenocorticotrophic hormone, azathioprine, methotrexate, ciclosporin, tacrolimus, mycophenolate mofetil, pentoxifylline and clopidogrel.[3] Intravenous immunoglobulin may have a role in treatment of MAP but it requires further investigation.

The relationship of MAP to other diseases, in particular SLE, is not clear. In 2003, Ball and Ackerman proposed that MAP is merely a variant of LE.[21] Specifically, they suggested that MAP is analogous to LE in the sense that each is fundamentally a systemic pathological process involving several organs, among them the skin, and that in fact MAP is usually a manifestation of LE. They adduced that histopathologically, MAP is indistinguishable from one expression of cutaneous LE and that immunopathologically, some patients with morphological findings stereotypical of MAP display signs characteristic of LE and episodically of dermatomyositis and rheumatoid arthritis, thus MAP is a distinctive pattern rather than a specific disease.

Because of the broad overlap in clinical and histological findings of lupus and MAP, High contended in 2004 that MAP may not be a specific entity but, rather, may represent a common end point of a variety of vascular insults, many of which have not been fully elucidated.[22] Scheinfeld has disputed High, and contends that systemic MAP is not a collagen vascular disease and is probably a distinct entity characterized by: (i) unresponsiveness to therapy, (ii) frequent presence of cellular virus-like inclusions, (iii) negative direct immunofluorescence findings, (iv) a grim prognosis that cannot be said to be uniformly fatal, (v) lack of photosensitivity and (vi) lack of facial lesions.[23] Scheinfeld believes that MAP is a thrombotic rather than an autoimmune disease.

In conclusion, MAP has a variety of presentations. It can range from a purely cutaneous variant[24] to a systemic disease, with diverse internal, radiological and immunological findings.[25] If skin lesions only are present, the prognosis is good, with no significant morbidity or mortality. MAP is a rare disease with about 200 cases reported; however, because of its complications an understanding of it is important. The cause of MAP has yet to be defined. Although many diseases can present with white atropic papules, it seems that systemic MAP has a constellation of findings that make it a real disease entity. It is hoped that some effective treatment will be devised for this lethal disease.

References

1 Kohlmeier W. Multiple Hautnelnosen bei Thromboangiitis obliterans. *Arch Dermatol Syphilol* 1941; **181**: 783–4.
2 Degos R. Malignant atrophic papulosis. *Br J Dermatol* 1979; **100**: 21–35.
3 Scheinfeld N. Degos disease. In: *Dermatology*. eMedicine Medical Textbooks. http://www.emedicine.com/derm/topic931.htm (accessed 15 March 2007).
4 Coskun B, Saral Y, Cicek D, Ozercan R. Benign cutaneous Degos' disease: a case report and review of the literature. *J Dermatol* 2004; **31**: 666–70.

5 Farrell AM, Moss J, Costello C. Benign cutaneous Degos' disease. *Br J Dermatol* 1998; **139**: 708–12.
6 Harvell JD, Williford PL, White WL. Benign cutaneous Degos' disease: a case report with emphasis on histopathology as papules chronologically evolve. *Am J Dermatopathol* 2001; **23**: 116–23.
7 Dubertret L. Malignant atrophic papulosis. In: *Dermatology in General Medicine* (Freedberg IM, Eisen AZ, Wolff K *et al.*), 6th edn. New York: McGraw-Hill, 2003.
8 Ryan TJ. Malignant atrophic papulosis. In: *Textbook of Dermatology* (Champion RH, Burton JL, Ebling F), 6th edn. Oxford: Blackwell Scientific; 1998.
9 Lankisch MR, Johst P, Scolapio JS, Fleming CR. Acute abdominal pain as a leading symptom for Degos' disease (malignant atrophic papulosis). *Am J Gastroenterol* 1999; **94**: 1098–9.
10 Subbiah P, Wijdicks E, Muenter M *et al.* Skin lesion with a fatal neurologic outcome (Degos' disease). *Neurology* 1996; **46**: 636–40.
11 Egan R, Lessell S. Posterior subcapsular cataract in Degos disease. *Am J Ophthalmol* 2000; **129**: 806–7.
12 Sibillat M, Avril MF, Charpentier P. Malignant atrophic papulosis (Degos' disease): clinical review. Apropos of a case. *J Fr Ophtalmol* 1986; **9**: 299–304.
13 Asherson RA, Cervera R. Antiphospholipid syndrome. *J Invest Dermatol* 1993; **100**: 21–7S.
14 Caux F, Aractingi S, Scrobohaci ML *et al.* Abnormal fibrinolysis in Degos disease. A study of 3 cases. *Ann Dermatol Venereol* 1994; **121**: 537–42.
15 Fernandez-Perez ER, Grabscheid E, Scheinfeld NS. A case of systemic malignant atrophic papulosis (Kohlmeier-Degos' disease). *J Natl Med Assoc* 2005; **97**: 421–5.
16 Ackerman AB, Chongchitnant N, Sanchez J *et al*, eds. *Histologic Diagnosis of Inflammatory Skin Diseases: an Algorithmic Method Based on Pattern Analysis*, 2nd edn. Baltimore: Williams & Wilkins, 1997: 771–2.
17 Katz SK, Mudd LJ, Roenigk HH Jr. Malignant atrophic papulosis (Degos' disease) involving three generations of a family. *J Am Acad Dermatol* 1997; **37**: 480–4.
18 Torrelo A, Sevilla J, Mediero IG *et al.* Malignant atrophic papulosis in an infant. *Br J Dermatol* 2002; **146**: 916–18.
19 Bogenrieder T, Kuske M, Landthaler M, Stolz W. Benign Degos' disease developing during pregnancy and followed for 10 years. *Acta Derm Venereol* 2002; **82**: 284–7.
20 Requena L, Farina C, Barat A. Degos disease in a patient with acquired immunodeficiency syndrome. *J Am Acad Dermatol* 1998; **38**: 852–6.
21 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**: 308–20.
22 High WA, Aranda J, Patel SB *et al.* Is Degos' disease a clinical and histological end point rather than a specific disease? *J Am Acad Dermatol* 2004; **50**: 895–9.
23 Scheinfeld N. Degos' disease is probably a distinct entity: a review of clinical and laboratory evidence. *J Am Acad Dermatol* 2005; **52**: 375–6; author reply 376–8.
24 Pinault AL, Barbaud A, Weber-Muller F, Schmutz JL. Benign familial Degos disease. *Ann Dermatol Venereol* 2004; **131**: 989–93.
25 Yoshikawa H, Maruta T, Yokoji H *et al.* Degos' disease: radiological and immunological aspects. *Acta Neurol Scand* 1996; **94**: 353–6.

