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Case Report

Malignant atrophic papulosis (Degos' disease)

惡性萎縮性丘疹病(Degos 氏病)

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A 25-year-old Chinese female presented with a few weeks' history of erythematous papular eruption over the forehead, upper back and scalp. The lesions typically consisted of a necrotic or atrophic centre with peripheral erythema and crusting. Skin biopsy showed histological features consistent with malignant atrophic papulosis (Degos' disease). The patient was also found to have anaemia, thrombocytopaenia, positive ANA and anti-dsDNA. She was treated as a case of malignant atrophic papulosis with features of systemic lupus erythematosus and idiopathic thrombocytopaenia on the basis of clinical, histological and further investigative findings.

患者女， 25歲。近數週於前額，上背部及頭皮出現紅色丘疹。皮損典型地由壞死及萎縮的中央及周圍的紅斑及結痂組成。組織病理檢查顯示惡性萎縮性丘疹的病理學特徵，病人有貧血、血小板減少、抗核因子及抗雙鍵脱氧核糖核酸陽性。根據臨床，組織病理及其他檢查，本例患者以惡性萎縮性丘疹病伴系統性紅斑狼瘡及特發性血小板減少症處理。

Keywords: Degos' disease, Malignant atrophic papulosis

關鍵詞：Degos 氏病、惡性萎縮性丘疹病

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Introduction

Malignant atrophic papulosis (MAP) is a rare occlusive vasculopathy of unknown aetiology. It is characterised by porcelain-white atrophic papules with peripheral erythema and telangiectasia. Two main subtypes are recognised: the purely cutaneous variant and the systemic variant. Although the condition is uncommon, recognition is important since thrombosis of vessels and tissue infarction of the skin, gastrointestinal tract, central nervous

system and other organs are possible, leading to significant morbidity and mortality. The condition is of interest to dermatologists since the cutaneous features often provide clues to the diagnosis.

Case report

A 25-year-old Chinese female presented with a history of erythematous facial papular eruption for three weeks, which first appeared while she was on a vacation in Japan. The eruption was asymptomatic and subsequently spread to the back and chest. There was no fever, arthralgia or other systemic symptoms. No hair loss or oral ulcer was noted. She was initially treated as folliculitis by a general practitioner without any improvement. The patient enjoyed good past health and was not on any regular medication. She was a non-smoker and a non-drinker. As for family history, her younger sister suffered from systemic lupus erythematosus (SLE).

Physical examination showed multiple erythematous papules ranging from 0.5 cm to 1.0 cm in diameter located on the forehead, cheek and upper back with a few on the scalp (Figures 1-3). An individual papule typically consisted of a necrotic or atrophic centre with peripheral erythema and some crusting. There was no petechia, vesicle or pustule. The nails and mucosal membranes were unremarkable. Clinical differential diagnoses for the cutaneous lesions included atrophie blanche-like papules of systemic lupus erythematosus, antiphospholipid syndrome, malignant atrophic papulosis, atrophie blanche, guttate lichen sclerosis and guttate morphea. Blood tests showed mild hypochromic, microcytic iron-deficiency anaemia with a haemoglobin level of 10.7 g/dL and MCV 67.7 fL. Haemoglobin pattern was normal. Total white cell and lymphocyte count were decreased at 2.6 x 10^9/L and 0.6 x 10^9/L respectively. Thrombocytopaenia was present with a platelet count of 23 x 10^9/L.

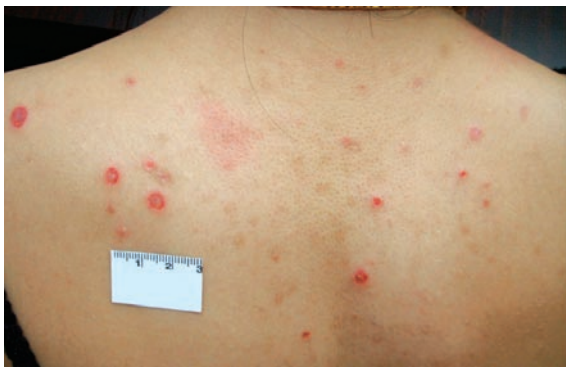

Figure 1. Multiple papules with necrotic or atrophic centres and peripheral erythema over the upper back.

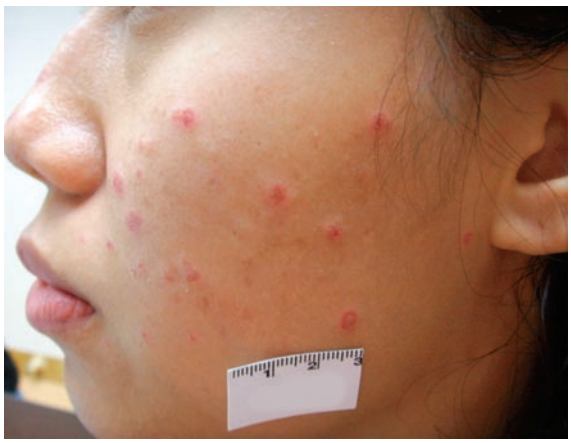

Figure 2. Multiple papules with necrotic or atrophic centres and peripheral erythema over the cheek.

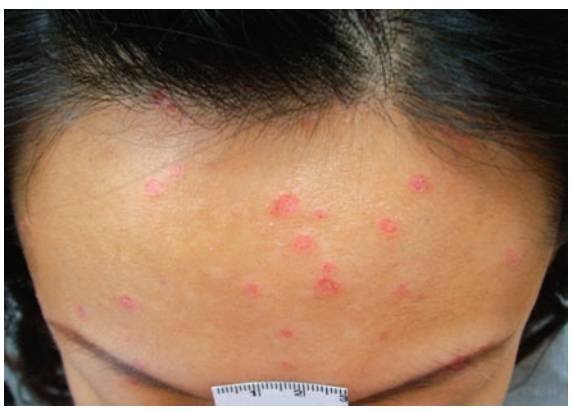

Figure 3. Multiple papules with necrotic or atrophic centres and peripheral erythema on the forehead.

Renal function and liver enzymes were normal. Albumin was decreased at 28 g/L. ANA was 1:160, anti-dsDNA 200 IU/mL and anti-ENA negative. C3 and C4 were normal. Anti-cardiolipin antibody and lupus anticoagulant were negative.

An incisional skin biopsy showed focal epidermal necrosis associated with a wedge-shaped area of dermal necrosis (Figure 4). The epidermis adjacent to the necrotic epidermis was atrophic with overlying hyperkeratosis and parakeratosis. Basal cell vacuolation was also present. In the dermis, there was moderate perivascular lymphocytic infiltrate (Figure 5). The blood vessels were lined by plump endothelial cells. No fibrinoid necrosis or leukocytoclasis was seen. Immunofluorescence studies showed weak staining with fibrin in the blood vessel wall. No staining was demonstrated with IgA, IgM, IgG and C3. Histological features together with clinical appearance of the cutaneous lesions were consistent with the diagnosis of malignant atrophic papulosis (Degos' disease). The patient subsequently underwent further investigations for associated diseases, especially systemic lupus erythematosus, and for evaluation of systemic involvement. Bone marrow examination showed features of iron deficiency anaemia and megakaryocytic hyperplasia, consistent with consumptive thrombocytopaenia. Stool for occult blood was negative. Upper endoscopy with biopsy showed gastritis and no evidence of *H. pylori* or malignancy. Colonoscopy was normal. Twenty-four hour urine showed no proteinuria. Features from the albumin scintiscan were compatible with intermittent protein loss from the gastrointestinal tract. Small bowel follow-through showed no lesions.

In view of the haematological and immunological findings, the patient was treated as systemic lupus erythematosus with thrombocytopaenia. She was started on prednisolone 20 mg twice daily, which was subsequently reduced. Other medications included ferrous sulphate 300 mg twice daily, aspirin 80 mg daily, hydroxychloroquine 200 mg daily and azathioprine 100 mg daily. On follow-up, no new malignant atrophic papulosis skin lesions had appeared since the start of systemic treatment. Many of the old skin lesions had resolved, some leaving atrophic scars.

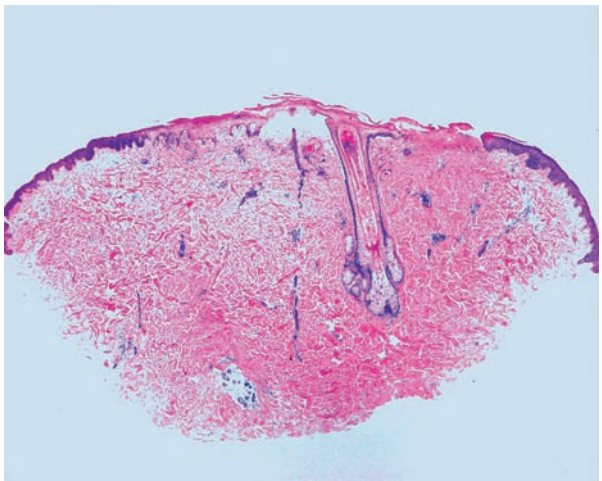

Figure 4. Histology shows central epidermal necrosis with wedge-shaped dermal infarction. There is sparse superficial and deep perivascular inflammatory infiltrate. (H&E, Original magnification x 20)

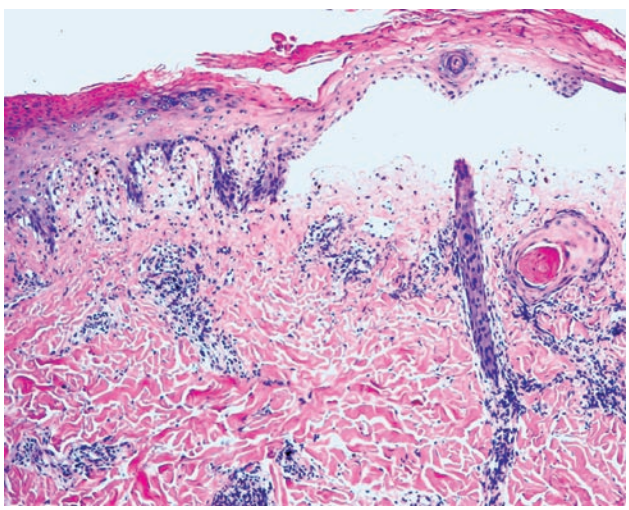

Figure 5. Histology shows central epidermal atrophy and necrosis with adjacent epidermal hyperplasia. There is mild basal vacuolar alteration. Mild perivascular lymphocytic infiltrate is also present. (H&E, Original magnification x 100)

Discussion

Malignant atrophic papulosis (Degos' disease) is a rare and clinically distinctive occlusive vasculopathy of unknown aetiology affecting small to medium-sized vessels. Narrowing and occlusion of the vessel lumen by intimal proliferation and thrombosis lead to tissue ischaemia and infarction of the dermis, gastrointestinal tract, central nervous system and other organs. Clinically, the skin lesions are characterised by the appearance of porcelain-white, atrophic papules with peripheral erythema and telangiectasia.

The first case of MAP was described by Köhlmeier in 1941.[1] A year later, Degos recognised it as a distinct clinical entity in a patient who died of intestinal perforation secondary to systemic involvement of MAP. More than two hundred cases have so far been reported in the literature worldwide. MAP affects all ages and both sexes, but it usually occurs in 'young adults' in the third to fourth decade. The male to female ratio is approximately 3:1.[2] Two main types of MAP have been recognised. The first type is the purely cutaneous form which is also known as 'benign cutaneous Degos' disease'. This type is thought to have a better outcome compared to other variants.[3] The second type is the systemic variant with cutaneous manifestations, which has multi-organ involvement and a more aggressive course. It is associated with a worse prognosis and is often lethal. Other less common variants include familial Degos' disease, atrophie blanche and connective tissue disease with Degos'-like features.

The cutaneous features of MAP are indistinguishable for the different variants of the disease. Typically, the lesions begin as pink or red papules of 2-15 mm in diameter, which progress to develop central necrosis and later heal with scars consisting of central porcelain-white atrophic centres. The papules often have peripheral telangiectatic rims and may be dome-shaped. The end-stage lesions may have a clover-like configuration and can resemble atrophie blanche. The eruption can be limited or extensive, with the number of papules ranging from less than twelve to more than six hundred. They occur more on the proximal than the distal body areas, and are more widespread on the back than on the abdomen. Involvement of the face, palm, sole, buccal and genital mucosa have been reported. The lesions are mostly asymptomatic but can have slight burning sensation. Other less common cutaneous features which have been reported include urticaria, ulcer-pustular lesions and gumma-like nodules. The typical cutaneous lesions in MAP can be confused clinically with other differential diagnoses, which include atrophie blanche, atrophie blanche-like papules in connective tissue diseases (e.g. SLE, dermatomyositis), dermal mucinosis, guttate lichen sclerosis, guttate morphea, scleroderma, scar, vitiligo and idiopathic guttate hypomelanosis. These can be distinguished histologically.

Systemic features in MAP usually manifest after the onset of cutaneous lesions, with a possible delay of three weeks to three years. Systemic involvement signifies extremely poor prognosis with death in nearly all patients. Affected patients usually die within two to three years from the onset of systemic involvement, often due to intestinal perforation. Many organ systems can be involved, including gastrointestinal tract, central nervous system, cardiopulmonary system, eyes, liver and renal systems. Involvement of the gastrointestinal tract is seen in 50-61% of the reported systemic MAP cases, which include bowel perforation, bleeding and enterocutaneous fistulae formation. The presenting symptoms can be abdominal pain, haematemesis and bleeding per rectum.[4] The central nervous system is involved in approximately 20% of the systemic MAP cases.[5]

Bleeding, ischaemia, myelopathy and polyradiculoneuropathy have been reported. These patients can present with a range of specific and non-specific symptoms, such as headache, dizziness, seizures, paraesthesia, hemiplegia, paraplegia, aphasia, gaze palsy and memory loss. Ophthalmic involvement has been reported in thirty-five out of the one hundred and five cases published in 1986.[6] Posterior subcapsular cataracts, third cranial nerve palsy, blepharoptosis, scleral plaques, papilloedema and optic atrophy can present with diplopia, ptosis and visual field defects. When the cardiopulmonary system is affected, patients can experience chest pain, shortness of breath and weakness as a result of pleuritis, pleural effusion, myocardial infarction, pericardial vasculitis and constrictive pericarditis. Involvement of the hepatorenal system in systemic MAP may be associated with vasculitis. Thickening of afferent glomerular arterioles and capillary basement membrane have also been reported. Since systemic MAP is a rare condition, several other more common multisystem diseases should be excluded before considering the diagnosis of MAP. These include Crohn's disease, polyarteritis nodosa, SLE and antiphospholipid syndrome.

The diagnosis of MAP depends on clinical features together with compatible histological findings. Histologically, MAP is an occlusive arteriopathy with different stages of evolution.[7] Even though the histological findings can be highly suggestive of MAP when interpreted by experienced pathologists, some features can overlap with collagen vascular diseases, particularly those with thrombosis. In an early stage, there is superficial and deep perivascular, periadnexal and perineural chronic inflammatory infiltrate with interstitial mucin deposition. Vacuolar interface reaction can be seen in the epidermis of the papules, which can mimic lupus erythematosus. In a later stage, fully developed papules histologically demonstrate wedge-shaped degeneration of collagen. Interface reaction can be prominent with squamatization of the dermoepidermal junction, melanin incontinence and epidermal atrophy. The interface reaction is usually confined to the central, porcelain-white area seen clinically. Marked endothelial swelling and occasional platelet-fibrin thrombi are often noted in the dermal vessels. Wedge-shaped area of ischaemia extending into the deep dermis has also been observed. Direct immunofluorescence examination does not give definitive results, although perivascular fibrin and complement can be present.

The pathogenesis of MAP is still not fully understood. The condition has been classified as a vaso-occlusive thrombotic disorder, a vasculitis and a mucinosis. Some authorities suggest that either a primary endothelial cell defect, alterations in platelet function or impaired fibrinolytic activity causes secondary thrombosis, which then leads to cutaneous infarction. This is consistent with the observation of increased Weibel-Palade bodies, which contain factors needed for haemostatsis, and increased staining of von Willebrand factors in the endothelial cells of the lesions.[8] The postulation of MAP being a vasculitis has less supporting evidence as inflammation of the vessel walls is minimal and immune complexes have not been consistently found. A viral aetiology has also been suggested, since virus-like inclusions have been observed by electron microscopy in the endothelial cells and fibroblasts.

The relationship of MAP with other diseases, especially SLE and antiphospholipid syndrome, is intriguing albeit controversial. Currently, there are several schools of thoughts. Ball, Newburger and Ackerman proposed in 2003 that MAP is a variant of lupus erythematosus (LE), and that MAP is analogous to LE in several aspects.[9] Firstly, both conditions are systemic pathological

process involving several organs. Some patients with cutaneous lesions typical of MAP display other features characteristic of LE, as in the case of our patient. Some of the MAP cases also display features of dermatomyositis and rheumatoid arthritis. Secondly, the histology of MPA can be indistinguishable from cutaneous LE. Thirdly, some patients with MAP have been found to have lupus anticoagulant or antiphospholipid antibodies, suggesting a link between MAP, LE and antiphospholipid syndrome. Since there is a broad overlap in the clinical and histological features of LE and MAP, High proposed in 2004 that MAP may not be a specific entity, but rather represents a common end-point to a variety of vascular insults which have not been fully elucidated.[10] In contrast to all the concepts proposed above, Scheinfeld contended that MAP is likely to be a distinct entity with a thrombotic origin, which is unrelated to collagen vascular diseases.[11] This is supported by the observations that i) MAP is often unresponsive to therapy, ii) negative direct immunofluorescence in MAP, iii) lack of photosensitivity in MAP in contrast to SLE, and iv) the overall grim prognosis in MAP which is, nevertheless, not universally fatal.

The standard treatment for both cutaneous and systemic MAP remains to be defined. The choice of treatment depends on whether the disease is purely cutaneous or has systemic involvement. For purely cutaneous 'benign' MAP, anti-platelet drugs such as aspirin and dipyridamole, may reduce the number of new lesions. Transdermal nicotine patch once daily to increase peripheral cutaneous blood flow has been shown to halt the formation of new lesions. However, the success in treatment of cutaneous lesions may simply reflect the natural course of the disease, rather than the effect of treatment. For systemic MAP, the mainstay of treatment is supportive. For intracranial bleed, gastrointestinal bleed, perforation and infarction, surgical intervention is needed. Many different treatments have been tried but without consistent success These include topical and systemic corticosteroids, azathioprine, methotrexate, cyclosporine, tacrolimus, mycophenolate mofetil, intravenous immunoglobulin, arsenic, sulphonamides, heparin, warfarin, streptomycin, urokinase, streptokinase, stanazolol, phenformin and ethyloestrenol.

For patients who present with cutaneous MAP, the disease can remain confined to the skin for a lifetime or progress to systemic involvement. Therefore, it is important to reassess these patients periodically. If the disease involves only the skin, there is generally no significant morbidity or mortality. In contrast, prognosis of systemic MAP is much worse, with death occurring within two to three years from the onset of systemic involvement. The causes of death are usually intestinal perforation and infarction, cardiopulmonary collapse, cerebral infarction and haemorrhage.

In conclusion, MAP can range from purely cutaneous to systemic disease affecting different organ systems. The cutaneous presentation typically consists of white atrophic papules as in our case. Although the condition is rare, it is important to recognise it because of its potentially lethal systemic complications. Currently, it is still controversial as to whether MAP is a distinct disease entity or a common clinical and histological endpoint to different vascular insults of unknown origin. Our case supports the proposed concept that MAP is related to LE. MAP limited to the skin has a good prognosis. However, purely cutaneous MAP may develop systemic disease after many years, so regular follow-up is required. Although treatment of systemic MAP does not alter its disease course, treatment of the gastrointestinal and neurological complications may prolong the patient's life. Finally, dermatologists should be aware of MAP since the most visible manifestation of this entity is in the skin.

References

1. Köhlmeier W. Multiple Hautnelnosen bei Thromboangiitis obliterans. Arch Dermatol Syphilol 1941;181:783-4.
2. 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.
3. 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.
4. 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.
5. Subbiah P, Wijdicks E, Muenter M, Carter J, Connolly S. Skin lesion with a fatal neurological outcome (Degos' disease). Neurology 1996;46:636-40.
6. Sibilat M, Avril M, Charpentier P, Offret H, Bloch-Michel E. Malignant atrophic papulosis (Degos' disease): clinical review. Apropos of a case. J Fr Ophthalmol 1986;9:299-304.
7. 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.
8. Fernández-Pérez ER, Grabscheid E, Scheinfeld NS. A case of systemic malignant atrophic papulosis (Köhlmeier-Degos' disease). J Natl Med Assoc 2005; 97:421-5.
9. Ball E, Newburger A, Ackerman A. 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.
10. 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;50:895-9.
11. Scheinfeld N. Degos' disease is probably a distinct entity: a review of clinical and laboratory evidence. J Am Acad Dermatol 2005;52:375-6.