A case of bilateral plantar pseudo-Kaposi sarcoma successfully treated with propranolol

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INTRODUCTION

Pseudo-Kaposi sarcoma (PKS), also known as acroangiodermatitis, is a benign cutaneous reactive angiomatosis, the clinical and histopathologic characteristics of which resemble those of Kaposi sarcoma (KS). There are 2 variants of PKS: the Mali type, which is associated with venous hypertension, and the Stewart-Bluefarb type, which is associated with an arteriovenous malformation or an acquired iatrogenic arteriovenous fistula in patients with chronic renal failure.[1] Histologically, a slight proliferation of endothelial cells often in a lobular structure with extravasation of red blood cells; dermal fibrosis; and a perivascular, superficial infiltrate consisting of lymphocytes, histiocytes, and eosinophils are observed in PKS.[1] We describe a patient with PKS treated with propranolol, a nonselective β-adrenergic blocker. Propranolol has been suggested to improve vascular diseases, such as proliferating infantile hemangioma and other vascular diseases, owing to its vasoconstrictive and angiogenesis-inhibiting effects.

CASE REPORT

A 57-year-old Japanese man suffering from painful erythema on both his soles for 4 years consulted our clinic. At his first visit, physical examination showed relatively well-defined dark purple-red patches with tenderness and induration on both his soles. Cutaneous manifestations and a skin biopsy showed mild leukocytoclastic vasculitis, fibrosis, and proliferation of capillaries in the upper dermis, but did not suggest a diagnosis. Direct immunofluorescence tests were negative. Treatment with topical steroids and systemic dapsone ameliorated his clinical symptoms and was discontinued 2 months later.

Abbreviations used:

KS: Kaposi sarcoma
PKS: pseudo-Kaposi sarcoma

Ten years later, he consulted our clinic again because his symptoms flared despite reinstitution of the previously prescribed drugs. Consequently, he had difficulty walking due to pain and tenderness in both soles. Physical examination showed relatively well-defined sclerotic and erythematous plaques with scale on his soles surrounded by small erythematous papules (Fig 1, *A*). Oral steroid treatment (prednisolone 20 mg/day) failed to improve his skin lesions and tenderness. A blood test revealed a normal white blood cell count and normal range values for serum c-related proteins, D-dimer, fibrin/fibrinogen degradation products, and serum immunoglobulins. Tests for HIV antigen and antibodies, antinuclear antibodies, and anticardiolipin antibodies were negative. Histologic examination showed a perivascular lymphocytic infiltrate and proliferation of dilated capillaries in the upper dermis (Fig 1, *B*). Contrast-enhanced magnetic resonance imaging showed subcutaneous venous dilatation in the skin (Fig 2, *A*). Doppler stethoscopy revealed shunt sounds on the papules with tenderness. A venous ultrasound revealed no venous insufficiency but arteriovenous fistulas on Doppler view (Fig 2, *B*). We provisionally diagnosed multiple arteriovenous fistulas of the soles. Compression therapy of his feet with elastic bandages mildly improved erythema and pain. However, after 6 months, painful red plaques had developed at other sites of the foot (Fig 3, *A*). Another skin biopsy was performed and revealed

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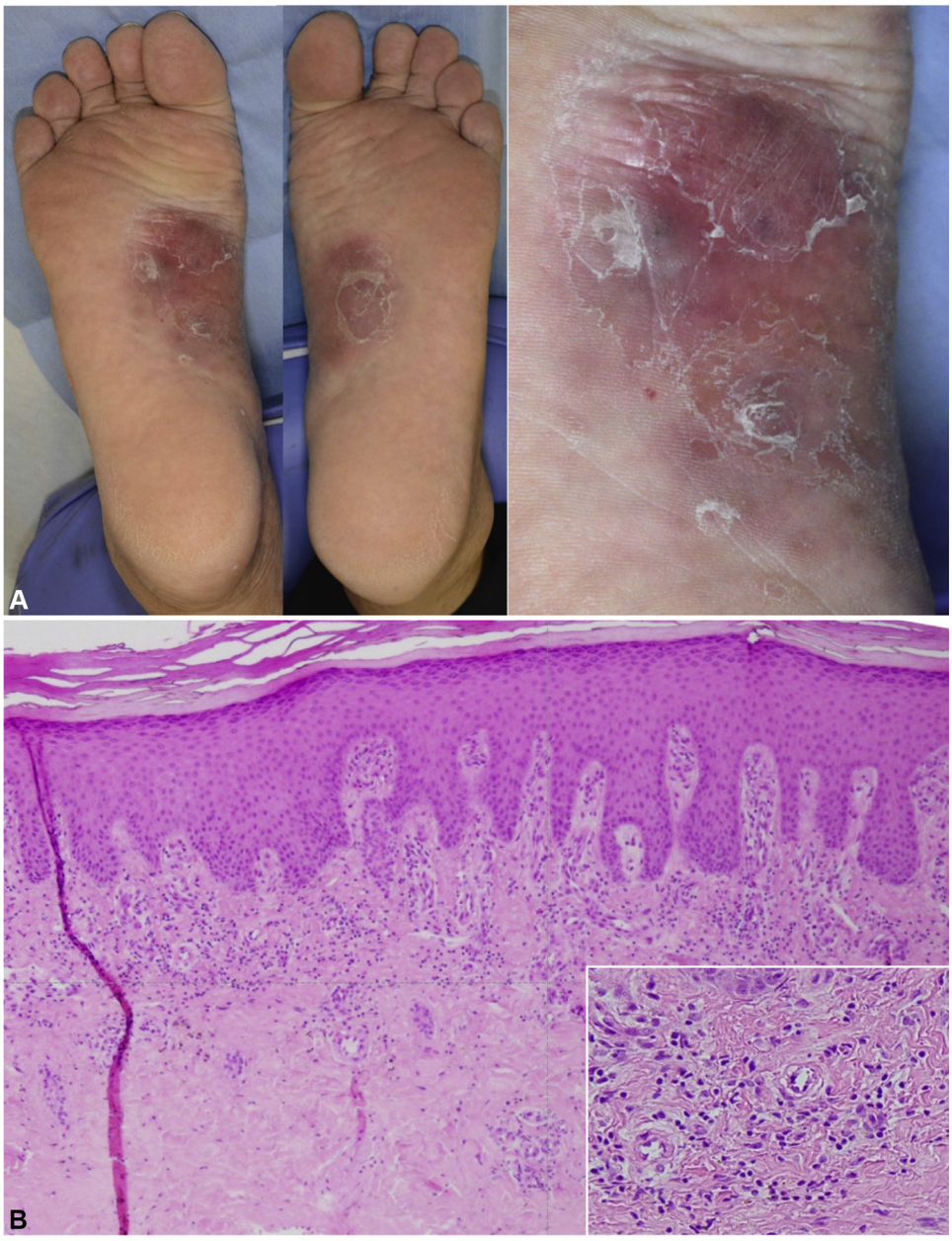

Fig 1. Clinical and pathologic features of the patient. **A**, Photograph taken when the patient's symptoms worsened. The patient showed relatively well-defined sclerotic erythematous plaques with scales on his soles. **B**, A skin biopsy revealed dermal inflammatory cell infiltration (hematoxylin-eosin stain, original magnification ×40) and proliferation of dilated capillaries in the upper dermis (original magnification ×200, *inset*).

hyperplasia of dermal vessels in a lobular arrangement formed by $CD31^+$ vascular endothelial cells without signs of vasculitis or malignancy (Fig 3, *B* to *D*). Based on these pathologic findings, we established the diagnosis of PKS. Propranolol 30 mg daily was initiated and increased to twice daily 2 months later. Thereafter, the erythematous plaques gradually improved and disappeared, leaving pigmentation (Fig 4). His symptoms have not recurred during 2 years of observation. He had no side effects from propranolol and continued it as a treatment for hypertension.

DISCUSSION

PKS is a rare disease among cutaneous reactive angiomatoses and is thought to be characterized by a

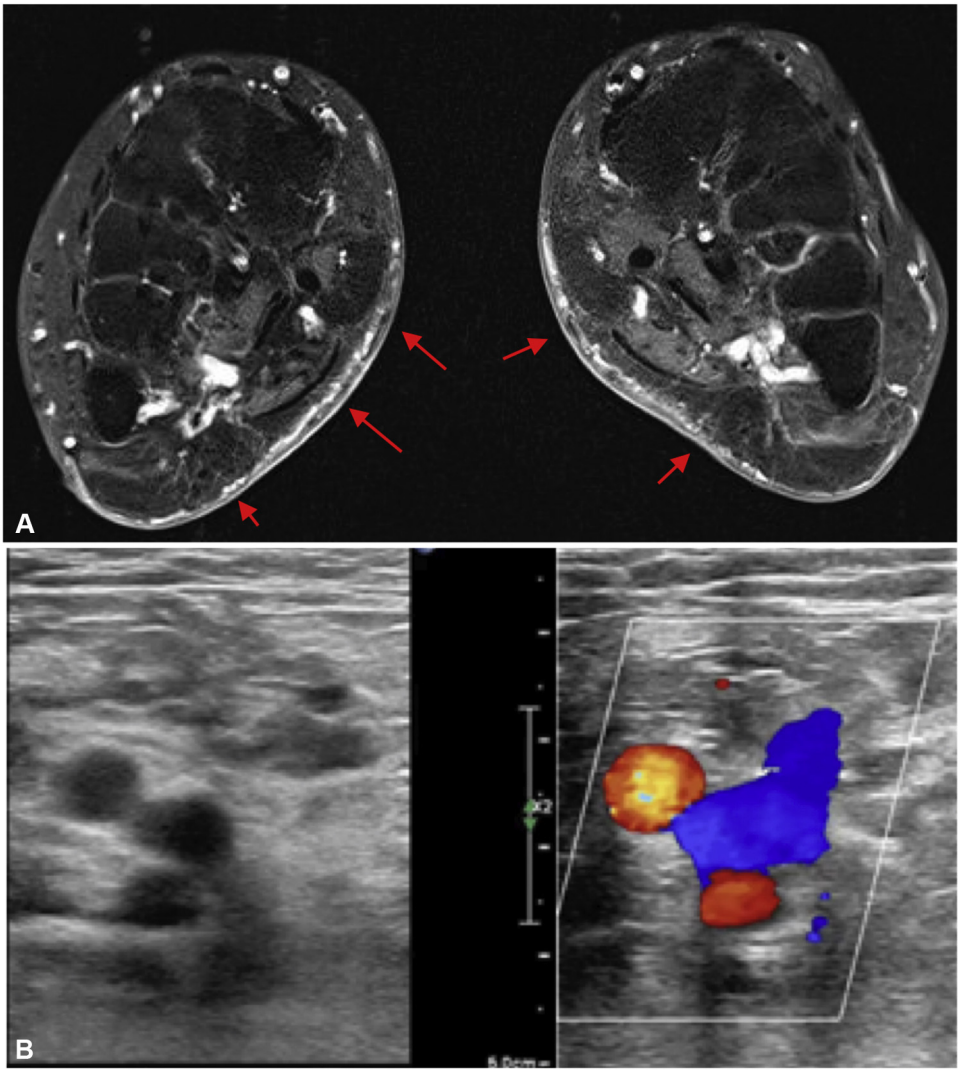

Fig 2. A, Contrast-enhanced magnetic resonance imaging showed subcutaneous venous dilatation in the skin. *Arrows* indicate dilated veins. **B**, A vein echocardiogram revealed multiple arteriovenous fistulas on Doppler view.

vascular abnormality followed by histiocyte recruitment and endotheliocyte and pericyte hyperplasia. PKS typically presents with violaceous papules and plaques, which are usually located on the lower limbs.[1] We provisionally diagnosed a disease with multiple arteriovenous fistulas and then changed the diagnosis to PKS because the patient's histopathologic characteristics developed to resemble those of KS. In most cases, PKS is part of the course of venous hypertension or arteriovenous fistula development. Our case did not show obvious venous insufficiency in the lower extremity but multiple arteriovenous fistulas in the skin lesion. An adult case of bilateral plantar PKS[2] also showed no obvious predisposition to PKS and suggested congenital malformation. Likewise, in our case, we speculated that the patient had an unknown congenital condition for developing PKS, which was gradually worsened by venous pressure due to chronic pressure stimulation at the sole, suggesting that our case may be a variant of the Mali type. The patient with PKS has shown 3 different histologic presentations over the clinical course. We might have observed the development and aggravation of PKS due to increased venous pressure with arteriovenous fistula.

Treatment of PKS tends to be conservative. Compression therapy heals ulcers secondary to PKS and leads to regression of lesions. Other more aggressive treatments include ultrasound-guided sclerotherapy, embolization, and surgical management of the fistula. Propranolol is a nonselective β-adrenergic blocker that competitively blocks the

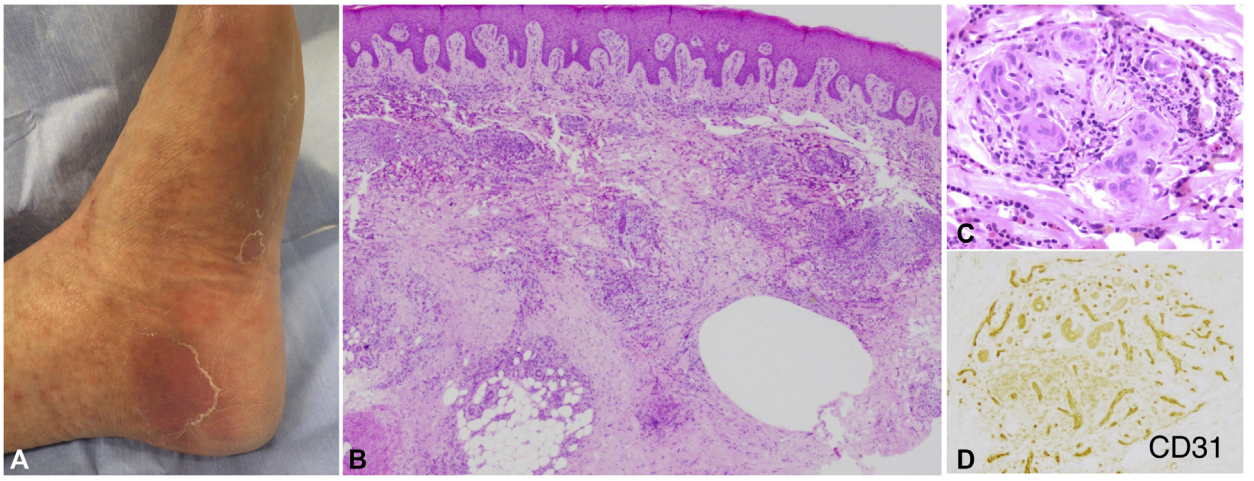

Fig 3. **A**, After 6 months, despite compression therapy, other red plaques emerged. Another skin biopsy was performed. **B**, A histologic image (hematoxylin-eosin stain, original magnification ×20) revealed multiple granulomatous nests formed by $CD31^{+}$ vascular endothelial cells. **C**, Hematoxylin-eosin stain, original magnification ×200. **D**, Immunostaining for CD31, original magnification ×200. These were similar to hemangiomas without signs of vasculitis or malignancy.

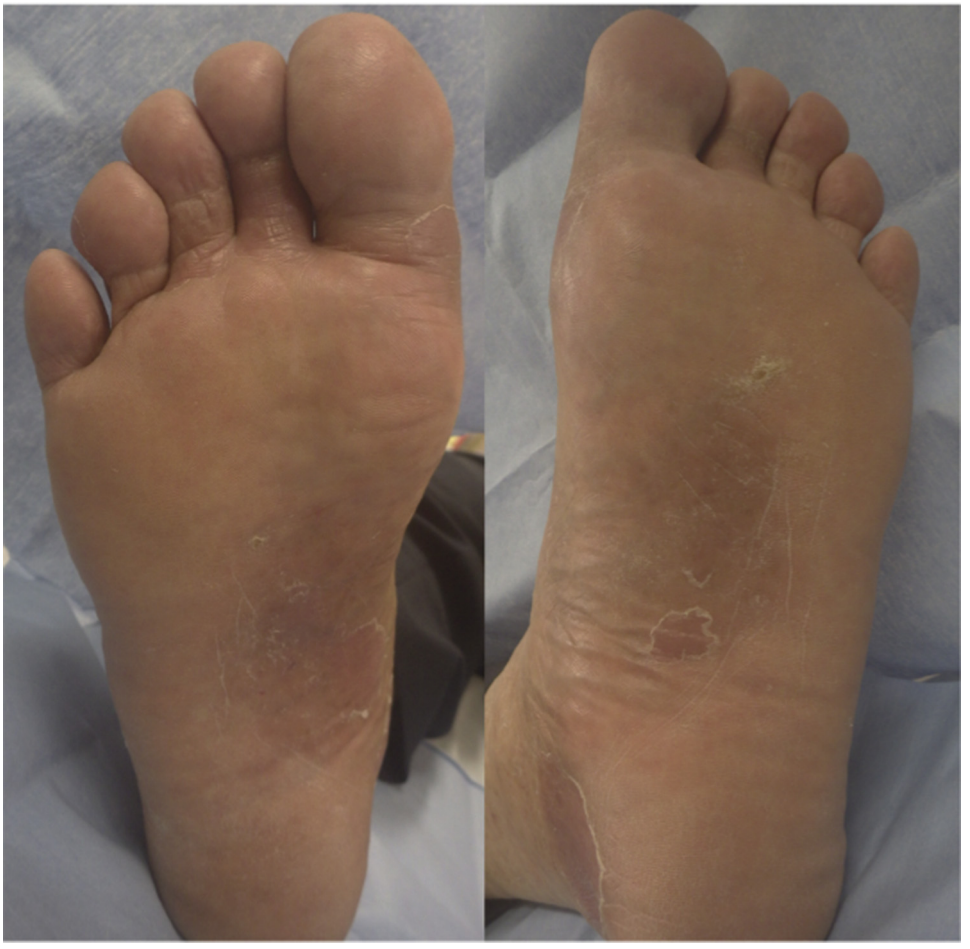

Fig 4. The erythematous plaques gradually improved and turned into pigmentation only.

response to β1- and β2-adrenergic stimulation and is used to treat hypertension and arrhythmia. Oral propranolol and topical beta-blockers are an established treatment for proliferating infantile hemangiomas due to vasoconstrictive and angiogenesis-inhibiting effects.[3,4] Similarly, there are case reports of propranolol improving other vascular diseases such as arteriovenous malformations,[3] cavernous hemangioma,[5] angiolymphoid hyperplasia with eosinophilia,[6] pyogenic granuloma,[7] angiosarcoma,[8] KS,[9] and other reactive angiomatoses (reactive angioendotheliomatosis and graft-versus-host disease-associated angiomatosis).[4] Regression of classic KS lesions treated with topical β-blocker has been noted.[10] Propranolol can be employed to treat a wide range of abnormal vascular changes similar to PKS, such as proliferating infantile hemangioma and other vascular diseases.

Conflicts of interest

None disclosed.

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