A Japanese Gentleman with Reticulate Pigmentation

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CASE SUMMARY

History

A 52-year-old Japanese businessman who had been staying in Hong Kong for the past 16 years complained of an asymptomatic pigmented rash at his axillae, buttocks, back, arms and thighs since teenage. The extent of the skin rash was slowly progressing over the years.

The patient enjoyed good health all along. He had a neck mass excised more than 20 years ago in Japan. The exact diagnosis was not known. There was no family history of similar pigmentation. His two siblings and his two teenage sons were not affected.

Physical examination

A reticulate hyperpigmented macular rash was present at the axillae, groins, extensor aspect of the upper limbs, buttocks, and thighs (Figure 1). Poikilodermatous changes were observed, with hypopigmented macules, epidermal atrophy and telangiectasia (Figure 2). Erythematous patches with epidermal atrophy were also seen, especially over the abdomen and chest (Figure 3). There were no mucosal lesions, palmar pits or nail dystrophy. No lymph nodes were palpable and hepatosplenomegaly was not detected.

Differential diagnoses

The differential diagnoses include mycosis fungoides and its variants, collagen vascular diseases like dermatomyositis and lupus erythematosus, and poikiloderma-like cutaneous amyloidosis. Genodermatoses with reticulate hyperpigmentation, and pigmented disorders which are more commonly seen in Japanese are also considered, in view of the early onset and ethnicity. The former include Dowling-Degos disease, dyskeratosis congenita, Rothmund-Thompson syndrome, Bloom's syndrome, Weary & Kindler syndrome, and Kindler syndrome. The latter consists of dyschromatosis universalis, prurigo pigmentosa and reticulate acropigmentation of Kitamura.

Investigations

Complete blood picture, liver, renal and thyroid function tests were normal. Blood smear for Sezary cells was negative. Anti-nuclear factor was present at a titre of 1/160, with a speckled pattern. Anti-DNA and anti-

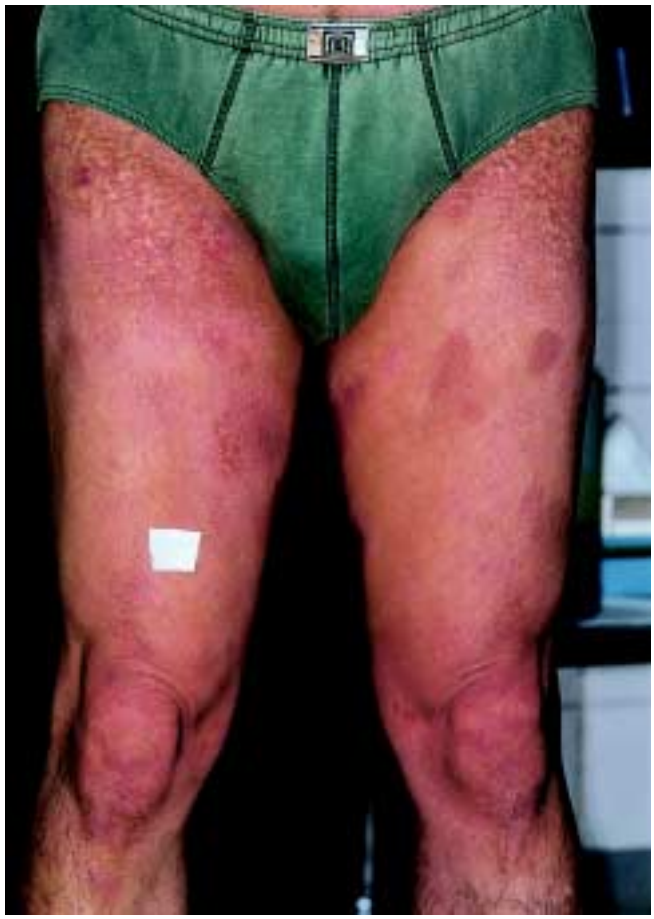

Figure 1: Reticulate pigmentation at the groin area. Erythematous patches with mild epidermal atrophy were seen on the thighs

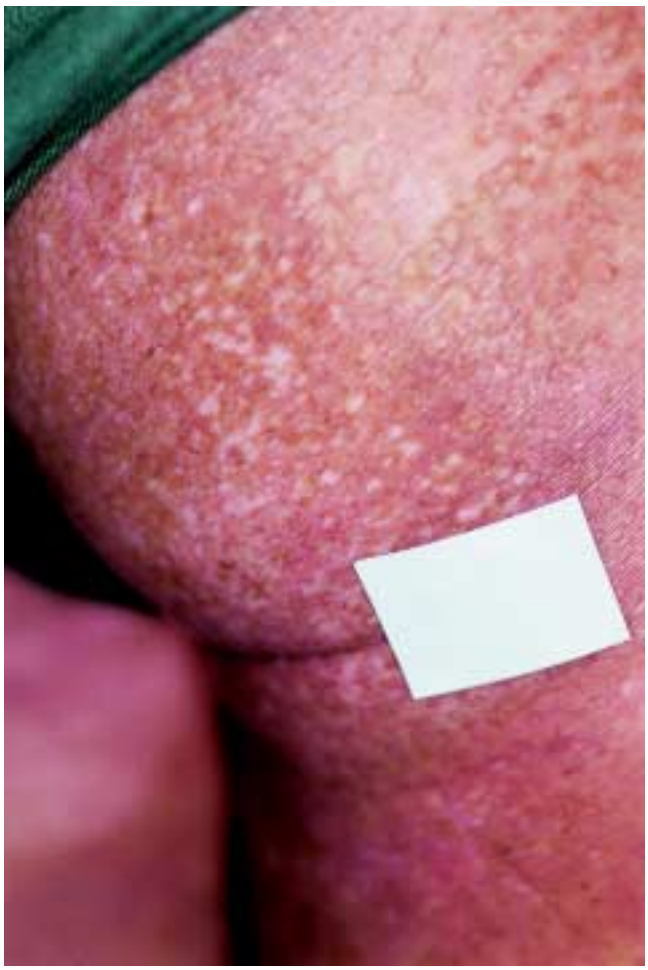

Figure 2: Poikilodermatous changes (reticulate hyperpigmentation, hypopigmentation, telangiectasia and atrophy) prominent over the buttocks

ENA antibodies were absent. Immunoglobulin pattern showed a mildly raised IgG of 1892 mg/dL (819-1725 mg/dL). No monoclonal immunoglobulin was detected by serum electrophoresis. Bence-Jones protein was negative in urine. Chest X-ray and ultrasound sonography of the abdomen did not reveal any abnormalities.

Histology

The first skin biopsy was taken at the thigh where poikilodermic changes were prominent. A lichenoid reaction with focal epidermal atrophy and telangietasia (poikilodermatous change) was present. Prominent epidermotropism by atypical lymphoid cells with pericellular halo was noted. Some of these lymphoid cells were large in size with irregular nuclear outline. T-cell receptor gene rearrangement study by polymerase chain reaction showed a dominant band in a reactive

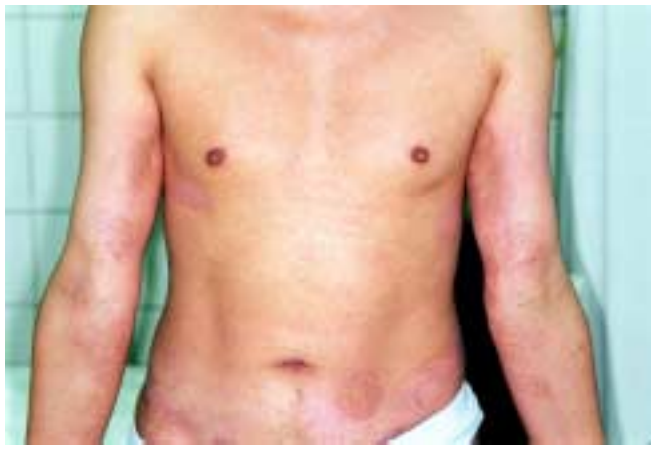

Figure 3: Well-defined, atrophic erythematous patches at the chest and abdomen. Reticulate pigmentation at the axillae and along the inner sides of the upper limbs

background. Congo red and crystal violet stains for amyloid deposit were negative.

A second skin biopsy taken from an erythrodermic patch at the chest showed an atrophic epidermis with elongated rete ridges and a vague band-like lymphocytic infiltrate in the papillary dermis. Prominent epidermotropism with atypical lymphoid cells was again noted. Large Pautrier's microabscresses were absent but there were aggregates of atypical lymphoid cells. T-cell receptor gene rearrangement revealed an abnormal band identical to the band in the previous biopsy.

Diagnosis

Mycosis fungoides, stage IB.

Treatment

The patient was started on PUVA therapy.

REVIEW ON STAGE IB MYCOSIS FUNGOIDES

Poikilodermatous mycosis fungoides and poikiloderma atrophicans vasculare

The salient feature in this patient was the long-standing history of the poikilodermatous lesions which were present for more than 25 years. It cannot be ascertained whether the poikilodermatous lesions started as premycotic lesions which later evolved to mycosis

fungoides, or whether the lesions represented a slow progressing form of mycosis fungoides.

Samman studied 107 patients with poikiloderma atrophicans vasculare ("prereticulotic poikiloderma" or "atrophic parapsoriasis").[1] In about one-fifth, the age of onset was less than 20 years old. From studying the first 50 cases in the series, it was observed that the condition could remain non-progressive for many years: three patients progressed to mycosis fungoides or reticulosis, five died (one due to mycosis fungoides and one due to leukaemia), four had complete resolution, and 28 remained more or less static, including 11 in whom the condition present for more than 20 years.

Prognosis of stage IB mycosis fungoides

Mycosis fungoides is usually staged using the TNM classification (Table 1 and 2). Kim et al studied the long-term outcome of 176 patients with generalized patch and/or plaque stage (T2) mycosis fungoides.[2] Most subjects were treated with topical nitrogen mustard or total skin electron beam therapy (TSEBT). The relative risk of death compared with race, age and sex-matched controls was 2.3 (95% C.I. 1.9-2.8). The calculated survival rates at five, 10 and 20 years were 73%, 55% and 27%, respectively. Patients who were younger than 58 years old had longer median survival than older ones (18.2 years vs 7.1 years). Nineteen percent of the deaths were due to mycosis fungoides. Disease progression occurred in 24% of patients in stage IB. There was no significant difference between the survival rates of those with stage IB and IIA disease.

Table 1. TNM classification for mycosis fungoides

Classification	Description
T (Skin)	
T1	Limited patch/plaque (<10% of total skin surface)
T2	Generalized patch/plaque (>10% of total skin surface)
T3	Tumours
T4	Generalized erythroderma
N (Nodes)	
N0	Lymph nodes clinically uninvolved
N1	Lymph nodes enlarged, histologically uninvolved
N2	Lymph nodes clinically uninvolved, histologically involved
N3	Lymph nodes enlarged and histologically involved
M (Viscera)	
M0	No visceral involvement
M1	Visceral involvement

In van Doorn et al's series, 135 patients were diagnosed as stage IB mycosis fungoides, with a median age of 61 at diagnosis.[3] The majority were treated with psoralen plus ultraviolet-A (PUVA) phototherapy. The overall survival at 10 years was found to be 61% with a disease-specific survival of 83%. Thirty percent had complete remission on initial therapy. Progression to a more advanced stage occurred in 24%. The survival rate of stage IB patients was found to be the same as stage IA patients. The study also found that complete remission on initial treatment was significantly related to survival in stage IB patients.

Treatment options for stage IB/T2 mycosis fungoides

Phototherapy

PUVA is the most popular choice of phototherapy in the treatment of mycosis fungoides. Herrmann et al achieved a 59% complete clinical & histological response rate, and a 35% partial response rate with PUVA in 49 stage IB patients.[4] The average dose to initial clearing was 140 J/cm^2. The freedom from relapse rate at five years was 25%.

Broadband UVB was able to induce complete clinical response in 83% of six stage IB patients with patch lesions in Ramsay et al's study. However, it was not able to induce remission in any patients with plaque lesions.[5] The median time to remission was five months, and the median duration to relapse was 22 months.

Narrowband UVB achieved a complete clinical response in 75-83% for stage IA/B patients with patch lesions.[6,7] The mean time to complete clearance was short, within 10 weeks. However, the relapse rates were

Table 2. Clinical staging system for mycosis fungoides

Clinical stages	T	N	M
IA	T1	N0	M0
IB	T2	N0	M0
IIA	T1-2	N1	M0
IIB	T3	N0-1	M0
IIIA	T4	N0	M0
IIIB	T4	N1	M0
IVA	T1-4	N2-3	M0
IVB	T1-4	N2-3	M1

high. In Hoger et al's study, all patients relapsed within five months.[7]

Zane et al used UVA1 (340-400 nm) at a dose of 100 J/cm^2 five times per week.[8] An 88% complete clinical and histological response was achieved in eight stage IB patients. Twenty-nine percent relapsed during a mean follow-up duration of 7.2 months, but they responded to a second course of UVA1 treatment.

Topical corticosteroids

Zackheim et al documented the efficacy of topical corticosteroids for the treatment of early stage mycosis fungoides.[9] The complete remission rate for stage T1 and stage T2 patients were 63% and 25% respectively, and the corresponding partial remission rates were 31% and 57%. Temporary depression of serum cortisol occurred in 13%, and was more common among T2 patients.

Other single therapy

For T2 mycosis fungoides, topical nitrogen mustard and carmustine had complete response rates of 26% and 48%, respectively.[10, 11] Total skin electron beam therapy cleared all lesions in 92% of stage IB patients[12] and 71% of T2 pateints.[13] Systemic retinoids are rarely used on their own in the treatment of mycosis fungoides. A novel RXR-selective retinoid, bexarotene, is undergoing phase three trial for early stage mycosis fungoides which were resistant to other forms of therapy.[14] Other modalities, such as interferon-α, systemic chemotherapy, photophoresis and photodynamic therapy are not usually used in the initial treatment of early stage mycosis fungoides.

Combination therapy

Aggressive treatment with multiple modalities is sometimes used, for example a combination of oral isotretinoin, interferon-α, TSEBT and nitrogen mustard.[15] Whether this approach will have any benefits on long-term survival over less toxic single therapy in the treatment of early stage mycosis fungoides remains to be determined.

Learning points:
Mycosis fungoides should be included in the differential diagnoses for poikilodermic lesions, even for cases with early onset, as the condition can remain non-progressive for many years.

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