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Case Report

A case of hard-to-diagnose Papuloerythroderma of Ofuji in an elderly male

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Abstract Papuloerythroderma of Ofuji (PEO) is a rare form of dermatosis, frequently regarded as a diagnosis of exclusion. The clinical manifestation comprises brownish-red flat papules characteristically sparing the skin fold area, giving the tell-tale "deck chair" sign. Despite the distinctive presentation, many PEO cases are relatively difficult to be recognized, owing to the largely nonspecific clinical and histopathologic features. Various conditions, including atopy, infection, medication, and malignancy, especially cutaneous T-cell lymphoma (CTCL), are often associated with the disease. Herein we described an elderly Indonesian male with erythematous plaques on the head and trunk initially diagnosed as psoriasis vulgaris, in whom PEO was established after two months of evaluation. Treatment with oral cyclosporine and methylprednisolone resulted in clinical improvement. This case illustrates that albeit rare, PEO, and more importantly CTCL, need to be ruled out in this particular demographic setting.

Key words
Cyclosporine; Geriatric; Malignancy; Papuloerythroderma of Ofuji.

Introduction

Papuloerythroderma of Ofuji (PEO) was first reported by Ofuji *et al.* in 1984. It is considered a rare form of dermatosis with a prevalence of approximately 1.5 cases per one million population, but more commonly found among elderly Asian men.[1] This condition is characterized by an itchy erythematous eruption consisting of flat, red-brown papules that coalesce to form plaques. The deck chair sign, i.e. sparing of the skin folds, is one of the classical signs of PEO, although it has also been reported in other dermatoses.[2] The majority of cases are idiopathic; however, causality of malignancies, including cutaneous T-cell lymphoma (CTCL), is reported frequently.[3] CTCL is usually considered as a differential diagnosis of PEO; therefore, ruling out its possibility at the initial suspicion is imperative.[1,3] This case report addresses the challenges in diagnosing PEO in a 69-year-old male patient who was initially identified with psoriasis vulgaris and psoriatic arthritis.

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Case report

A 69-year-old male came with pruritic erythematous and brown plaques on almost his entire body worsening around three months ago. It started two years ago as itchy and scaly erythematous papules on his arms which later coalesced into plaques. No history of fever bouts prior to the skin breakout. Since eight months ago, the lesions had extended to the scalp, face, neck, trunk and both legs, and pruritus had become more severe. They were not triggered by sun exposure. The patient experienced neither

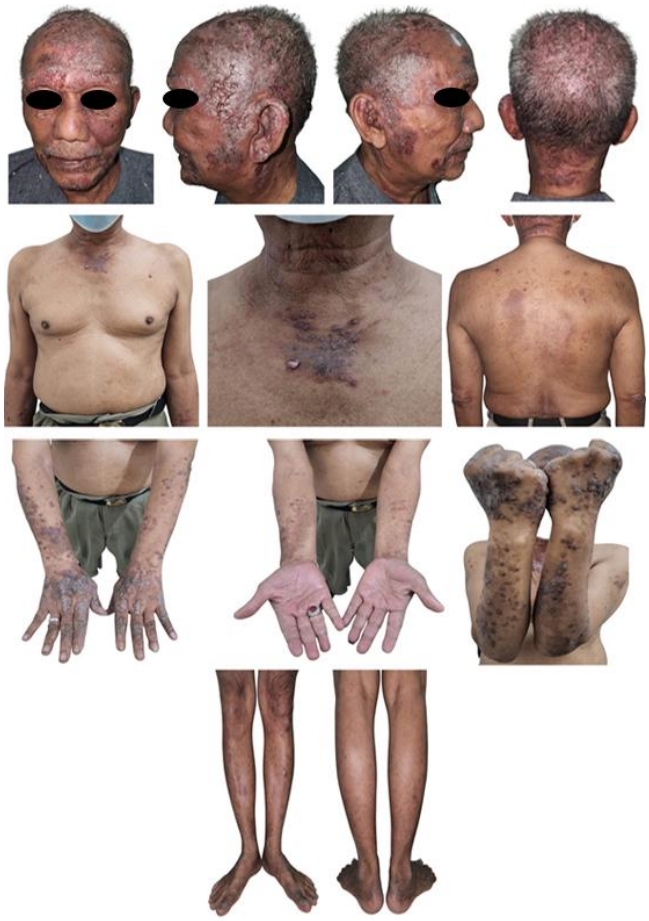

Figure 1 A 69-year-old male suffered from erythematous and hyperpigmented, scaly papules and plaques for two years duration, worsening since the past three months, despite methotrexate and steroid treatment for psoriasis vulgaris. The lesions mainly located in the sun-exposed areas, especially the scalp and head. Some sparing of skin creases on the neck were observed (red arrows).

intermittent fever, stomatitis, fatigue, nor weight loss. There were no nail or mucosal involvements as well. No evidence of hypertension, diabetes, dyslipidemia, or other systemic diseases were present. Past and family history of childhood eczema, asthma, and allergic rhinitis were denied. In addition, the patient suffered from recurrent pain on both knees and hips. Initially, an internist established the diagnoses as psoriasis and psoriatic arthritis and prescribed methotrexate 10 mg/week, increased by 2.5 mg every two weeks until reached the maximum dose of 17.5 mg/week, and folic acid 5 mg/week. As for further evaluation and management of the skin problem, a referral to the dermatology outpatient clinic was conducted.

On inspection, erythematous and hyperpigmented plaques with white, thick, adherent scales and varying degree of ulceration were observed on the scalp, face, preauricular, neck, upper chest, back, arms, dorsal hands, dorsal hand, and feet. Skin creases on the neck was spared (**Figure 1**). Lymph node enlargement was not found. Subsequent dermoscopic evaluation revealed perifollicular white halo, red dots, white scales, brown globules, erythema structureless area on cutaneous lesion, without periungual telangiectasia on the nails (**Figure 2**). On the other hand, laboratory examination demonstrated increased blood sedimentation rate (111 mm/h) and CRP (9.1 mg/L), leukocytosis (11.670/µL), eosinophilia (650/µL), and elevated

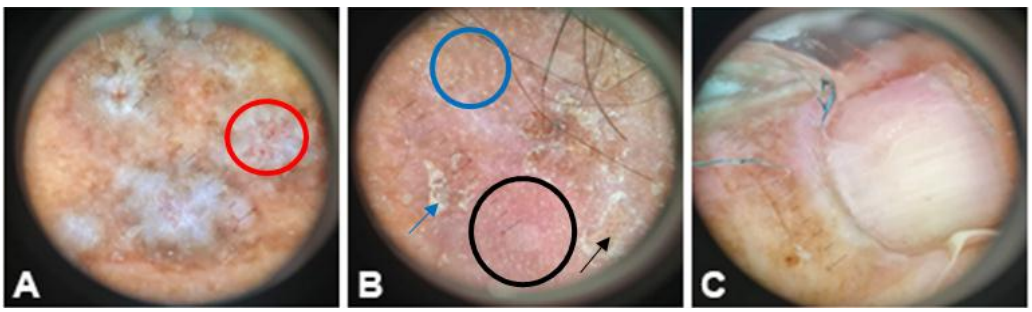

Figure 2 Dermoscopic examination showed: (A) red dots (red circle); (B) perifollicular white halo (blue arrow), white scales (black arrow), brown globules (blue circle), structureless erythema area (black circle) on cutaneous lesion; and (C) no periungual telangiectasia on the nails.

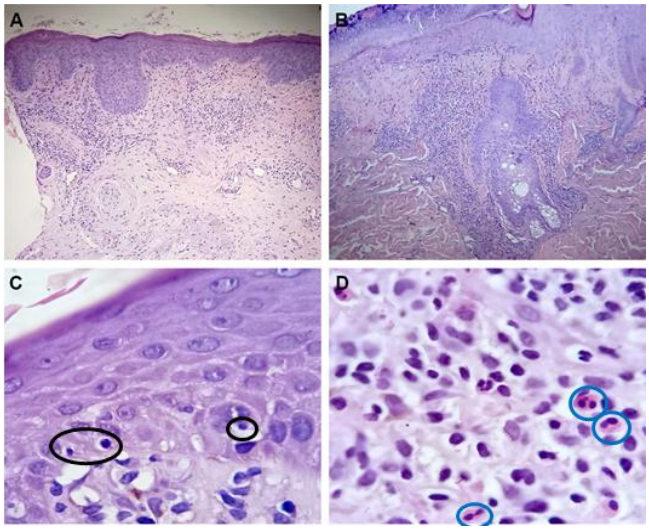

Figure 3 (A) Histopathology from a lesion on the face showing primarily interface dermatitis. (B) Adjacent to the dermoepidermal junction, heavy lymphocytic infiltrates were found around hair follicles. (C) Some lymphocytes were found reaching into the epidermis (black ovals) and (D) eosinophils were conspicuous (blue ovals). Note that the classical features of psoriasis were absent.

total IgE levels (145.4 IU/ml). Sézary cells were not found in peripheral blood examination. Antinuclear antibody (ANA) titer was 1/320 (coarse, speckled pattern) but anti ds-DNA was within normal limit (3.3 IU/ml). Due to the minimal clinical improvements following two months treatment with methotrexate, skin biopsy was performed two weeks after stopping the regimen. Histopathologic findings from plaques on the left cheek and left arms consisted of acanthosis, parakeratosis, some epidermal necrosis, vacuolar alteration, perivascular and interstitial lymphocytes, but most strikingly, melanin deposits, large number of eosinophils, and few atypical lymphocytes (**Figure 3**). Papuloerythtroderma of Ofuji and CTCL were considered as the differential diagnoses. Immunohistochemistry staining showed CD3 and CD5 were positive in most cells; CD20, CD4, CD30, CD56 were negative; CD8 and CD7 were positive in some cells; and Ki67 was positive, consistent with reactive, non-neoplastic process, that the diagnosis of PEO was settled on.

Given the final diagnosis, the treatment was switched into the combination of 200 mg cyclosporine and 12 mg methylprednisolone daily, resulting in decreasing pruritus and resolving of some lesions, except for plaques on the nape, neck, and the dorsal hands (**Figure 4**). He was consulted to hematology-oncology division for successive evaluation and screening for malignancy.

Discussion

Psoriasis vulgaris is characterized by well-demarcated erythematous plaques with silvery-white scales, primarily on the extensor extremities, scalp, trunk, lumbosacral area, and buttocks.[4] Multiple joint involvements are often found in psoriasis, as seen in this case. However, failure to respond with adequate psoriatic treatment led us to explore another possible differential diagnoses, such as subacute

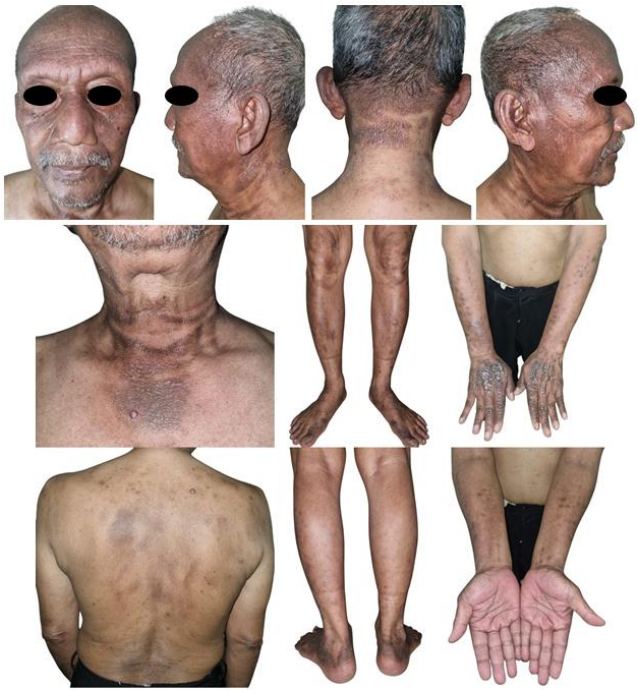

Figure 4 Improvement of the PEO cutaneous features following cyclosporine and methylprednisolone treatment. However, lesions on the nape, neck, presternal area, and dorsal hands were still present.

cutaneous lupus erythematosus (SCLE), lichen planus, seborrheic dermatitis, and CTCL.

In SCLE, the typical clinical features are papulosquamous lesions or hyperkeratotic annular plaques in sun-exposed skin areas.[5] Although the distribution of lesion in this case was consistent with SCLE, that was not the case with the morphology. Furthermore, they were not exacerbated by sunlight. ANA examination showed a positive result, but other diagnostic criteria of SLE were not fulfilled.

The predominant morphology was flat papules which coalesced to form plaques, suggesting a probable diagnosis of lichen planus (LP). However, LP lesion is usually violaceous and accompanied by Wickham striae, attributes that were absent in our case. The main predilections of lichen planus are the wrist, hands, and lower limbs, and rarely affects the scalp.[6]

The lesion distribution on the scalp, face, retroauricular, and upper chest resembled those of seborrheic dermatitis, nevertheless, they were characterized by yellowish scales and generally responsive to topical corticosteroids.

The histopathological pattern in this case was decidedly interface dermatitis, which should raise a suspicion to CTCL. However, further immunohistochemical evaluation favored a reactive (non-neoplastic) condition. The findings and the rising of blood eosinophils led to the conclusion of PEO.

The non-specific clinical properties of PEO often result in the delayed diagnosis,[3] such as in this case. The average duration from the onset until the diagnosis of PEO is about seven months,[1] while the diagnosis of this patient was reached after two months of evaluation.

In 2010, Torchia *et al.* proposed a set of diagnosis criteria consisting of five major and five additional minor criteria.[1] Our patient satisfied three major criteria, i.e. (1) eruptions resembling erythroderma evolving from multiple brownish-red flat papules coalescing into plaques; (2) deck chair sign on the lateral neck area; and (3) pruritus. Despite the result of immunohistochemistry, the possibility of CTCL could not be completely ruled out as histological marks may notoriously be found only after repeated biopsies in a considerable span of time. Currently, the patient is evaluated in the hematology-oncology clinic for possible underlying malignancy. Thus, the other major criteria, exclusion of malignancy could not be ascertained yet. Four of the five minor criteria were met: (1) male; (2) age over 55 years; (3) increased eosinophils in peripheral blood and tissues; and (4) elevated total IgE serum. No peripheral lymphopenia was noticed.

The dysregulation of T cell function is thought to be involved in the pathogenesis of PEO, although the exact mechanism is unclear. Numerous cytokines produced by Th2 and Th22 triggers tumor progression by suppressing immune responses. This might account for the association of PEO with malignancies.[7,8] Approximately 51.3% of malignancies in PEO originate from the gastrointestinal tract,[7] especially gastric cancer in the Japanese population,[8] and the others are sourced from colon, esophageal, prostatic, lung, and blood precursors.[9] PEO is sometimes regarded as a variant of mycosis fungoides, specifically the folliculotropic type. Several reports suggest that PEO may potentially be a CTCL so that T-cell receptor (TCR) clonality testing is required to rule this out.[3,7] Biopsy results in this patient were nonspecific for CTCL, whilst immunohistochemical examination showed a reactive process. T-cell receptor (TCR) clonality test was not performed due to unavailability in our setting.

PEO is also frequently associated with atopic conditions, infections, and medications.[8] A history of atopy is present in approximately 20% of the patients, but non-specific histologic features complicated the distinction. Infection, for instance by human immunodeficiency virus (HIV), fungi, and parasites has also been incriminated. Remission after treatment of viral infection with interferon alfa seems to support the hypothesis. Additionally, common drugs such as aspirin, furosemide, isoniazid, nifedipine, and ranitidine have been reported to trigger the lesions.[9]

Replacement of previous therapy with cyclosporine after diagnosis of PEO in our patient dramatically improved most of his lesion within two weeks. The use of cyclosporine has been beneficial in a case of PEO with sternoclavicular arthritis. After administering cyclosporine at a dose of 2 mg/body weight/day for three months, cutaneous remission was achieved and joint complaints improved to allow the dose decrements. Unfortunately, the skin lesions recurred after discontinuation.[10]

To date, no management guidelines for PEO have been universally adopted. Treatment options comprised oral corticosteroids, psoralen and UVA (PUVA), oral retinoids, and other modalities. A systematic review by Mufti *et al.* described that single therapy of oral retinoids and PUVA was superior to oral corticosteroids in terms of efficacy. The effectiveness of the combination of PUVA with topical corticosteroids or oral retinoids has been proven, with a complete resolution was attained in up to 60% of patients.[11] Most PEO cases have a favorable prognosis, but it is essential to exclude CTCL as the latter may negatively affect the outcomes.[1,9]

Conclusion

The diagnosis of PEO should be considered especially in male patients older than 55 years of age with an eruption resembling erythroderma consisting of flat papules that coalesce to form plaques, without the involvement of skin fold areas (deck chair sign). Laboratory abnormalities such as increased eosinophils in peripheral blood and tissue, elevated serum IgE levels, and lymphopenia support the diagnosis. Ruling out CTCL is important when the diagnosis of PEO is suggested. Routine histologic examination might not always clearly differentiate the two, hence additional investigations such as immunohistochemistry and T-cell receptor clonality testing are required.

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