CASE NO. 9

Patient: A 62–year-old Thai female from Singburi province

Chief complaint: Multiple asymptomatic nodules for 4 months

Present illness: The patient had a 4-month history of progressively asymptomatic skin lesions.

Past history: She was diagnosed with corneal ulcer of her left eye with abnormal revascularization suspected peripheral ulcerative keratitis (PUK) since 2007. She had no history of fever, arthralgia, arthritis, prior GI or URI symptoms. No diarrhea, anorexia and weight loss were demonstrated.

Family history: unremarkable

Physical examination: unremarkable

Skin examination: Multiple discrete symmetrical, rubbery to firm, erythematous to violaceous papules and nodules which some lesions were confluent to plaques predominately on extensor aspects of forearms, hands, knees and upper thighs (Fig. 9.1, 9.2)

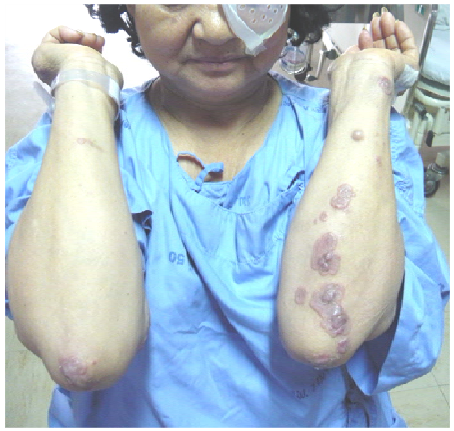

Fig. 9.1

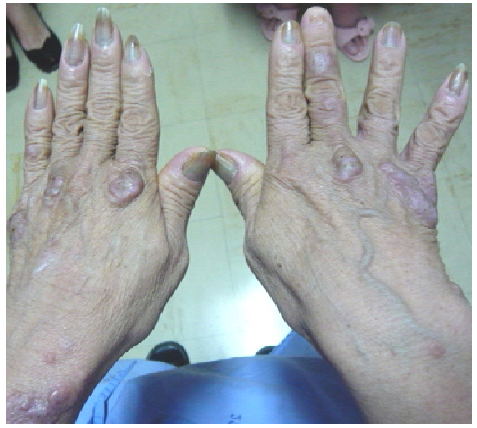

Fig. 9.2

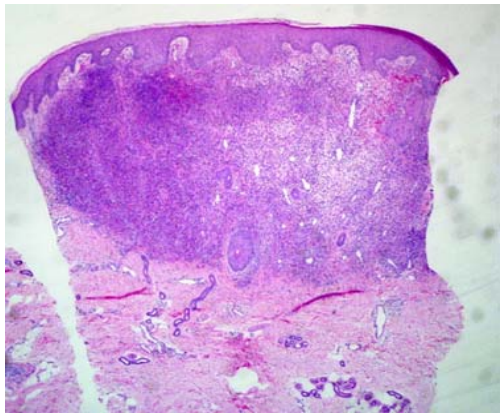

Fig. 9.3

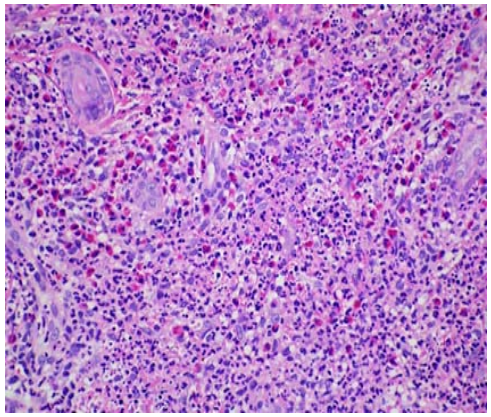

Fig. 9.4

Histopathology: (S09-2363B) (Fig. 9.3, 9.4)

- Dense diffuse inflammatory infiltrate of mostly neutrophils, nuclear dusts, intermingled with lymphocytes, histiocytes, eosinophils and extravasated erythrocytes in the dermis.
- Increase numbered of thick-walled blood vessels lined by plump endothelial cells.
- Edema of the upper dermis.

Investigation:

CBC: WBC 3,600 /μl, N 36%, L 38%, M 11%, Eo 15%, Hct 35.8%, platelets 429,000/μl

LFT: Total protein 76.1 mg/dl, Alb 46 mg/dl, AST/ALT 49/41 U/L, GGT 110 U/L

Hepatitis profile: HBsAg negative, AntiHBs positive >1,000 mIU/ml

Anti HIV: Negative

ANA: Positive 1:80, homogenous pattern

Rheumatoid factor: Negative
CXR: unremarkable

Diagnosis: Erythema elevatum diutinum

Treatment: Dapsone

Presenter: Punnaya Sirithanabadeekul

Consultant: Penpun Wattanakrai

Premjit Viyavajamai

Discussion:

Erythema elevatum diutinum (EED) is a rare form of chronic cutaneous vasculitis. Due to its characteristic late stage demonstrating granulation response with a proliferation of dermal spindle cells, it is sometimes called fibrosing leukocytoclastic vasculitis (LCV). EED was firstly described by Bury and Hutchinson in the late 1880s[1]. Previously, EED was divided into Bury type, typically occurring in young women with rheumatologic disease and the Hutchinson type, presenting in elderly men. However, it is currently considered to be only one entity regardless of patient's underlying illness[1].

Clinically, typical lesions are multiple, symmetrical, firm, tender, red to reddish brown or purplish papules and nodules which then may coalesce to yellow-brown large nodules or plaques with eventual dyspigmentation. The extensor aspects of extremities especially prominence elbows, knees, ankles, dorsal sides of hands and feet are classic distribution; although, periauricular, truncal[2], fingertips[3], palms and soles[4] involvement and penile ulcer[5] had been reported. Cold exposure can exacerbate lesions to be more raised and erythema. EED is commonly found in patients in the fourth to the sixth decade of life with slightly male predominance. The lesions generally demonstrate intermittent and chronic relapsing course over several years; however, it may resolute spontaneously after 5-10 years[6]. Partial involution may give a yellowish or brownish hue, resembling xanthomas.

The etiology of EED is not clear. Nevertheless, it is presumed to represent an immune-complex disease. Several mechanisms including repeated immune complex deposition within vessel walls, complement fixation, inflammatory responses and vascular destruction may involved.

Histopathologically, consistent changes are described in early and late stages. Dense perivascular infiltration of neutrophils admixed with lymphocytes and histiocytes, papillary dermis and perifollicular involvement without a grenz zone are found in the early lesions. In contrary, minimal inflammatory infiltration and marked perivascular fibrosing thickening are characteristic findings in late lesions. Vascular endothelium of EED stained positive for CD31, CD34, VEGF and factor VIIIa[7]. Depending on the stage of lesions, EED can be confused clinically and histopathologically with several dermatoses including granuloma annulare, granuloma faciale, sweet's syndrome, xanthoma, necrobiotic xanthogranuloma, fibrous histiocytoma or dermatofibroma and Kaposi's sarcoma. However, the diagnosis of EED is based on characteristic clinical presentations and histopathologic findings.

Although the pathogenesis is unclear, EED has been associated with numerous medical conditions. Streptococcal, hepatitis B and HIV infection are importantly associated infectious entity of which EED might be a cutaneous reaction. Hematologic malignancy such as B-cell lymphoma, chronic lymphocytic leukemia, polycytemia vera and IgA monoclonal gammopathy are the most common malignant associations, and should be ruled out. Concurrent rheumatoid arthritis, autoimmune etiologies or even insect bite reaction have been reported.

Regarding to the chronic and recurrent course of disease, EED treatment is quite difficult. However, treatment of the underlying disease or the associated condition can improve the results. Generally,

dapsone is the first line drug of choice. Dramatic and rapid response has been shown within 48 hours after dapsone administration and nearly complete resolution has been achieved in weeks or months. Nevertheless, it may be less effective in late stage due to the fibrotic formation. Unfortunately, EED may recur when dapsone is discontinued. Alternatively, tetracycline, niacinamide, colchicine, chloroquine, intralesional, potent topical steroid and systemic corticosteroids have been prescribed.

To the best of our knowledge, our patient is the fifth peripheral ulcerative keratitis associated condition with EED. The first three cases developed PUK concomitant with EED eruption[8]. Similarly, all cutaneous lesions dramatically responded to dapsone while eye problem was improved in two of them. In the forth case, EED was diagnosed more than 1 year prior the PUK development[9]. As a result, PUK could be found concomitant, prior to or after EED eruption. Therefore, complete ophthalmic examination for PUK should be considered in patients with EED. Our patient's lesions have been significantly improved after the dapsone administration.

Reference:

1 Gibson LE, el-Azhary RA. Erythema elevatum diutinum. Clin Dermatol 2000; 18: 295-9.

2 Hatzitolios A, Tzellos TG, Savopoulos C et al. Erythema elevatum diutinum with rare distribution as a first clinical sign of non-Hodgkin's lymphoma: a novel association? J Dermatol 2008; 35: 297-300.

3 Hansen U, Haerslev T, Knudsen B et al. Erythema elevatum diutinum: case report showing an unusual distribution. Cutis 1994; 53: 124-6.

4 Barzegar M, Davatchi CC, Akhyani M et al. An atypical presentation of erythema elevatum diutinum involving palms and soles. Int J Dermatol 2009; 48: 73-5.

5 Yoshii N, Kanekura T, Higashi Y et al. Erythema elevatum diutinum manifesting as a penile ulcer. Clin Exp Dermatol 2007; 32: 211-3.

6 Wilkinson SM, English JS, Smith NP et al. Erythema elevatum diutinum: a clinicopathological study. Clin Exp Dermatol 1992; 17: 87-93.

7 Wahl CE, Bouldin MB, Gibson LE. Erythema elevatum diutinum: clinical, histopathologic, and immunohistochemical characteristics of six patients. Am J Dermatopathol 2005; 27: 397-400.

8 Takiwaki H, Kubo Y, Tsuda H et al. Peripheral ulcerative keratitis associated with erythema elevatum diutinum and a positive rheumatoid factor: a report of three cases. Br J Dermatol 1998; 138: 893-7.

9 Aldave AJ, Shih JL, Jovkar S et al. Peripheral keratitis associated with erythema elevatum diutinum. Am J Ophthalmol 2003; 135: 389-90.