Eruptive pseudoangiomatosis (EPA) is a benign, asymptomatic and self-resolving disorder that is characterized by the sudden appearance of angiomatous-like papules [1, 2]. The consensus that EPA preferentially affects children had not been queried until Navarro et al. [3] reported their first adult case in 2000. We herein report a frequently relapsing adult case that was successfully controlled with pimecrolimus 1% cream.

A 69-year-old Chinese female complained of angiomatous papules on the face and the dorsal surfaces of her hands. The lesions had first appeared on the face and the extensor surface of the hands 6 months earlier, however they had not been accompanied by a high fever or other prodromal symptoms. Since then, similar lesions had relapsed at the same site after a quiescent period of approximately 10 days. Each occurrence lasted 12–18 days, and occurred without sequelae. There was no itching or other abnormal sensations, nor were there urticaria, purpura, ulceration, papulovesicle or overlying scales. The patient was otherwise well and she denied a previous history of insect bites or drug use. Previous treatment with oral citirizine tablets had been unsuccessful and had not prevented relapses. On examination, angiomatous papules with diameters of between 2 and 5 mm were noted on the face and dorsal surfaces of the hands. Scales, ulcerations and crusts were not observed (fig. 1, 2). There were no similar lesions on other parts of the body. The red papules blanched completely with pressure and rapidly refilled from the center after release. Analyses of the lymph nodes, spleen and liver revealed no abnormalities. Routine laboratory tests were normal, and serological testing for echovirus, cytomegalovirus, parvovirus B19, hepatitis B and C viruses and human immunodeficiency virus were all negative. Autoantibodies and a serial of tumor markers (AFP, CEA, FER, β2Mg, CA-50, CA125) were all in normal ranges. A skin biopsy revealed di-
lated vessels which were lined with plump endothelial cells. Mild perivascular lymphocytes and sparse eosinophilic cells had infiltrated the superficial and midermis. Fibrinoid degeneration was an occasional microscopic finding, but there was no sign of thrombus formation or extravasation of red blood cells. The vascular number was within the normal range and the epidermis was normal (fig. 3, 4). On the basis of the clinical and histological findings, a diagnosis of EPA was made. The patient had received no therapy for at least the 4 months before this consultation. After the patient had provided written consent, she was treated with pimecrolimus 1% cream (Elidel, Novartis Pharma, China) once daily on the affected areas. Complete resolution was seen 5 days later, and no recurrence was observed during the following 12 weeks of consecutive pimecrolimus topical application. However, since completion of the initial treatment, the patient has had 4 relapses during 6 months of follow-up. Each recurrence responded similarly well to the pimecrolimus cream. No skin irritation or any local adverse effects were observed during the treatment.

Discussion

Almost 60 cases of EPA have been documented in the English-language literature since the condition was first reported in 1969 [1]. Most cases had their onset in summer and were characterized by asymptomatic, erythematous papules that typically measured between 2 and 4 mm in diameter. EPA preferentially affects the face and the hands. If other parts, except the face, are involved, a blanching halo is likely to surround the papules. The erythematous color tends to vanish in response to pressure, and refills with release. Children and adults are equally affected, though several of the earliest reports were about youngsters. In pediatric patients, fever, headache or upper respiratory tract infection are common prodromal symptoms, which contrasts with the adult condition that tends to lack these symptoms (as seen in our case). Lesions are supposed to resolve quicker in the adult case (1–2 weeks) than in children (usually 1 month) [4–6]. All 15 adult patients so far reported (including the present case) were females, if cases with mosquito or insect bite were excluded. This indicates that females may be vulnerable to EPA as adults.

In EPA, dilated blood vessels with plump endothelial cells are the most prominent histological features. Mild perivascular lymphocytic and sparse eosinophilic infiltration are obvious in the superficial and midermis [5]. Extravasation of red blood cells is an occasional pathological finding [7]. Furthermore, the absence of vascular proliferation differentiates EPA from other skin disorders that have similar clinical presentations. In our case, besides some pathological features typical of EPA, a small proportion of vessels showed plump endothelial cells and mild fibrinoid degeneration without thrombus formation; however, the pathological significance of this has not been determined.

EPA can be misinterpreted as erythema punctatum Higuchi, which is clinically characterized by haloed erythema due to mosquito bites. Histological studies revealed prominent capillary dilatation without hobnail endothelial cells, which is exclusively present in EPA [8]. Distinction from disseminated pyogenic granulomas is easy as angiomatous tissue tends to occur in discrete masses, surrounded by myxoid stroma containing scattered spindle- and stellate-shaped connective tissue cells [9]. The main distinguishing feature of eruptive cherry angioma is that the dome-shaped papules are composed of numerous newly formed capillaries with narrow lumina and prominent endothelial cells arranged in a lobular fashion in the subpapillary region [10]. Drug-induced photodistributed telangiectasia is a kind of iatrogenic spider-like telangiectasia that mimicks EPA; however, it occurs secondary to the administration of lithium, thiotixene, interferon-α, cefotaxime, isotretinoin and other drugs [11]. The medical history provided points of differentiation.
EPA seems to have no single etiology. A dermal hypersensitivity reaction to viral infection or a direct viral effect on the vascular endothelium are supposed to be involved in the pathogenesis [2]. Like some other cases, our patient experienced onset in summer, and the lesions were exclusively distributed on exposed areas such as the face and dorsal surfaces of the hands. It is likely that a specific wavelength of ultraviolet switched on a successive process of photoimmunological damage to the blood vessels through an as yet unknown mechanism. The vasodilatation could be the result of a kind of photoimmunological effect on endothelial cells. Most EPAs resolve spontaneously and need no treatment. However, those that recur repeatedly require medical intervention. Our case was the most intensely relapsing one that required effective treatment for cosmetic reasons. Oral antihistamines and topical methylprednisolone are reported to be effective in repetitive cases. However, some authors have argued that topical steroids cannot alter the natural prognosis of EPA. We have gained a favorable result in the treatment of EPA with pimecrolimus 1% cream. Complete remission was noted after 5 days of consecutive topical application (in contrast to 12–18 days without intervention). No recurrence was observed during the treatment. Reaplication of pimecrolimus was equally effective, though relapse seems to be an unchangeable process with such a remedy.

Pimecrolimus is a new treatment for inflammatory cutaneous diseases. It has been shown to be effective in atopic dermatitis, allergic contact dermatitis, psoriasis, cutaneous lupus erythematosus, seborrheic dermatitis, lichen planus pigmentosus, oral lichen planus, Schamberg’s disease and other diseases [12]. This is the first successful application of pimecrolimus for the treatment of EPA.

There is no report that pimecrolimus has an antiangiogenic effect. Pimecrolimus can inhibit the production and release of tumor necrosis factor-α, interleukin-2 and other proinflammatory cytokines in T cells. Cytokines, especially tumor necrosis factor-α, may interfere with endothelial function by generating oxygen free radicals and by modulating endothelial NO release, which may be partially responsible for the vasodilation through membrane-associated phospholipase A₂ [13]. As perivascular lymphocytic infiltration is a very common pathological finding in EPA, it is likely that pimecrolimus has a certain indirect vasoconstriction effect through its inhibitory effect on the release of tumor necrosis factor-α by T lymphocytes. However, the exact pharmaceutical mechanism of pimecrolimus in EPA remains to be elucidated.

References


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