TNPM presents as subcorneal or intraepidermal pustules composed mainly of neutrophils; this finding helps to differentiate TNPM from NTE, in which there is a predominance of eosinophils, 1,3,7,10. In conclusion, we must be aware that TNPM is a benign condition with no systemic manifestations and it does not require treatment. This entity can be confused with serious infections, and patients with TNPM may be administered empirical antibiotic treatment or undergo invasive tests. It is essential that pediatricians and dermatologists are aware of TNPM in order to avoid unnecessary additional tests or treatments.

References

Multifocal Fixed Drug Eruption Probably Induced by Mefenamic Acid

Exantema fijo medicamentoso múltiple probablemente inducido por ácido mefenámico

To the Editor:

Mefenamic acid is a nonsteroidal anti-inflammatory inhibitor of cyclooxygenase 1 and 2 that is marketed in Spain under the name of Coslan (Pfizer). According to the summary of product characteristics, it is indicated for the treatment of pain, inflammation, and fever of any etiology, dysmenorrhea, menorrhagia due to dysfunctional causes, rheumatoid arthritis, and acute or chronic gout. It can cause cardiovascular, genitourinary, gastrointestinal, hepatic, hematologic, respiratory, and cutaneous adverse effects. Fixed drug eruption (FDE), and multifocal FDE in particular, is an infrequent cutaneous adverse effect of mefenamic acid. 1

A 36-year-old woman with no relevant medical history apart from occasional treatment with mefenamic acid for dysmenorrhea (Coslan capsules, 250 mg/8 h) consulted for 4 skin lesions that had appeared some months earlier. She reported that the lesions occasionally caused a burning sensation but that there were no other associated symp-

ones are antibiotics (particularly co-trimoxazole), anticonvulsants, and analgesics.3

Mefenamic acid is an anthranilic acid derivative that inhibits prostaglandin synthesis. It was recently described as an inducer of FDE and has also been implicated in bullous pemphigoid,4 anaphylaxis,7 Stevens-Johnson syndrome,8 and linear immunoglobulin A dermatosis.9

Although mefenamic acid has been widely used in a range of medical fields, only a few cases of mefenamic acid–induced FDE have been reported to date.1,4,10 Furthermore, less common clinical manifestations have been reported in several of these cases, including multifocal dalmatian dog–like lesions,1 reticulated lesions,3 and lesions mimicking erythema multiforme.4

Diagnosis is based on clinical history and characteristic skin findings. An oral challenge test with the relevant drug is the gold standard for confirming clinical suspicion of FDE, as occurred in our case. Patch testing of lesional and healthy skin is a safe, noninvasive alternative, but it has variable sensitivity, with results differing according to the concentration and penetration of the test substance, the vehicle used, and the thickness of skin at the test site. A negative patch test result, therefore, does not rule out FDE.2

References

To the Editor:

The term calciphylaxis has been used since the 1960s\(^1\) to describe skin ulceration secondary to vascular calcifications in patients with terminal renal failure and secondary hyperparathyroidism.\(^2\) However, nonuremic causes have been reported and the mechanism of cutaneous vascular calcification has now been investigated more extensively.\(^3\) The condition is currently considered a complex multifactorial process and not a simple deposition. Daudén et al.\(^4\) proposed a new classification of these processes, using cutaneous vascular calcification (CVC) as a general term, and we are in agreement with this terminology.

We report the case of an 80-year-old woman with a history of severe refractory osteoporosis, hypertension, obesity, atrial fibrillation, and polymyalgia rheumatica treated with corticosteroids. As her osteoporosis was resistant to the usual treatments, she was prescribed the human recombinant peptide teriparatide. The active fragment is a 34 amino-acid sequence of parathyroid hormone (rhPTH). The agent is administered subcutaneously at a dose of 20 \(\mu\)g every 24 hours. Two months after starting treatment, the patient developed painful necrotic ulcers on the legs on areas of skin with a livedoid appearance (Fig. 1). The echo-Doppler study, renal function tests, calcium-phosphate product, and autoimmune studies were all normal. Skin biopsy (Fig. 2) showed ulceration and necrosis of the epidermis, dilatation of the dermal vessels, and circumferential calcification in walls of small arteries at the dermal-epidermal junction. Immunofluorescence was negative. These findings were consistent with calciphylaxis, but renal failure was not present. However, on administration of teriparatide, which acts like endogenous parathyroid hormone (PTH), a pharmacological state of hyperparathyroidism had been induced. The drug was withdrawn and, at 3 weeks after discontinuation, the patient’s lesions improved progressively. She died from progression of her heart failure 6 months after onset of her skin condition. At the time of death, she was free of skin lesions (Fig. 3).

CVC usually occurs in patients with certain predisposing factors, such as obesity, chronic inflammation, corticosteroid treatment, and menopause, and also in individuals with abnormal calcium phosphate metabolism and PTH levels. In recent years, the pathogenic relationships between these factors have been determined. The vascular endothelial cells are seen to adopt an osteogenic phenotype in these patients. Both vascular endothelial cells and osteoblasts, osteoclasts, and vascular smooth muscle cells can express the receptor activator of nuclear factor \(\kappa\)B (RANK) and its ligand RANKL on their membranes; when RANK is activated, the

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**Figure 1** Necrotic ulcers on the legs on areas of skin with a livedoid appearance.

**Figure 2** Circumferential calcification on the wall of small arteries. Hematoxylin and eosin, original magnification \(\times 100\).