University Hospital Robert Debré, Department of Dermatology, Reims[a] *and Medical Dermatology Practice, Epernay,*[b] *France*

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Correspondence to: Delphine Anuset, BM, Service de Dermatologie, Hôpital Robert Debré, 51092 Reims, France

E-mail: danuset@chu-reims.fr

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Alitretinoin: A new treatment option for hereditary punctate palmoplantar keratoderma (Brauer-Buschke-Fischer syndrome)

To the Editor: Punctate palmoplantar keratoderma type I (Brauer-Buschke-Fischer syndrome or PPKP1) is one of a group of heterogeneous disorders characterized by abnormal keratinization of the palms and soles. It is an autosomal dominant genodermatosis, and lesions appear within the first 2 decades of life. Molecular genetic studies have shown loss-of-function mutations in AAGAB, encoding α- and γ -adaptin-binding protein p34, located at locus 15q22.[1]

Since PPKP1 is a rare disease, no standardized treatment has been established. Therapeutic approaches are based on traditional systemic retinoids (e.g., acitretin), although a successful response is not always seen.

We describe a 41-year-old Caucasian woman with a 20-year history of hyperkeratotic lesions on the palms and soles. She complained of pruritus and pain, as well as difficulty walking and performing manual activities. Previous treatments, which included various keratolytic creams/ointments and potent topical steroids, did not produce a significant improvement. Similar skin lesions were present in her brother and grandmother.

Dermatologic examination demonstrated multiple, yellow-gray crater-like hyperkeratotic papules on the palms and soles. The papules coalesced to form diffuse plaques of approximately 1 to 2 cm in diameter, especially over pressure points on the feet (Fig 1, *A*). There was no keratoderma transgrediens.

Histopathology of a skin biopsy specimen from a palm lesion revealed marked hyperkeratosis, parakeratosis, and mild acanthosis without any change in

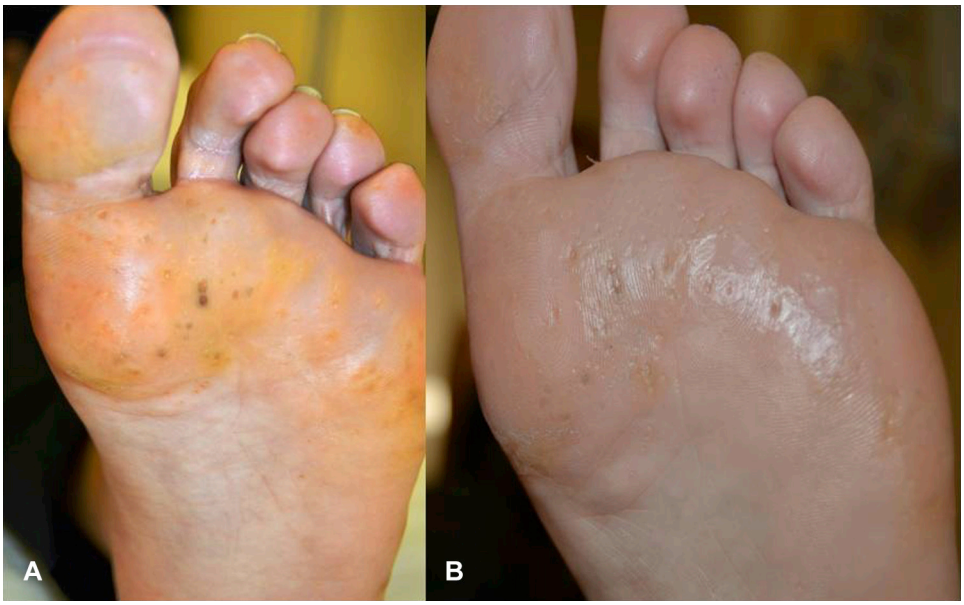

Fig 1. Hereditary punctate palmoplantar keratoderma. Multiple, *yellow-gray* hyperkeratotic lesions on left sole, coalescing to form diffuse plaques **(A)** before treatment with oral alitretinoin. After 8 months of therapy, lesions had nearly completely resolved **(B)**.

the dermis, consistent with a diagnosis of PPKP1. Molecular studies were not performed due to lack of availability. Routine hematologic investigations were normal and pregnancy test was negative.

Oral alitretinoin 30 mg/day was administered for 8 months as a trial of treatment. Contraceptive therapy was initiated 1 month earlier and continued for 10 months. Almost complete clinical remission of PPK was achieved after 8 months of treatment (Fig 1, *B*). No local or systemic adverse events were observed. Two months into the follow-up period the patient had not experienced any recurrence. An "8-months-on, 4-months-off" protocol for alitretinoin therapy was planned.

Traditional systemic retinoids are used for treatment of PPK by many authors.[2,3] We elected not to treat with acitretin because of its long-lasting teratogenicity (3 years after stopping treatment) and the need for long-term contraception.[4] Alitretinoin (9-*cis*-retinoic acid) is a new retinoid, with immunomodulatory and anti-inflammatory effects, which binds to retinoic acid receptors A and X. It regulates keratinocyte differentiation with fewer adverse events than traditional retinoids and requires only 1 month of contraception once therapy is completed.[5] We therefore consider oral alitretinoin to be a useful alternative treatment for women of childbearing age who suffer with PPKP.

Beatrice Raone, MD, Roberta Raboni, MD, and Annalisa Patrizi, MD

Dermatology, Department of Specialized, Experimental and Diagnostic Medicine, Sant'Orsola—Malpighi Hospital, University of Bologna, Italy

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Correspondence to: Beatrice Raone, MD, Dermatology, Department of Specialized, Experimental and Diagnostic Medicine, University of Bologna, Sant'Orsola—Malpighi Hospital, Via Massarenti, 140138 Bologna, Italy

E-mail: beatrice.raone@libero.it

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Supraumbilical cutaneous lesions after transcatheter arterial chemoembolization for hepatocellular carcinoma

To the Editor: Transcatheter arterial chemoembolization (TACE) is a palliative procedure for the treatment of hepatocellular carcinomas and unresectable liver metastases. It involves the catheterization of the right or left branches of the hepatic artery with subsequent administration of microspheres loaded with a chemotherapeutic agent, usually Adriamycin, occluding the vessels that feed the tumor and producing a local chemotherapeutic effect. Supraumbilical cutaneous lesions secondary to TACE are a rare complication.[1-5]

Multicentric hepatocellular carcinoma was diagnosed 2 years ago in a 67-year-old male patient with a history of liver cirrhosis. He underwent two TACE procedures in 2012 without complications. In March 2013, a magnetic resonance imaging scan revealed a 2-cm nodule in the liver. A third TACE was performed with Adriamycin loaded into 100- to 300-μm microspheres. Twenty-four hours later, painful reticulated violaceous cutaneous lesions developed in the patient's supraumbilical area (Fig 1). A skin biopsy showed focal necrosis in the sebaceous gland of the pilosebaceous unit in the dermis and an arterial vessel with intraluminal thrombotic material in the hypodermis (Fig 2).

Topical antibiotics were prescribed and complete re-epithelization of the lesions was achieved within 2 months. Later, when reviewing the angiographic images, we observed that the hepatic falciform artery (HFA), partially responsible for the periumbilical irrigation, had been accidentally chemoembolized.

Supraumbilical skin lesions after TACE are an infrequent complication. They are most likely due to the inflow of the chemotherapeutic agent into the HFA and the subsequent ischemia caused by the occlusion of the distal arterioles of this artery.[1,3-5] The HFA is a small terminal branch of the left or middle hepatic artery running through the falciform hepatic ligament, and its branches are distributed around the navel.[1,2] According to various angiography series, HFA is present in a variable percentage (2% to 24.5%) of patients. However, in postmortem studies its presence increases to up to 67% , possibly