

## Labial Melanotic Macule After Application of Topical Tacrolimus: Two Case Reports

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Tacrolimus ointment (Protopic<sup>®</sup>, Fujisawa) is a topical calcineurin inhibitor used to control the symptoms of moderate to severe atopic dermatitis (AD). We report here two patients with AD who developed labial melanotic macules after topical application of tacrolimus ointment 0.1%.

### CASE REPORTS

**Patient 1.** A 16-year-old Caucasian boy with long-standing moderate AD presented to our department with numerous eczematous lesions involving predominantly the folds, the neck and the face and with a very severe involvement of the perioral and periocular areas. In the past he had been treated with emollients, topical steroids, oral antihistamines, and antibiotics with temporary and partial improvement. We started treatment with tacrolimus ointment 0.1% initially twice daily (3 weeks) and then once daily on all affected areas, with excellent clinical improvement. Approximately 9 months after starting tacrolimus he developed a melanotic lesion, sized 2 × 3 mm, on his lower lip (Fig. 1). Dermoscopy showed linear and curved brown lines in a regular parallel pattern (Fig. 2). As this pattern has been described for labial melanotic macule (1), and it is well established that labial melanotic macule can be diagnosed with dermoscopy alone (2), we decided not to perform a biopsy and we continued treatment under close follow-up. Over a 3-month period the lesion persisted unchanged.

**Patient 2.** A 25-year-old Caucasian woman with long-lasting AD presented with persistent cheilitis. She reported having been treated for years for her dermatosis with topical steroids, antihistamines and emollients with only partial improvement. After puberty her dermatitis had greatly improved except for the cheilitis. Treatment with tacrolimus ointment 0.1% once daily was started, with a significant clinical improvement. Three months later she developed two brown macules on her lower lip, sized 1 × 1 and 3 × 2 mm. Dermoscopy showed a structureless pattern (1). As for the former patient, no biopsy was performed. The patient decided to stop tacrolimus. After discontinuation the macules persisted unchanged over a 6 month period. Both patients denied sun exposure in the months preceding the onset of the lesions. Labial melanotic macule is a small brown to black macule, well-circumscribed, mostly occurring on the lower lip. Histology shows an augmented melanin production by basal melanocytes. Melanocytes are usually normal in number and localization. In the upper portion of lamina propria melanophages with melanin pigment can be observed (3). With dermoscopy three main patterns can be seen: structureless, parallel and reticular-like (1). Patient 1 showed a parallel pattern, while patient 2 showed a structureless pattern.



Fig. 1. Labial melanotic macule on the lower lip of a 16-year-old boy after 9 months treatment with topical tacrolimus.



Fig. 2. Dermoscopy of the lesion showed a regular parallel pattern, with linear and curved brown lines.

### DISCUSSION

We hypothesize that topical tacrolimus may have induced the onset of the labial melanotic macules. The development of melanotic macules in our patients could also have been favoured by sun exposure and/or inflammation. However, our patients had had a long-standing inflammation treated with topical steroids, and, furthermore, the patients had often earlier been sun exposed. In the last months before the development of the macules, both patients had had very limited sun exposure. Thus, the only change in their habits had been topical treatment with tacrolimus. Three cases of lentigines induced by topical tacrolimus have been reported, 3, 5 and 6 months after starting tacrolimus (4). This delay could be partially explained by limited sun exposure and by the time required for local immunosuppression. Tacrolimus could induce melanocyte activation, both by a direct mechanism and by its immunosuppressive activity (5). Topical tacrolimus efficacy and safety have been established. However, a careful follow-up to assess long-term evolution of labial melanotic macules is mandatory.

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