

# Facial Involvement in Progressive Macular Hypomelanosis

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## PRACTICE POINTS

- Progressive macular hypomelanosis should be considered in the differential diagnosis for hypopigmented facial lesions.
- Progressive macular hypomelanosis proves to be a diagnosis of exclusion.

Progressive macular hypomelanosis (PMH) is a skin disorder that historically has been described as having a predominantly truncal distribution. We report 4 adult cases of PMH with facial involvement. The diagnosis was made for all 4 patients after excluding other hypopigmented diseases. This report underscores the importance of considering PMH as part of the differential for hypopigmented lesions on the face.

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**P**rogressive macular hypomelanosis (PMH) is a non-inflammatory skin disorder characterized by ill-defined, nummular, hypopigmented, and nonscaly macules. Historically, various names have been used to describe this entity. Several of these terms, including *cutis trunci variata* and *nummular and confluent hypomelanosis of the trunk*, reflected its predominantly truncal distribution.<sup>1,2</sup> Less frequently, involvement on the neck, buttocks, and arms and legs has been noted.<sup>1,2</sup> A lack of facial involvement previously has been highlighted as a key clinical feature of PMH.<sup>3</sup>

Progressive macular hypomelanosis is a diagnosis of exclusion. Hypopigmented diseases commonly considered in the differential include those caused by fungi and yeasts (eg, tinea versicolor, seborrheic dermatitis), inflammatory skin disorders (eg, pityriasis alba, postinflammatory dyschromia), and mycosis fungoides (MF) as well as leprosy.

The hypopigmented macules of PMH have nonspecific histopathologic findings; lesional skin often shows minimal alterations as compared to normal skin. A sparse perivascular lymphocytic infiltrate often is observed,<sup>4,5</sup> and at times, a decrease in epidermal melanin content can be detected.<sup>1-3,6,7</sup>

We report 4 cases with considerable facial involvement of hypopigmented macules that were determined to be consistent with PMH. We propose that characteristic macules that are not clinically or histopathologically consistent with other disease entities are compatible with a diagnosis of PMH, regardless of the distribution. A diagnosis of PMH should be considered in the differential when there are suggestive facial lesions in addition to truncal lesions.

## Case Reports

**Patient 1**—A 40-year-old man presented with hypopigmented macules on the face (Figure 1), trunk, chest, arms, and legs of 2 years' duration. The lesions were asymptomatic and had started on the forehead as hypopigmented macules, then progressed to the trunk, arms, and legs. The patient denied any prior rash, injury, or hyperpigmentation associated with the distribution of the lesions.

A rapid plasma reagin (RPR) test was conducted to rule out secondary syphilis and was nonreactive. During a series of clinical encounters over several months, a total of 5 biopsies of lesions on the face and back were performed. All specimens contained mild mononuclear perivascular inflammation (Figure 2). In some foci, staining for Melan-A revealed a decrease in epidermal melanocytes (Figure 3). Periodic acid-Schiff staining performed on one section revealed a few pityriasis spores but no hyphal elements, suggesting colonization rather than infection.

The patient initially was started on tacrolimus ointment 0.1% once daily and narrowband UVB phototherapy twice weekly for 3 months without benefit. A diagnosis of tinea versicolor was revisited and the patient

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was switched to ketoconazole shampoo 1% two to 3 times weekly on the face, trunk, arms, and legs for 10 to 15 minutes prior to rinsing, and ketoconazole cream 2% was applied twice daily to the affected areas for 2 months without notable improvement. Once-weekly 150-mg pulse doses of oral fluconazole for 8 weeks were started but proved equally ineffective. Antibiotic therapy aimed at eradicating *Propionibacterium acnes* was considered following a provisional diagnosis of PMH after the patient failed 5 months of therapy for tinea versicolor.

**Patient 2**—A 54-year-old man presented with hypopigmented to depigmented nonscaly macules on the face, trunk, chest, and arms of several months' duration. The patient initially noted hypopigmentation on the face that gradually spread to the rest of the body. The patient denied any prior rash or hyperpigmentation in the affected areas. At the initial visit to our clinic, a potassium hydroxide (KOH) preparation of the face and back was positive for tinea versicolor. The patient was treated with ketoconazole shampoo 1% two to 3 times weekly for several weeks on the scalp, face, trunk, arms, and legs for 10 to 15 minutes prior to rinsing and 2 total doses of oral fluconazole 150 mg taken 1 week apart.

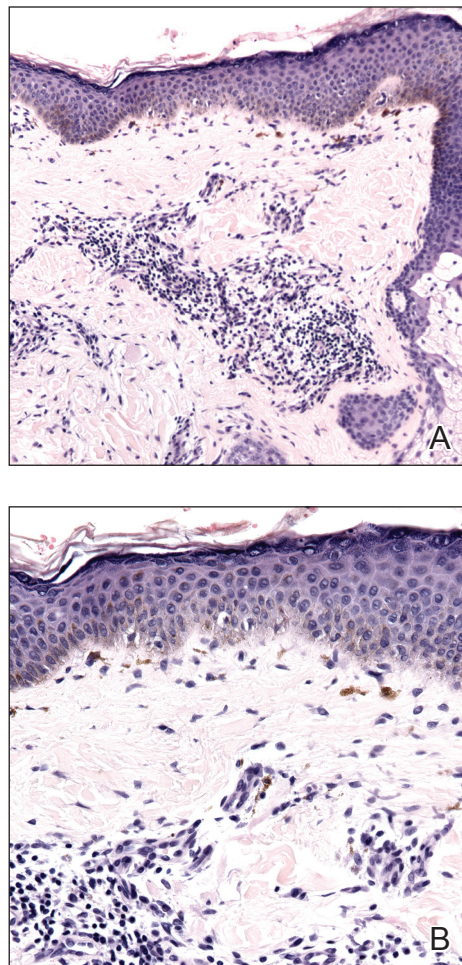
Three months later the patient returned with no improvement of the existing lesions and with progression of the disease to previously uninvolved areas of the trunk, arms, and legs. Biopsy of a facial lesion was performed, and laboratory studies including RPR, thyroid-stimulating hormone, and antinuclear antibody tests were conducted to screen for possible systemic disease. Microscopic analysis of the biopsied facial lesion

revealed a sparse perivascular infiltrate of lymphocytes and plasma cells but no evidence of yeast or hyphal elements. Melan-A staining did not reveal a decreased number of epidermal melanocytes. All laboratory studies were negative or within normal limits. Desonide ointment 0.05% was prescribed to relieve the patient's occasional pruritus. Although the patient's symptoms resolved, the hypopigmented macules continued to progress, making a diagnosis of PMH more likely given the lack of improvement on treatment for tinea versicolor. Pimecrolimus cream 1% was started with discontinuation of desonide for steroid-sparing therapy.

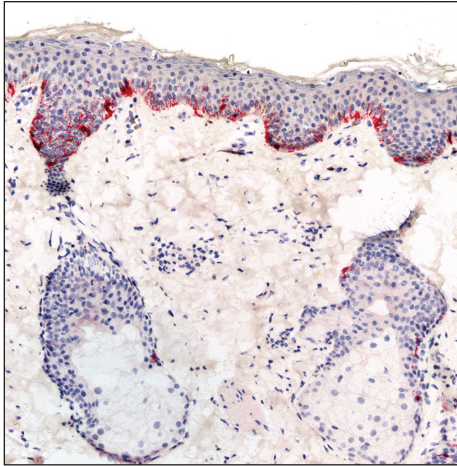
**Patient 3**—A 63-year-old man presented with progressive nonscaly and asymptomatic hypopigmented macules on the face, trunk, abdomen, and back of 5 years' duration. He first noted lesions on the abdomen and they subsequently spread to the rest of the body. The patient denied any prior rash, hyperpigmentation, or other lesions in the involved areas.



**FIGURE 1.** Progressive macular hypomelanosis. Hypopigmented macules noted on the face of a 40-year-old man (A and B).



**FIGURE 2.** Progressive macular hypomelanosis. Mild mononuclear perivascular inflammation with a few melanophages present within the papillary dermis (A and B)(H&E, original magnifications  $\times 20$  and  $\times 40$ ).



**FIGURE 3.** Progressive macular hypomelanosis. Melan-A staining revealed a normal number of epidermal melanocytes across most of the biopsy except for a small foci with a decreased number of epidermal melanocytes (original magnification  $\times 20$ ).

One year prior to the current presentation, KOH scrapings from the lesions performed by an outside physician were negative. During his initial visit to our clinic, an abdominal biopsy was performed, and histopathologic analysis showed postinflammatory pigmentary alteration; however, the patient denied any prior history of rash or injury in the distribution of the lesions that would correlate with the histopathologic findings of postinflammatory pigmentation. Because the histopathologic findings showed postinflammatory pigmentary alteration, additional stains including Melan-A were not performed.

The patient was provisionally treated with ketoconazole shampoo 1% two to 3 times weekly on the face, trunk, arms, and legs for 10 to 15 minutes prior to rinsing and ketoconazole cream 2% twice daily to the affected areas. After several months on this regimen, the patient did not report any improvement. An abdominal skin biopsy was again performed and revealed similar histopathology. Periodic acid–Schiff staining was negative for fungus. A diagnosis of PMH was made, and the patient was started on benzoyl peroxide wash 5% and clindamycin lotion.

**Patient 4**—A 45-year-old woman presented with hypopigmented, nonscaly macules on the face, neck, chest, trunk, and back. She first noted the lesions on the face and trunk more than 8 years prior, and they subsequently progressed. Potassium hydroxide scrapings performed on the lesions at the current presentation were negative, and a skin biopsy from the neck revealed postinflammatory pigmentary alteration, although the patient had no history of rash or injury in the areas in which the lesions were distributed.

Fontana–Masson and Melan-A staining of the skin biopsy of the neck revealed a normal distribution of melanocytes and pigment at the dermoepidermal junction. An

RPR test was nonreactive. A diagnosis of PMH was made, and the patient was started on benzoyl peroxide wash 5% and clindamycin phosphate lotion 1%.

### Comment

The 4 cases of PMH reported here showed extensive facial involvement in addition to the characteristic hypopigmented lesions on the trunk, arms, and legs. It is unclear why the lesions in these patients had a predominantly facial distribution. Involvement of the face in PMH has not been commonly reported in the literature. Martínez-Martínez et al<sup>3</sup> reported 12 PMH patients with lesions only presenting in lumbar and abdominal distributions. Kim et al<sup>8</sup> presented a series of 23 PMH patients treated with narrowband UVB in whom 56% (9/16) saw repigmentation in 90% of the lesions following treatment. The most commonly affected area was the lower back, followed by the abdomen, upper back, chest, sacral region, flank, and shoulders, respectively.<sup>8</sup> In a review by Relyveld et al,<sup>1</sup> PMH is described as a predominantly truncal disease that can occasionally extend to the neck, face, and proximal arms and legs; however, no specific cases were reported.

Previous case series have reported PMH primarily in adolescents and young adults, with mean ages ranging from 26 to 30 years.<sup>1,3</sup> The 4 patients reported here were older, ranging in age from 40 to 65 years. This discrepancy in age may contribute to the facial distribution encountered in this patient population; however, given the small number of patients in our case series, such extrapolation is premature. Most recently, Westerhof et al<sup>6</sup> demonstrated a relationship between the presence of *P acnes*, a common skin commensal of the face, and the hypopigmented macules of PMH. The investigators suggested that some strains of *P acnes* produce a factor that is yet to be identified that interferes with melanogenesis. The response of PMH lesions to topical treatments such as benzoyl peroxide, clindamycin, and phototherapy has lent credence to the potential etiologic role of *P acnes* in this condition.<sup>9,10</sup> The interplay between age, PMH distribution, and *P acnes* requires further investigation.

The biopsies in our 4 patients were consistent with the nonspecific histopathologic characteristics of PMH lesions. Biopsies in all 4 patients revealed a sparse perivascular lymphocytic infiltrate, and in 2 of the cases, postinflammatory pigmentary alteration was noted. Such changes often are described in PMH lesions.<sup>4,5</sup> In other cases detailed in the literature, lesional and nonlesional skin often are indistinguishable on hematoxylin and eosin staining.<sup>11</sup> In the 3 patients for whom we performed additional immunohistochemical studies, results were mixed: Melan-A staining revealed a decreased number of melanocytes in Patient 1 but not in Patients 2 or 4. Many reported cases in the literature have not demonstrated a decrease in melanocyte density but instead show a decrease in melanin content in lesional skin.<sup>1-3,6,7</sup> Although additional stains performed in Patient 4 revealed neither



a decrease in the number of melanocytes nor a decrease in the melanin content, such histopathologic findings of PMH often are subtle. Additional stains were not performed in Patient 3. More studies are needed to characterize the immunohistochemical staining patterns of lesional skin in patients with PMH.

Tinea versicolor, pityriasis alba, mycosis fungoides, sarcoidosis, leprosy, and syphilis typically are included in the differential diagnosis for PMH. Tinea versicolor traditionally is diagnosed based on the combination of irregular hypopigmented or hyperpigmented scaly macules and a KOH preparation that is positive for hyphae and spores. Similar to PMH, tinea versicolor is most often found on the trunk, but unusual cases have been reported involving the face.<sup>12</sup>

Patient 2 reflected how it can be difficult diagnostically to distinguish between tinea versicolor and PMH. Although this patient initially had a KOH scraping suggestive for tinea versicolor, adequate treatment with oral fluconazole and ketoconazole shampoo did not result in improvement. The hypopigmented lesions in this patient continued to progress despite therapy. Additionally, his hypopigmented to depigmented nonscaly macules were more clinically consistent with the characteristic description of lesion configuration in PMH than with the irregular, more sharply defined, asymmetric, and scaly spots of tinea versicolor. Furthermore, the inflammatory findings on biopsy favored a diagnosis of PMH.

Pityriasis alba, most frequently presents on the face in the form of hypopigmented, sometimes slightly scaly macules but also can occur on the body. It usually occurs in younger patients who often have an atopic diathesis. Histologic findings generally are nonspecific, but discrete eczematous changes can sometimes be appreciated in the epidermis and dermis. None of our patients had histories suggestive of an atopic diathesis or lesion distributions typical of pityriasis alba. Histologic findings also were more consistent with PMH than pityriasis alba.

A diagnosis of patch-stage hypopigmented MF should also be entertained in patients with hypopigmented macules, as it can appear similar to the lesions of PMH. Hypopigmented MF often is associated with subtle atrophy, scaling, poikiloderma, and erythema. These features were not present in the 4 cases presented here. Histologically, atypical lymphocytes with prominent epidermotropism and tagging of the epidermis by large lymphocytic infiltrates are seen in cases of hypopigmented MF. These findings were not present in biopsies from our patients.

Hypopigmented sarcoidosis, leprosy, and syphilis are other systemic diseases associated with hypopigmented lesions. Histologically, noncaseating granulomas in the dermis or subcutaneous tissue would favor a diagnosis of sarcoidosis over PMH. In patients who live in endemic

areas, a diagnosis of leprosy for an anesthetic hypopigmented lesion would be higher in the differential. Finally, it is important to rule out secondary syphilis when diagnosing PMH. Known as the great imitator, secondary syphilis may present in a patient in the form of hypopigmented macules. Patients 1, 2, and 4 had nonreactive RPR tests; unfortunately, RPR was not checked in Patient 3. He denied all risk factors for syphilis.

Various topical and oral treatments were prescribed for each patient, but so far none have been unequivocally effective. In the literature, there are reports supporting the efficacy of topical antimicrobial agents targeting *P. acnes*.<sup>9,10</sup> One case report noted improvement in a patient with PMH after isotretinoin use.<sup>13</sup> Phototherapy also has been reported to improve PMH in several case reports<sup>4-8</sup>; however, consistent response to these therapies has not been documented. Unfortunately for patients with a diagnosis of PMH, a lack of effective treatment options often exists.

This series of 4 cases highlights the importance of considering PMH in the differential of hypopigmented macules, even when they appear predominantly on the face.

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