Melasma is a relatively common, but under-diagnosed, skin condition that can be a challenge to treat for primary care physicians. Our case involves a 39-year-old G3P2A1 Hispanic female not on any hormonal manipulation for birth control and no significant past medical history who presented with a facial rash of 4 years' duration which had not been relieved by moisturizer and over-the-counter steroid creams. Examination was remarkable for hyperpigmented macules found exclusively on her cheeks (see Figs. 1 and 2). There had been no progression of the rash since the onset, which notably began 1 year after her last labor. She denied associated symptoms of pain, arthralgias, myalgia, fevers, or history of autoimmune disorders, but reported occasional mild pruritus. She was prescribed hydroquinone cream 0.4% to be applied twice daily.

Melasma affects approximately 5 million people in the United States (1) with a prevalence rate up to 40% in certain populations (2). It presents as hyper-pigmented macules or patches distributed symmetrically on sun-exposed areas such as the upper lip, chin, forehead, or, as in our case, the cheeks. Distribution can be classified into three groups: centrofacial, involving the areas of the forehead, cheeks, nose, upper lip, and chin; malar, which involved only the nose and cheeks; and mandibular, involving solely the ramus of the mandible. Distribution is hypothesized to be related to sebaceous gland density. In rare instances, melasma can occur in extensor aspect of forearms and upper chest.

Melasma is much more common in women and has a presumptive genetic component, as 48% have reported a positive family history according to a 2009 survey (3). Pathophysiology of melasma involves excess sunlight/radiation which causes peroxidation of lipids in the cellular membrane that further generates free radicals subsequently stimulating excess melanin. Melanin is increased in the epidermis and/or dermis. Melanocyte numbers are not increased, but they tend to be larger, more dendritic, and more active. This condition is also seen in pregnancy and is possibly related to hormonal stimulation from...
melanocyte stimulating hormones, estrogen and/or progestosterone. The exact genes or hormones involved remain unknown.

Melasma can be confused with other causes of hyperpigmentation, including postinflammatory hyperpigmentation, drug-induced hyperpigmentation, and pigmented contact dermatitis. There is no specific diagnostic test to differentiate these disorders; therefore, a good history and physical examination remain the cornerstones of making the diagnosis of melasma. Postinflammatory hyperpigmentation should be suspected if there is underlying history of inflammatory skin disorders like acne, contact dermatitis, etc. Drug-induced hyperpigmentation is more diffuse and less irregular. History of exposure to drugs like tetracycline and amiodarone should be obtained. Pigmented contact dermatitis occurs after repeated contact with cosmetic agents; hence history of exposure should be obtained. It presents with gray–brown reticular pigmentation.

No labs are presently indicated for the workup of melasma, although there may be a role in the future for ordering thyroid function tests as thyroid hormones and thyroid autoimmunity have been implicated in pathogenesis in some studies; further study is needed to evaluate this finding (4). The Melasma Area and Severity Index has been used in clinical trials to standardize subjective evaluation; however, this has yet to be validated (5).

Treatment is difficult with expected time course of very gradual resolution. The mainstay therapy includes hydroxyquinone cream and avoiding exposure to sun and estrogen. Hydroxyquinone is a topical depigmentation agent which acts to inhibit tyrosinase, which is an enzyme that converts the rate-limiting step of L-tyrosine to L-DOPA in the melanin synthesis pathway (1).

Chemical or laser treatment might be beneficial in certain individuals but is typically reserved as second line (6). The most effective means of prevention is prophylactic management which includes avoidance of sun exposure, discontinuing usage of oral contraceptive pills (OCPs), and regular usage of broad-spectrum sunscreens (7). Of these, OCP discontinuation is perhaps most important, as this has found to be linked with melasma in patients even without genetic predisposition.

Topical retinoids (trans-retinoic-acid) have been found to increase keratinocyte turnover and decrease melanocyte activity. An added benefit is they also potentially increase epidermis permeability which can make adjunct therapy more effective (8). Due to the teratogenic property of retinoids, prescribers must first rule out pregnancy. To recruit all known treatment modalities in a single medication, a triple combination therapy of hydroxyquinone 4%, tretinoin 0.05%, and fluocinolone acetonide 0.01% has been approved by the FDA (9).

Conflict of interest and funding

The authors have not received any funding or benefits from industry or elsewhere to conduct this study.

References

1. Grimes PE. Melasma. Etiologic and therapeutic considerations. Arch Dermatol 1995; 131(12): 1453–7.
2. Werlinger KD, Guevara IL, González CM, Rincón ET, Caetano R, Haley RW, et al. Prevalence of self-diagnosed melasma among premenopausal Latino women in Dallas and Fort Worth, Tex. Arch Dermatol 2007; 143(3): 424–5.
3. Ortonne JP, Arelanno, Berneburg M, Cestari T, Chan H, Grimes P, et al. A global survey of the role of ultraviolet radiation and hormonal influences in the development of melasma. J Eur Acad Dermatol Venereol 2009; 23(11): 1254–62.
4. Pandya AG, Hynan LS, Bhore R, Riley FC, Guevara IL, Grimes P, et al. Reliability assessment and validation of the Melasma Area and Severity Index (MASI) and a new modified MASI scoring method. J Am Acad Dermatol 2011; 64(1): 78–83, 83 e1–2.
5. Chan R, Park KC, Lee MH, Lee ES, Chang SE, Leow YH, et al. A randomized controlled trial of the efficacy and safety of a fixed triple combination (fluocinolone acetonide 0.01%, hydroquinone 4%, tretinoin 0.05%) compared with hydroquinone 4% cream in Asian patients with moderate to severe melasma. Br J Dermatol 2008; 159(3): 697–703.
6. Çakmak SK, Özcan N, Kılıç A, Koparal S, Artüz F, Çakmak A, et al. Etiopathogenetic factors, thyroid functions and thyroid autoimmunity in melasma patients. Postepy Dermatol Alergol 2015; 32(5): 327–30.
7. Kópera D, Hohenleutner U. Ruby laser treatment of melasma and postinflammatory hyperpigmentation. Dermatol Surg 1995; 21(11): 994.
8. Burke H, Carmichael AJ. Reversible melasma associated with tretinoin. Br J Dermatol 1996; 135(5): 862.
9. Sheth VM, Pandya AG. Melasma: A comprehensive update: Part II. J Am Acad Dermatol 2011; 65(4): 699–714.