Minocycline pigmentation of the vulva masquerading as a melanocytic lesion

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INTRODUCTION

This is a novel case of a patient with a pigmented vulvar lesion who was referred to a dermatologist by her gynecologist to determine a follow-up strategy for this lesion and consider a complete resection to rule out melanoma. This lesion was later discovered, through further examination and histologic analysis, to be the result of mucosal minocycline deposition.

CASE REPORT

A 67-year-old white woman presented to the dermatology clinic for further assessment of a pigmented vulvar lesion near the urethral meatus that was discovered incidentally 4 months prior. The patient had been examined by 3 gynecologists since discovery of this lesion, which consisted of mostly black pigmentation with some various shades of grey (Fig 1). A punch biopsy section taken by the second gynecologist showed findings of spongiosis within the epithelium with moderate to numerous superficial melanophages (Fig 2). The differential diagnosis included postinflammatory hyperpigmentation, fixed drug eruption, and irritant contact dermatitis, but a regressed mucosal melanoma was also considered. The third gynecologist started the patient on local estrogen therapy for severe vulvovaginal atrophy and pain, which resulted in a fading of the lesion from a black to grey color along with resolution of the atrophic tissues. The patient did not want to proceed with an additional biopsy at that time, but when the lesion remained unchanged after 3 months, the patient agreed to a second punch biopsy of the vulvar lesion at a site distal from the first biopsy location. Similar histologic results to the first biopsy were found. The patient was referred to the dermatology clinic for consultation regarding whether to perform scouting biopsies or full resection to completely rule out melanoma. Physical examination of the patient's vulvar vestibule displayed irregular grey patches of pigmentation, which were not erythematous or tender, with uniform pigment distribution under dermoscopy. The pigmentation extended over the urethra, onto the lateral surrounding vestibule, and against the posterior vaginal wall. The skin examination was also significant for widespread, irregular speckled macules of varying shades of grey and small patches of dyspigmentation throughout the patient's body, most notably on her legs, arms, eyes and face (Fig 3), which was also observed by her third gynecologist. The patient's medical history was significant for vaginal atrophy, hypothyroidism, and high cholesterol. She also had cystic acne that she was treating with minocycline consistently for the last 7 years but also noted intermittent use for last 20 years. The minocycline was prescribed by both her outside dermatologist and primary care physician.

Iron stain of her prior tissue biopsy section was recommended to look for possible minocycline deposition given the patient's extended minocycline use and widespread cutaneous pigmentation. Results of this iron staining were positive and consistent with minocycline superficial dermal

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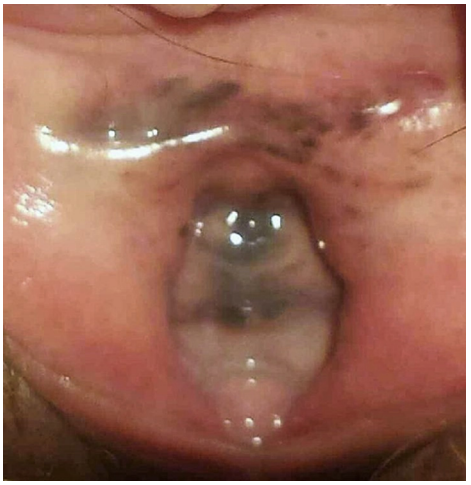

Fig 1. Minocycline pigmentation of the vulva. Irregular pigmentation patch seen on the patient's vulva during examination.

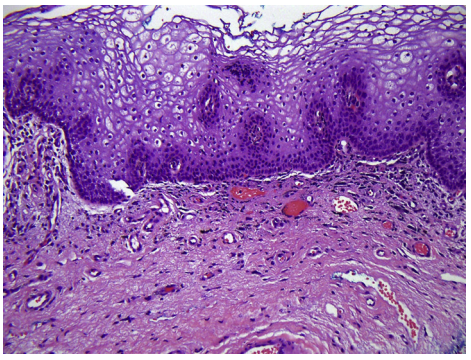

Fig 2. Histopathologic findings from the pigmented lesion biopsy taken from the vestibule/periurethral area. Spongiosis of the epithelium and moderate to numerous superficial melanophages were seen on histology. (Hematoxylin-eosin stain; original magnification: ×20.)

pigmentation (Fig 4). The residual pigmentation remaining within the patient's vulvar vestibule was found to be not related to a melanoma and would not require future surveillance biopsies. The patient was instructed to cease further use of minocycline. She switched to tretinoin 0.025% cream and clindamycin 1% lotion for her new acne regimen. At follow-up 2 months later, the patient already noticed reduction of her minocycline-induced pigmentation on her face, arm, and legs.

DISCUSSION

Minocycline is frequently used in dermatology and is more lipophilic compared with other tetracycline group members.[1] Minocycline binds to plasma proteins and has a propensity for depositing into soft tissues rich with collagen. This lipophilic nature allows for an extended half-life that conversely leads

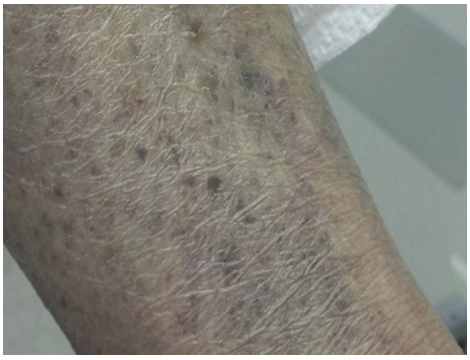

Fig 3. Left forearm examination shows a small portion of the widespread, irregular speckled macules and patches of grey dyspigmentation present diffusely throughout the patient's skin surface.

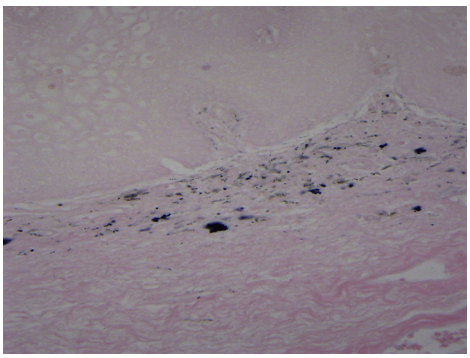

Fig 4. Histopathologic findings from the prior biopsy after staining with iron. The biopsy section shows positive areas of black and brown pigment in the papillary dermis consistent with minocycline dermal pigmentation. (Iron staining; original magnification: ×40.)

to its higher incidence of adverse effects seen with long-term treatments.[2] One of the common adverse effects with extended use is a blue-black/grey pigmentation of the skin, which stems from the oxidation of the aromatic D-ring within the minocycline structure that forms a paraquinone imine that has similar properties to that of the quinone present in eumelanin.[3,4]

Minocycline hyperpigmentation is divided into 3 types. Type I is the most common and appears as blue-black/grey pigment staining in areas of acne scarring or inflammation as seen in this patient.[5] Type II appears as blue-grey pigment on normal skin most commonly on the shins, legs, and forearms, also seen in this patient. Type III presents as diffuse muddy-brown discoloration on sun-exposed areas of the skin. Both types I and II stain for iron and melanin on hematoxylin-eosin and resolve slowly over time after minocycline is stopped. Type III stains for melanin only and remains indefinitely.[3] In our patient case, a type I hyperpigmentation was

present in her vulvar lesion caused by the chronic inflammation associated with her vaginal atrophy, resulting in progressive minocycline deposition in the dermis as seen on histology. This case distinguishes itself from a possible lichen sclerosis condition, which can also cause vaginal atrophy and hyperpigmentation but hyperpigmentation seen in lichen sclerosis present in the epidermis.[6]

Because of the uniqueness of this pigmented lesion's location, a possible vulvar melanoma could not be definitively ruled out before referral to the dermatology clinic, thus, leaving the patient with options of ongoing future visits involving multiple random biopsies or possible complete resection of the lesion. The concern of possible vulvar melanoma, although rare, was warranted because it is an aggressive tumor that accounts for less than 1% of all malignant melanomas and carries a poor prognosis, with a 5-year survival rate of 5% to 25%.[7,8] After the patient's dermatology referral visit and subsequent discussion between dermatology, dermatopathology, and gynecology departments, this patient's biopsy slides were re-examined with iron staining, which showed the minocycline deposition. The patient was give assurance that her vulvar pigmentation was not melanoma and would not require further biopsies or a complete resection.

This patient's case not only highlights this novel presentation of vulvar minocycline pigmentation but also emphasizes how management and therapy can be maximized when colleagues between specialties partner together during unique and challenging cases for the betterment of care.

REFERENCES

1. Cockings J, Savage NW. Minocycline and oral pigmentation. *Aust Dent J*. 1998;43(1):14-16.
2. Aronson JK. *Meyler's Side Effects of Antimicrobial drugs*1st ed. New York, NY: Elsevier; 2010.
3. Geria A, Tajirian AL, Kihiczak G, Schwartz RA. Minocycline-induced skin pigmentation: an update. *Acta Dermatovenerol Croat*. 2009;17(2):123-126.
4. Enochs WS, Nilges MJ, Swartz HM. The minocycline-induced thyroid pigment and several synthetic models: identification and characterization by electron paramagnetic resonance spectroscopy. *J Pharmacol Exp Ther*. 1993;266(3):1164-1176.
5. Fiscus V, Hankinson A, Alweis R. Minocycline-induced hyperpigmentation. *J Community Hosp Intern Med Perspect*. 2014;4(3):http://dx.doi.org/10.3402/jchimp.v4.24063.
6. Fistarol S, Itin PH. Diagnosis and treatment of lichen sclerosus: an update. *Am J Clin Dermatol*. 2013;14:27-47.
7. Chaudhuri S, Das D, Chowdhury S, Gupta AD. Primary malignant melanoma of the vagina: A case report and review of literature. *South Asian J Cancer*. 2013;2(1):4.
8. Tjalma W, Monaghan JM, de Barros Lopes A, Naik R, Nordin A. Primary vaginal melanoma and long-term survivors. *Eur J Gynaecol Oncol*. 2001;22(1):20-22.