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Widespread dermoscopic alterations of multiple melanocytic nevi in a patient receiving vandetanib: implications for dermatological surveillance

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Dear Editor,

Regression-like dermoscopic and histopathological changes in pre-existing melanocytic nevi have increasingly been reported in patients undergoing modern oncologic therapies, particularly immune checkpoint inhibitors (such as ipilimumab, nivolumab, and pembrolizumab) and targeted agents including BRAF and MEK inhibitors.¹⁻³ In these settings, nevi may exhibit grey-blue discoloration, peppering, inflammatory infiltrates, and partial or total regression patterns, reflecting therapy-induced immune activation or microenvironmental modulation.^{1,2} Vandetanib (a multi-targeted tyrosine kinase inhibitor acting on EGFR, VEGFR, and RET pathways), has demonstrated therapeutic efficacy in advanced medullary thyroid carcinoma;⁴ however, similar widespread regression-like modifications of melanocytic lesions have not been clearly characterized in patients receiving this agent.

A 31-year-old Caucasian male presented to our department for an annual full-body skin examination. Two years earlier, he had undergone the same evaluation using a videodermatoscope (Vidix®, Intellistudio) at identical magnification settings, which revealed no atypical or suspicious melanocytic lesions. Over the preceding 12 months, the patient had been diagnosed with medullary thyroid carcinoma and subsequently developed multiple lateral cervical lymph node metastases as well as bulky mediastinal nodal involvement. Systemic therapy with vandetanib was therefore initiated. At the subsequent annual dermatologic follow-up, comparative assessment of archived dermoscopic images revealed diffuse and consistent changes affecting multiple pre-existing melanocytic nevi. Clinically, the lesions appeared darker. Dermoscopically, melanocytic lesions showed widespread peppering and greyish lichenoid-like areas, with an increased number of dots (Figure 1). Marked diffuse cutaneous xerosis was also observed. Reflectance confocal microscopy (RCM; VivaScope GmbH, Munich, Germany) was performed on 5 representative lesions and demonstrated bright dermal papillae with a superficial inflammatory infiltrate in the papillary dermis, characterized by numerous hyperreflective cells, without cytologic atypia (Figure 1). Excisional biopsy of 3 selected lesions confirmed compound melanocytic nevi with inflammatory infiltrate and melanophages consistent with treatment-related (vandetanib-induced) changes (Figure 2). At 3-year follow-up, the patient remains on vandetanib therapy and under regular dermatologic surveillance, with no need for excision of further suspicious pigmented cutaneous lesions.

Photosensitivity is a known adverse effect of vandetanib, whereas pigmentary changes are uncommon but have been reported.⁵⁻⁸ However, to date and to the best of our knowledge, simultaneous alterations involving multiple pre-existing melanocytic nevi characterized by pseudo-inflammatory, regression-like, and lichenoid dermoscopic features with diffuse grey areas have not been previously detailed

during vandetanib therapy. The pathogenesis of this cutaneous feature is not well known. Previous reports have described histopathological findings such as dermal iron and melanin deposition, with pigmented macrophages and inflammatory infiltrates in the dermis.^{5,6} However, these observations were not related to dynamic changes in pre-existing melanocytic lesions, and the reported cutaneous blue-gray dermoscopic pigmentation was attributed to dermal pigment deposition in healthy skin, rather than to widespread pseudo-inflammatory or regression-like modifications involving multiple nevi.^{5,8} A plausible hypothesis is that vandetanib-associated photoinduced inflammation, including lichenoid-type reactions, may promote pigment incontinence with dermal melanophage accumulation; this post-inflammatory pigmentary process could contribute to the diffuse grey structures observed dermoscopically in multiple pre-existing nevi.^{5,7} The marked diffuse xerosis observed is also consistent with EGFR pathway inhibition, as xerosis is a frequent class effect of EGFR-targeted therapies.^{5,9}

These findings suggest that patients receiving vandetanib may benefit from dermatological surveillance, as treatment-related inflammatory and pigmentary changes in melanocytic nevi could potentially mask or obscure clinically and dermoscopically suspicious features that might otherwise go unnoticed among more common therapy-induced alterations. Dermatological assessment in this setting is essential to enable early recognition and management of potentially relevant skin disorders and to avoid unnecessary alarmism, misdiagnosis, or unwarranted treatment discontinuation that could compromise the efficacy of life-saving oncologic therapies.

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Figure 1. Representative serial imaging of multiple pre-existing melanocytic nevi during vandetanib therapy. First row (right arm): baseline videodermoscopy acquired two years before presentation (**A**); follow-up videodermoscopy showing pigmentary changes with xerosis and diffuse grayish areas (**B**); and the corresponding RCM image demonstrating hyperreflective cells within the papillary dermis. Second row (left thigh): baseline videodermoscopy (**D**), follow-up videodermoscopy (**E**), and corresponding RCM image (**F**). Third row (deltoid): baseline videodermoscopy (**G**), follow-up videodermoscopy (**H**), and corresponding RCM image (**I**).

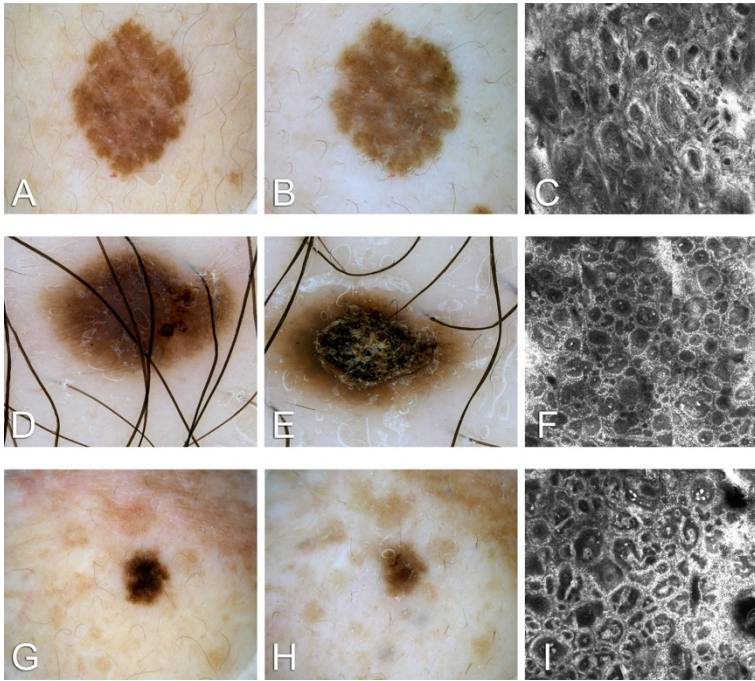


Figure 2. Histology of an excised pigmented lesion showed melanophages in the papillary dermis in the absence of cytoarchitectural atypia of melanocytes (hematoxylin & eosin).

