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Significant improvement of a nevus spilus-type congenital melanocytic nevus with oral selumetinib

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Abstract

Giant congenital melanocytic nevi (GCMN) can be cosmetically significant and can lead to melanoma. There is no standard pharmacologic treatment for GCMN. We present the case of an 8-year-old female with kaposiform lymphangiomatosis caused by an *NRAS* mutation whose nevus spilus-type GCMN improved on oral selumetinib.

KEYWORDS
kaposiform lymphangiomatosis, MEK inhibitor, nevus spilus, NRAS

To the Editors,

An 8-year-old female with a history of kaposiform lymphangiomatosis (KLA) and a GCMN (nevus spilus-type) presented for follow up in January 2024. Her nevus was noted at birth, asymptomatic, involved the upper back and neck in a shawl-like distribution with one right dorsal hand satellite patch, and had been followed by dermatology since 4 months of age. Her KLA was diagnosed in 2022 after evaluation of abdominal pain and thrombocytopenia that resulted in periportal edema and diffuse liver lesions. A liver biopsy demonstrated a spindle-celled vascular proliferation with positive *NRAS* (p.G13R, c.37G > C, variant allele frequency = 4.4%) mutation; pathology was positive for CD31, ERG, factor VIII, and D240. The KLA diagnosis was confirmed after pathology review by a multidisciplinary vascular anomaly team. Her KLA was treated with selumetinib 20 mg twice daily, a mitogen-activated protein kinase (MEK) inhibitor, with excellent disease control and few side effects.

After 14 months of treatment, her nevi were lighter, with almost complete disappearance of the right dorsal hand satellite patch (Figure 1) and overall lightening and decreased nevi on her upper back (Figure 2).

Large segmental nevus spilus containing congenital-pattern nevi are referred to as nevus spilus-type congenital melanocytic nevi (CMN)[1] and often contain missense activating *NRAS* mutations.[1,2]

Our case represents one of the first associations between CMN and KLA. Genetically, both disease processes can be driven by *NRAS* mutations. Our patient had a proven *NRAS* mutation in her KLA, so it is reasonable to presume her nevus spilus is caused by the same *NRAS* mutation. We did not have a clinical reason to biopsy her CMN to confirm this suspicion.

Several reports have previously noted treatment of GCMN with MEK inhibitors. In two case reports, treatment with the MEK inhibitor trametinib was associated with reduction in nevus-associated symptoms, with modest improvement in nevus pigmentation.[3,4] Another report documented two CMN with genetic hyperactivation of the MAPK pathway responding to oral trametinib with a reduction in CMN bulk, erythema, and pruritus.[5]

Our case contributes to the sparse literature on changes in GCMN while on MEK inhibitor treatment. Unlike the other cases, selumetinib was not initiated specifically for management of the GCMN, and we did not have sequencing of lesional skin demonstrating nevus susceptibility

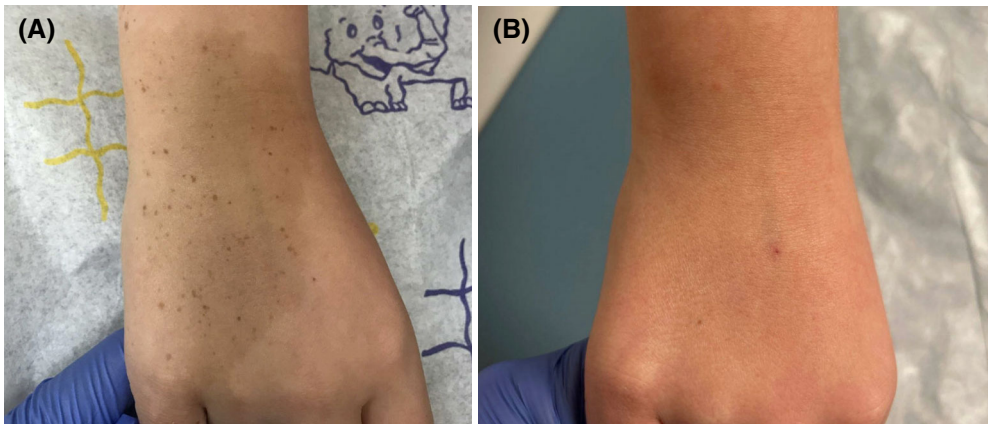

FIGURE 1 Satellite nevus on hand (A) before and (B)after mitogen-activated protein kinase inhibitor treatment.

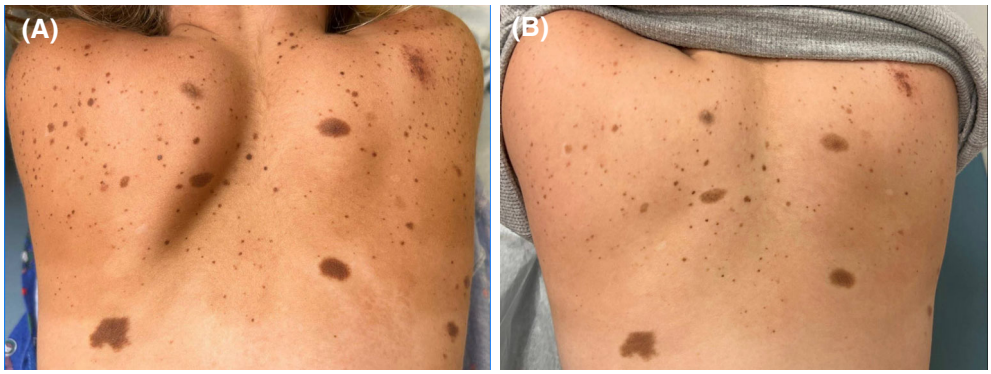

FIGURE 2 Giant nevus spilus on upper back (A) before and (B) after mitogen-activated protein kinase inhibitor treatment. Halo phenomenon is shown in the top-left section of (B).

to MEK inhibition. However, we noted almost complete clearance of a satellite lesion on our patient's right hand and observed significant lightening of the primary nevus. It is unclear if MEK inhibition is promoting immune recognition or inhibiting melanocytic proliferation leading to lightening. It is also unknown whether the response to MEK inhibition will persist with ongoing therapy. Regardless, this case further suggests that MEK inhibition may be a therapeutic option in GCMN that require therapy.

AUTHOR CONTRIBUTIONS

RB: Writing manuscript; editing; preparing for submission. **TH**: Writing manuscript; editing; preparing for submission. **DA**: Editing manuscript. **AM**: Editing manuscript. **JT**: Editing manuscript; preparing for submission.

CONFLICT OF INTEREST STATEMENT

The authors have no relevant conflicts of interest to disclose.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

INFORMED CONSENT

Informed consent was obtained from the patient and family prior to submission of this publication.

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