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RESIDENTS FORUM

RF - Drug-Induced Eruptive Melanocytic Nevi[☆]



FR - Nevus melanocíticos eruptivos asociados a medicamentos

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PALABRAS CLAVE

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The prestigious *Journal of the American Academy of Dermatology* recently published an interesting article that presents the results of an extensive review of the literature on eruptive melanocytic nevi that develop in association with medication use.¹ This type of lesion has historically been associated with severe blistering diseases (epidermolysis bullosa, toxic drug reactions, etc.) and with conditions

leading to immunodeficiency (renal transplantation, bone marrow transplantation, malignancy, AIDS, etc.).²

In order to differentiate eruptive nevi associated with medications (ENAM) from acquired melanocytic nevi, the authors propose the following criteria:

- Development of more than 5 palmoplantar melanocytic nevi at any age.
- Development of more than 10 melanocytic nevi bodywide outside of puberty or pregnancy.
- Development of more than 20 melanocytic nevi bodywide during puberty or pregnancy.

A diagnosis of ENAM is established when the patient meets 1 or more of these criteria in the last 6 months and there is a temporal relationship with the use of a particular medication. The authors also propose the classification of ENAMs according to the implicated medication ([Table 1](#)).

Using these criteria, the authors identified a total of 66 reported cases of ENAM. Thiopurines, azathioprine, and 6-mercaptopurine were the drugs most frequently associated with ENAM (34.8% of cases). Cases of ENAM in the last 10 years account for 66.2% of all cases reported in the literature, and 44.2% of these cases are associated with biologic therapies. No differences between sexes were identified and a certain predilection for lighter skin types was found. The lesions appear weeks or months after medication use begins and usually present as 1- to 3-mm light or dark brown macules. Dermoscopically, the lesions are usually characterized by globules arranged symmetrically at the periphery.³ Histologically, the lesions appear as compound nevi. ENAMs are

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Table 1 Types of Eruptive Nevi Associated With Medication and Drugs Involved.

Types of ENAM	Drugs Involved
Ia. Nonbiologic immunosuppressants	Azathioprine, 6-mercaptopurine, corticosteroids, cyclosporin, and methotrexate
Ib. Biologic immunosuppressants	Etanercept, alefacept, infliximab, and rituximab
IIa. Nonbiologic chemotherapeutics	Capecitabine, interferon alfa-2b, cyclophosphamide, and octreotide
IIb. Biologic chemotherapeutics	Vemurafenib, encorafenib, sorafenib, sunitinib, erlotinib, regorafenib, and rituximab
III. Melanocyte stimulators	Melanotan I and II and corticotrophin

Abbreviation: ENAM, eruptive nevi associated with medications.

more likely than acquired melanocytic nevi to be located on the palms and soles.⁴

The pathogenesis of ENAM and the potential risk of development or transformation to melanoma are not completely understood.⁵ It appears logical that immunosuppression could play an important role in the development of ENAM and larger numbers of nevi could be a risk factor for melanoma. However, further research is needed in order to provide more evidence. For now, in patients diagnosed

with ENAM, the authors recommend annual follow-up visits and identification of the drug responsible. They also suggest that alternative treatments be considered in patients with a personal or family history of melanoma.

The number of patients on immunosuppressive medications is on the rise and the subgroup receiving biologics is growing. Although ENAM is rare, the incidence of this entity is expected to rise in the coming years. An understanding of this causal relationship will favor early diagnosis, thereby minimizing the degree of uncertainty for both patient and physician and avoiding unnecessary complementary tests.

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