Long-term Follow-up of a Patient With Eruptive Melanocytic Nevi After Stevens-Johnson Syndrome

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Background: Eruptive melanocytic nevi (MN) are a rare phenomenon characterized by the simultaneous, abrupt onset of hundreds of MN, often in a grouped distribution. There are few studies on this topic in the literature. We followed up a patient who developed eruptive MN 38 years ago after Stevens-Johnson syndrome. Herein we document this patient’s progress and review the literature on this unusual phenomenon.

Observations: For 38 years, the patient’s lesions have remained stable, without signs of malignant degeneration. We discuss the possible etiology and natural history of this condition in 2 major patient populations: those with bullous disorders and those with systemic immunosuppression.

Conclusions: We postulate that the etiology and natural course of eruptive MN may differ between the 2 main populations of patients at risk for eruptive MN, with MN arising after bullous disorders being more likely to remain benign compared with those in patients with ongoing immunosuppression. However, this hypothesis has yet to be proved, and it will require long-term surveillance of individuals who have developed eruptive MN to determine its merit.

Arch Dermatol. 2007;143(12):1555-1557

Common acquired melanocytic nevi (MN) appear during the first 3 decades of life, reaching a peak of approximately 30 to 40 nevi per individual.1 They have a tendency to develop individually and to be distributed on sun-exposed sites of the skin. However, crops of MN may appear abruptly during adolescence and pregnancy. It has been suggested that common acquired MN tend to gradually disappear or decrease in number with increasing age,1 but this may be a cohort effect.

In contrast to this is the rare phenomenon of eruptive MN. Eruptive MN are characterized by the simultaneous, abrupt onset of hundreds of nevi, often in a grouped distribution. This condition was first described in 1868,2 and since that time there have been only a few subsequent reports.

Eruptive MN are most likely to arise in association with bullous dermatoses or systemic immunosuppression. With the former, eruptive MN have been reported in patients with erythema multiforme,3 Stevens-Johnson syndrome,4,5 toxic epidermal necrolysis,3,4,7 epidermolysis bullosa,8,9 and bullae induced by mustard gas.10 There have also been reports of eruptive nevi arising in patients with immunosuppression from human immunodeficiency virus infection,11,12 neoplastic disease,13,14 organ transplantation,13,16 Crohn disease,17-19 or chemotherapy.20 Eruptive MN have been described less frequently in association with Addison disease21 and psoralen–UV-A phototherapy.22 More recently,19 eruptive MN have been described in patients undergoing immunosuppressive therapy with azathioprine, biological agents (infliximab, etanercept, and alefacept), or combinations of these drugs. Occasionally, eruptive MN may arise without any apparent precipitating factors.6,7,17,23

We had the unique opportunity to follow up a patient who developed eruptive MN 38 years ago. This patient was first described by Kopf et al5 in 1977. Herein, we document the patient’s progress and review the literature on this unusual phenomenon.

Report of a Case

In 1969, an 8-year-old boy developed rubella complicated by a widespread bullous eruption diagnosed as Stevens-Johnson syndrome. He was extremely ill, and his disease resulted in temporary universal alopecia and exfoliation of the nail...
plates. Six to 8 weeks after the bullous lesions resolved, he abruptly developed hundreds of MN on his back, confined to areas that had previously blistered. The lesions appeared over several months, after which they did not change appreciably in appearance. The patient was examined 5 years later by Dr Kopf. At that time, 2 biopsies were performed, and photographs were taken (Figure 1). The biopsy findings were compatible with benign compound MN.5

Before being cared for by us, this patient had numerous biopsy specimens obtained from the areas of the eruptive MN. Most often these specimens showed benign compound MN, but occasionally these were described as MN with mild architectural or cytologic atypia consistent with atypical nevi. In 1990, one of us (J.K.R.) assumed the care of this patient, and as of October 2006, the patient has remained healthy, with no other intervening health issues. There was no personal or family history of multiple MN, atypical MN, or melanoma.

On recent examination, the patient was fair skinned with limited sun damage. He had typical MN distributed symmetrically across the cutaneous surface. However, on the middle thoracic region of his back were hundreds of 2- to 5-mm light to dark brown, round or oval MN. In addition, there were 2 zosteriform collections of MN on the right side of the middle thoracic region of his back and on the right flank (Figure 2). There was a single clinically atypical MN on the abdomen compared with photographs taken in 1974 and again in 1990. The eruptive MN have not changed appreciably during the past 38 years. At no time have there been any clinical or histologic findings suggestive of melanoma.

COMMENT

The development of eruptive MN is a rare event, and the reporting of long-term follow-up of such a patient is unique. A key question about eruptive MN is whether they pre-dispose the patient to an increased risk of melanoma. Although we cannot answer this question conclusively, we can comment on this patient who developed eruptive MN after Stevens-Johnson syndrome more than 38 years ago. During this time, his lesions have remained stable, with no evidence of malignant degeneration.

Eruptive MN occur in 2 major patient populations: those with bullous cutaneous disorders and those who develop this event in association with systemic immunosuppression. The pathogenesis of eruptive MN in the setting of bullous disorders remains unknown. Several researchers6,11,13 have postulated that during epidermal regeneration, specific cytokines and growth factors are elaborated and secreted, leading to epithelial regeneration and melanocyte proliferation. This hypothesis is consistent with the work of Lanschuetzer et al,9 who demonstrated several growth factors along with individual melanocytes in blister fluid overlying an “epidermolysis bullosa nevus,” an eruptive MN that occurred at the site of a previous bulla. Because most of the bullous disorders associated with eruptive MN are transient, the changes in local growth factors may also be transient. Therefore, we believe that without further stimuli, these MN would remain stable without a propensity to malignant degeneration. To our knowledge, no reports of malignant degeneration of eruptive nevi in a patient with a bullous disorder have been described.

In contrast, in patients with eruptive MN associated with immunosuppression, the pathogenesis and natural history may be quite different. Acquired MN are affected by a variety of factors, including genetics, phenotypic traits, and sun exposure.25 In addition, there is accumulating evidence of the role of the immune system in melanogenesis.19,25 In 1989, Ross26 first suggested that immune surveillance is integral in preventing melanoma growth in and around MN. This theory has been supported by some of the literature on eruptive MN. Several researchers believe that an intact immune system normally limits the proliferation of melanocytes, whereas a disordered one is unable to do so, leading to eruptive MN.5,12,13,15,16,19,27 To support this concept, Piaserico et al13 recently described fading and disappearance of eruptive MN on withdrawal of immunosuppressive therapy in a renal transplant recipient who was experiencing graft rejection. As other researchers25 have suggested, it seems...
that immunodeficiency itself, not the type of immunosuppression, plays a pivotal role in the development of eruptive MN.

It is possible that a dysfunctional immune system, unable to limit the proliferation of melanocytes, allows for the appearance of atypical cells, leading first to atypical/dysplastic MN and later to melanoma. It could be hypothesized that in immunosuppressed patients, eruptive nevi may be at greater risk for undergoing malignant degeneration. To our knowledge, no reports of malignant degeneration of eruptive nevi in a patient with systemic immunosuppression have been described. However, patients who are immunosuppressed have a significantly increased risk of melanoma.14-18,20 Why only a small percentage of patients in these populations experience eruptive MN remains to be determined.

In summary, we describe the long-term course of a patient who developed eruptive MN after a bullous disorder. After 38 years of follow-up, his lesions have remained stable, without signs of malignant degeneration. The etiology and natural course of eruptive MN may differ between the 2 main populations of patients at risk for eruptive MN, with MN arising after bullous disorders being likely to remain benign compared with those in patients with ongoing immunosuppression. However, this hypothesis has yet to be proved, and it will require long-term surveillance of individuals who have developed eruptive MN to determine its merit.

Accepted for Publication: June 4, 2007.

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Author Contributions: Dr Rivers had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Rivers. Acquisition of data: Rivers. Analysis and interpretation of data: Gelfer and Rivers. Drafting of the manuscript: Gelfer and Rivers. Critical revision of the manuscript for important intellectual content: Gelfer and Rivers. Administrative, technical, and material support: Gelfer. Study supervision: Rivers.

Financial Disclosure: None reported.

Additional Contributions: A. Kopf, MD, provided the photograph of the original eruption from 1974.

REFERENCES


