Agminated Atypical (Dysplastic) Nevi
Case Report and Review of the Literature

Ashfaq A. Marghoob, MD; Robin Blum, BS; Robert Nossa, MD; Klaus J. Busam, MD; Dana Sachs, MD; Allan Halpern, MD

Background: Patients with the atypical mole syndrome have multiple dysplastic nevi that appear to be randomly distributed on certain preferred anatomical sites such as the upper back. These dysplastic nevi are thought to be acquired melanocytic nevi that begin appearing at puberty. To our knowledge, the presence of agminated atypical (dysplastic) nevi has not been reported.

Observation: We describe a patient with the atypical mole syndrome who has more than 100 melanocytic nevi, many of which are clinically atypical and one of which proved to be a melanoma. Among his many melanocytic nevi is a cluster of approximately 50 nevi that are distributed in an area measuring 5 × 3 cm. The histopathologic features of these nevi are consistent with the diagnosis of “dysplastic nevus.”

Conclusions: To our knowledge, agminated atypical (dysplastic) nevi have not been described previously. The presence of agminated atypical (dysplastic) nevi in a patient with the atypical mole syndrome can be theorized to arise because of loss of heterozygosity.

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REPORT OF A CASE

A 44-year-old man was referred to the dermatology clinic for evaluation of multiple irregular moles. The patient reported that his nevi developed during his teenage years. He denied a family history of multiple moles or melanoma.

On physical examination, the patient had more than 100 melanocytic nevi, and a few of these nevi appeared clinically atypical. The largest nevus, on the right side of his chest, measured 1 cm in greatest diameter (Figure 1). The patient also had an irregular melanocytic neoplasm on the right side of his mandible that on subsequent biopsy proved to be melanoma in situ.

The patient had a cluster of approximately 50 melanocytic nevi on his right arm, all distributed in an area 5 × 3 cm in diameter (Figure 2 and Figure 3). The patient stated that this cluster of nevi first became apparent at the age of 15 years. No background café-au-lait pigmentation was noted clinically or with the aid of a Wood light examination. Dermoscopy revealed that all the nevi had a “diffuse and patchy” network pattern (Figure 4A). However, one area was darker (Figure 3) and on dermoscopy had black dots, globules, and structureless areas (Figure 4B). Because this area had nevi that differed from the other surrounding nevi, it was excised. The histopathologic findings revealed a lentiginous compound melanocytic nevus with architectural disorder of its intraepidermal component and irregu-
lar placement of nests of variable size and shape, fusion of nests, and asymmetric extension of the junctional component beyond the confines of the intradermal nevus component (Figure 5A). Several melanocytes contained abnormally large nuclei, some that were twice the normal size, and the nuclei had irregular contours. Furthermore, papillary dermal fibroplasia with a sparse lymphohistiocytic infiltrate was present (Figure 5B). In light of the presence of architectural disorder and cytologic atypia, a diagnosis of dysplastic nevus was made.

COMMENT

Atypical moles (dysplastic nevi) are acquired pigmented lesions that develop during puberty and continue to develop and change throughout life. Although they may appear anywhere on the body, they primarily develop on the trunk.

Clinically, atypical nevi share many features of malignant melanoma, including asymmetry, border irregularity, color variability, and a diameter greater than 6 mm.8 They can be multiple or solitary, and can develop in patients with or without a family history of similar lesions.

We describe a patient with the atypical mole syndrome who had an unusual presentation of multiple, clustered, clinically atypical (dysplastic) nevi. To our knowledge, this is the first reported case of agminated atypical (dysplastic) nevi. In this patient, the diagnosis of atypical (dysplastic) nevi was based on clinical and histologic features. Clinically, some of the patient’s nevi were irregular, demonstrated variegation of color, and were greater than 6 mm in diameter. The dermoscopic feature of a patchy network was also consistent with a diagnosis of dysplastic nevi.6 The histologic diagnosis of the biopsied section was that of a dysplastic nevus or a nevus with “architectural disorder and cytologic atypia.”9

A review of the literature revealed that the term agminated has been used to describe several different cutaneous lesions. Pigmented lesions that have been described as agminated include melanocytic nevi,3 congenital melanocytic nevi,10 Spitz nevi,11,12 nevi spilus,13,14 blue nevi,15,16 and multiple lentigines.17 Other nonpigmented agminated lesions reported in the literature include xanthogranulomas,18 angiofibromas,19 and neurilemmomas.20 Historically, atypical (dysplastic) nevi have not been reported to occur in an agminated distribution.

Based on this patient’s clinical and histologic features, the diagnosis of agminated atypical (dysplastic) nevi, and not any of the other previously reported agminated lesions, is most accurate. By definition, congenital melanocytic nevi are melanocytic nevi that are present at birth or develop shortly after birth. Because our patient’s nevi developed during his teenage years, it is unlikely that they were congenital melanocytic nevi.21 In addition, the histopathologic features were not consistent with congenital melanocytic nevi.

It is unlikely that the cluster of lesions were Spitz nevi. Although multiple agminated Spitz nevi have been reported,22 the histologic features of Spitz nevi are quite different and demonstrate admixed spindle and epithelioid cells arranged in irregular nests with occasional mitotic figures. These features were not seen in this patient’s biopsy specimen. In addition, the clinical features

Figure 1. Anterior chest and abdomen showing multiple melanocytic nevi. The patient’s largest nevus is on the right side of his chest near the midline.

Figure 2. The agminated atypical nevi are seen on the right arm.

Figure 3. The agminated atypical nevi. A biopsy of the area within the oval was performed. A indicates the area from which the dermoscopic image seen in Figure 4A was taken; and B, the area from which the dermoscopic image seen in Figure 4B was taken.
of agminated Spitz nevi are also different. Spitz nevi tend to develop in early childhood, predominately occur on the face, and are pink. In our patient, the nevi did not develop until puberty, occurred on his arm, and were brown.

The diagnoses of nevus spilus, blue nevi, and lentiginosis can be ruled out based on clinical and histologic features. Unlike our patient, who developed his “agminated atypical moles” at the age of 15 years, nevus spilus is usually apparent by early infancy or childhood. The diagnosis of nevus spilus is also not consistent with the clinical examination because of the obvious lack of background pigmentation, a feature commonly seen in a nevus spilus. Furthermore, the pathological features of our patient’s agminated lesions also failed to demonstrate the background of lentigo, as would be seen in a nevus spilus. The diagnosis of blue nevi was not made because clinically they did not appear as blue or black dome-shaped papules, and histologically they did not demonstrate dermal melanocytes grouped in irregular bundles admixed with melanophages. The diagnosis of agminated lentiginosis was not made because the histologic features did not demonstrate elongation of the rete ridges and hyperplasia of melanocytes.

It has been proposed that the atypical mole syndrome has either an autosomal dominant mode of inheritance with incomplete penetrance or a polygenic mode of inheritance. The specific gene or genes that predispose to the development of dysplastic nevi and the precipitants for the formation of individual melanocytic nevi have not been identified. However, sun exposure has been implicated in the development of melanocytic nevi. Furthermore, it has been postulated that some atypical melanocytic nevi may develop through loss of heterozygosity (LOH). Loss of heterozygosity is the loss of a normal wild-type allele, leading to the expression of a mutant or recessive allele. One mechanism for acquired loss of an allele may be through mutations induced by UV exposure. The specific etiology of agminated nevi is not known. Local environmental factors, such as UV radiation, may play a role in the development of clustered lesions. However, it is also possible that this agminated pattern may represent LOH, occurring during embryogenesis, as has been postulated to account for the segmental distribution of lesions such as neurofibromas, porokeratosis, and Becker nevi. In our patient, the agminated dysplastic nevi occurred in the presence of the atypical mole syndrome. Other examples of segmental clustering of skin lesions superimposed on a generalized less severe form of the condition may shed light on the pathogenesis in our case. Autosomal dominant skin disorders, such as neurofibromatosis, sometimes occur in a segmental pattern superimposed on a less severe but diffuse form of the same disorder. This phenomenon may be explained by an early postzygotic mutational event giving rise to LOH at the locus responsible for the trait. A person can also have a segmental manifestation of a polygenic skin disorder, such as segmental severe psoriasis, superimposed on symmetric involvement of ordinary psoriasis. This too can be explained by LOH occurring in a somatic cell during early embryogenesis, resulting in either homozygosity or hemizygosity for one of the genes predisposing to psoriasis. Future studies of the distribution of lesions in cases of agminated nevi such as ours coupled with genetic analysis of microdissected tissues may shed light on the timing and nature of these events.
In conclusion, based on a review of clinical entities occurring in an agminated distribution, we believe that our case is the first report of agminated atypical (dysplastic) nevi. This is a new, previously undescribed, clinical variant of atypical (dysplastic) nevi occurring in a patient with the atypical mole syndrome and adds to the phenotypic spectrum of this entity. In addition, this case raises the possibility that LOH may play a role in the development of some cases of dysplastic nevi or atypical mole syndrome.

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Corresponding author and reprints: Ashfaq A. Marghoob, MD, Dermatology Service, Memorial Sloan-Kettering Cancer Center, 1275 York Ave, New York, NY 10021.

REFERENCES