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Desmoplastic melanoma of the eyelid and conjunctival melanoma in neurofibromatosis type 1: A clinical pathological correlation

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ABSTRACT

A 56-year-old woman with neurofibromatosis type 1 (NF1) presented with a left upper eyelid amelanotic nodule with adjacent eyelid margin hyperpigmentation. Physical examination additionally revealed primary acquired melanosis (PAM) on the palpebral conjunctiva of the same eyelid. Full thickness eyelid excision and conjunctival map biopsy identified desmoplastic melanoma of the eyelid in addition to invasive conjunctival melanoma and conjunctival melanoma in situ. Sentinel lymph node biopsy was negative for metastasis. She was treated with surgical excision for the eyelid melanoma and topical mitomycin C for the conjunctival melanoma. We discuss the rare entity of desmoplastic melanoma of the eyelid and its possible association with NF1.

As a disease of neural crest derived tissue, neurofibromatosis type 1 (NF1) may also be linked to melanoma, a malignancy of melanocytes.[38] Both cutaneous and ocular variants of melanoma have been observed in NF1, and the risk of developing melanoma in NF1 is elevated.[3,4,11,18,38,40–42,46] Genetic analysis indicates mutations in the 17q11.2 locus of the *NF1* gene in certain melanoma cells.[2] Additionally, in vitro and mouse studies demonstrate that the loss of *NF1* reduces BRAF-induced senescence, which is a process that drives senescence rather than malignant transformation.[26] Furthermore, neurofibromas as seen in NF1 may express melanocyte differentiation markers.[33]

We describe a patient with NF1 with findings of two types of melanoma: desmoplastic melanoma of the eyelid and conjunctival melanoma. These two distinct types of melanoma in a patient with NF1 have, to our knowledge, not been previously described. We also review the literature on desmoplastic melanomas of the eyelid.

1. Case Report

A 56-year-old white woman presented for evaluation of a left upper lid lesion. She thought this had been present since early

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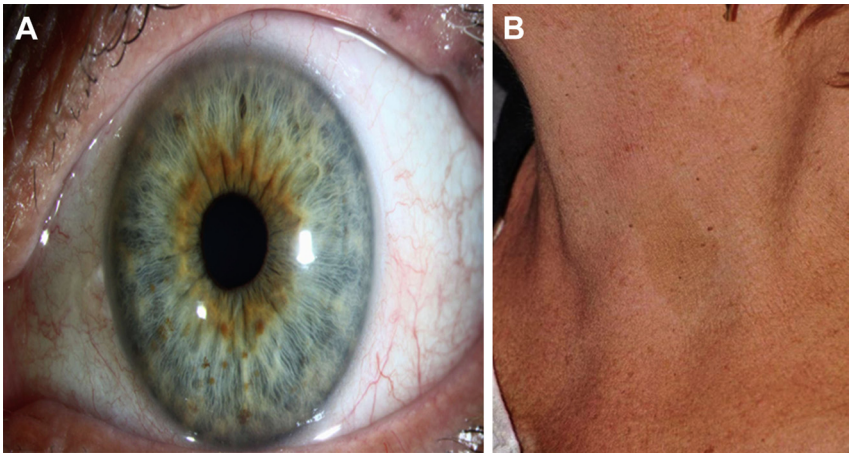

Fig. 1 – *A*: External photograph of the patient's left eye. Lisch nodules are seen on the iris. *B*: External photograph of the patient's neck with hyperpigemented macules consistent with café-au-lait spots.

adulthood, but it had become friable with bleeding over the past 5 months. She did not note a change in its size.

Her past medical history was significant for NF1 diagnosed at age 34 with the presence of café-au-le spots, axillary freckling, neurofibromas, and Lisch nodules (Fig. 1). Additionally, she had been treated with external beam radiation and lumpectomy for breast cancer 5 years previously with remission.

Her visual acuity was 20/20 bilaterally with correction. Pupils, extraocular movements, and intraocular pressures were normal. Examination of the eyelids demonstrated a 2×1 mm area of pigmentation of the left upper lid margin with a 1.5 mm amelanotic nodule adjacent to it. Slit lamp exam of the left eye demonstrated a 3×1 mm and a 5×4 mm area of primary acquired melanosis (PAM) on the palpebral conjunctiva without involvement of the bulbar conjunctiva (Fig. 2).

She initially underwent a shave biopsy of the upper eyelid that revealed a desmoplastic melanoma of at least 1.1 mm depth and perineural invasion with involvement of peripheral and deep margins. She subsequently had a pentagonal excision of the left upper eyelid, conjunctival map biopsies, and cryotherapy. Fresh-frozen sections of the lateral and medial margins were reported as negative, but permanent sections of the medial margins were positive, necessitating additional excision.

The main eyelid lesion demonstrated spindle cell proliferation within the dermis of the eyelid (Figs. 3–5). The proliferation was relatively hypocellular, as it was accompanied by abundant fibrotic stroma, but contained enlarged, hyperchromatic and pleomorphic nuclei. The overlying epidermis contained an atypical melanocytic proliferation with areas of pagetoid spread. Immunohistochemistry for S-100 protein and HMB-45 were positive in both the epidermal and dermal

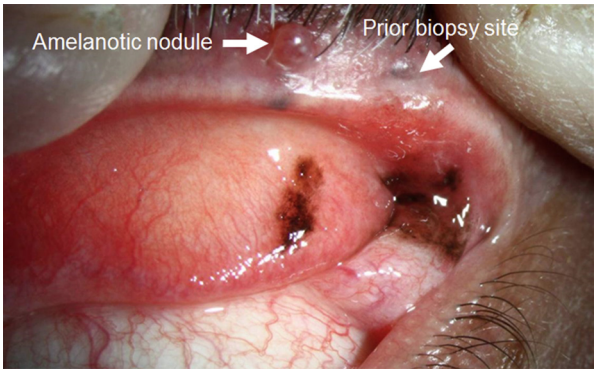

Fig. 2 – External photograph of the patient's everted left upper eyelid. Noted within the photograph is an amelanotic nodule (*large arrow*) next to the prior shave biopsy site (*small arrow*). Also visible within the photograph are hyperpigmented lesions within the palpebral conjunctiva resembling the clinical diagnosis of PAM.

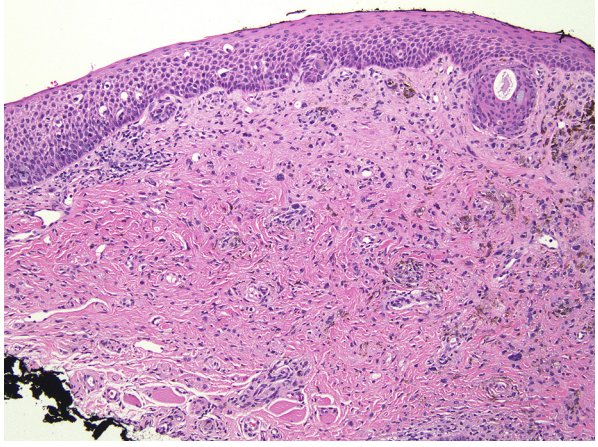

Fig. 3 – Initial biopsy specimen. The photomicrograph demonstrates atypical, but relatively paucicellular, dermal infiltrate embedded in a fibrous stroma on hematoxylin and eosin stain (10×). The overlying epidermis reveals scattered atypical, vacuolated cells with pagetoid spread.