A Neurofibroma with Unusual Morphology

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Sir,

Neurofibromatosis presents in a variety of clinical patterns. Some cases of neurofibromatosis are associated with anomalies of various systems other than skin. Usually, the cutaneous lesions of neurofibromas are easily recognizable and the morphological lesions are mollusca fibrosa (soft papules, pedunculated or sessile), café-au-lait macules (CALM), hyperpigmented macules other than CALM, freckle-like lesions in the axillary vaults and elsewhere, and fusiform soft to firm swellings, sometimes with the feel of a bag of worms, as in a plexiform neurofibroma. We report here a case of an unusual morphological presentation of a lesion of neurofibroma.

CASE REPORT

A 17-year-old girl presented to us with multiple hyperpigmented dark brown macules on her trunk and extremities present from early childhood, and multiple cutaneous papules and nodules that had been developing for about 3 years. There were no other systemic complaints. She had been born to healthy non-consanguineous parents following an uneventful pregnancy. She was the only affected member in the family, both her sisters being unaffected.

On examination, she had numerous (>6) CALM on her abdomen, back and extremities, ranging in size from 0.5 to 3 cm, along with numerous cutaneous neurofibromas, clinically fulfilling the criteria for a diagnosis of neurofibromatosis 1 (NF1). Ophthalmological assessment did not reveal Lisch nodules or any other abnormality. There were no bony defects and the systemic examination was normal.

Of interest was a 3×2 cm soft plaque on the right side of her abdomen, which was uniformly brown, oval in shape with one end somewhat angular, and had numerous indentations on its surface (Fig. 1). According to her history, this plaque had been preceded by a dark-brown hyperpigmented macule similar to her other CALM. The shape of this plaque also resembled that of a CALM. Clinically, we made a diagnosis of an unusual presentation of neurofibroma for this lesion, since it was well circumscribed, uniformly raised throughout and oval to irregular, but very soft on palpation, thus being unlike either a subcutaneous or a plexiform neurofibroma. However, the punch biopsy from this plaque revealed features typical of a neurofibroma, with numerous delicate fascicles composed of cells having spindle-shaped nuclei and scant cytoplasm, and a matrix containing delicate, wavy collagen bundles (Fig. 2).

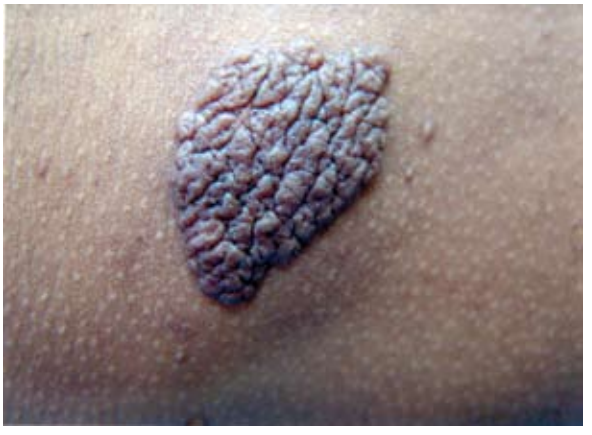

Fig. 1. The flat-topped, uniformly raised hyperpigmented well-defined plaque of neurofibroma.

DISCUSSION

NF1, an autosomal dominant disorder, is one of the most common neurocutaneous conditions and affects 1 in 3000 persons (1). Since NF1 may be considered a neurocristopathy primarily affecting tissues derived from the neural crest and since melanocytes originate in the neural crest, the presence of hyperpigmented lesions in the NF1 phenotype is to be expected, because of changes in melanocyte cell growth and differentiation (2). Hyperpigmentary manifestations of NF1, besides CALM and axillary freckling, may include a plexiform neurofibroma with hyperpigmentation on the surface. Rarely, neurofibromas may arise within pre-existing CALM (2). The hyperpigmentation of a plexiform neurofibroma may also be associated with hypertrichosis, clinically simulating a Becker's naevus (3). It may also resemble a naevus spilus (4).

The pathogenesis of CALM and neurofibromas has not been fully elucidated. Post-transcriptional reduction in neurofibromin levels has been suspected to be related to altered melanogenesis in melanocytes of NF1 patients and increase in CALM (5). The oblong to oval shape of the CALM has been theorised to be due to the diffusion of an unknown substance whose critical concentration level determines the increased melanin content in them (5). With regard to neurofibromas and neurofibroma-like neoplasms, some studies have linked aberrant fibroblast proliferation in response to passive and/or active mechanical stress to arrector pili muscles (6), while others indicate the causative role of mast cells in their pathogenesis (7).

CALM have been shown on electron microscopy to contain increased subepidermal and intra-epidermal nerves that belong to free nerve endings (8). This is the characteristic histological finding of a CALM in NF1, and an increase in the number of macromelanosomes may or may not be seen (9). As both melanocytes and

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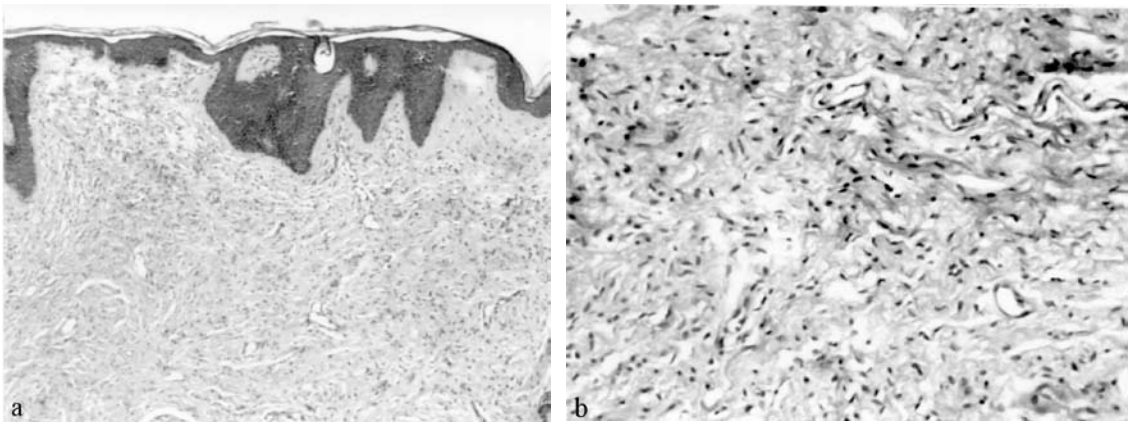

Fig. 2. The histopathology of the plaque, revealing numerous fascicles of cells with spindle-shaped nuclei and the matrix revealing delicate, wavy collagen bundles. (a) 40×; (b) 100×.

nerves are derivatives of the neural crest, a common growth factor can be speculated to lead to their co-existence in a CALM. Though the pathogenesis of the pigmentary changes in various dermatoses is complex, with more than one factor likely to be contributing, it may be speculated that the hyperpigmentation of a CALM is due to the free nerve endings present in increased numbers, considering the fact that in leprosy where nerve endings are destroyed, hypopigmentation often results.

The findings in our patient suggest that the pathogenetic pathways of the two cardinal cutaneous manifestations of neurofibromatosis, CALM and neurofibromas, are linked. The exact nature of these links, however, remains to be understood.

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