Dermal Melanocyte Hamartoma and Hereditary Motor and Sensory Neuropathy Type 2A

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Sir,

Dermal melanocyte hamartoma (DMH) is a rare clinico-pathological entity characterized by the persistence of ectopic melanocytes in the dermis after birth (1–6). Related entities are the pilar neurocristic hamartoma (7) and phakomatosis pigmentovascularis type IVa (8, 9), in which the blue-coloured spots are associated with naevus flammeus.

Here, we report a rare case of DMH associated with hereditary motor and sensory neuropathy type 2A (HMSN 2A), also known as Charcot Marie Tooth disease, a neurological disorder with recessive autosomal inheritance, characterized by a demyelinizing peripheral neuropathy and progressive myopathy (10).

CASE REPORT

A 54-year-old man presented with several congenital pigmented lesions, mottled with small, well-demarcated macular-papules of a dark-blue colour on the upper trunk and extensor region of the limbs, including hands, with characteristic mantle distribution (Fig. 1). During childhood the macules had increased in number with the appearance of new elements similar to blue naevus or cavernous hemangioma.

Skin biopsies from the large grey-blue patches on his back showed basal hyperpigmentation and slight orthokeratotic hyperkeratosis of the epidermis with normal number of intraepidermal melanocytes. In the upper dermis, a mild perivascular infiltrate was present with many melanophagic histiocytes. In the middle and lower dermis there were scattered spindle and elongated cells with dusty melanin cytoplasmatic granules disposed along collagen fibres (Fig. 2) or focally arranged in perineural and perivascular localization. An immunological test for S-100 protein performed with Avidin–Biotin–Complex (DAKO) and Diamino-Benzidine chromogen counterstained with Giemsa showed the nuclear and cytoplasmic positivity typical of neuro-ectodermal cells with the green dusty appearance of melanin. The nerve bundles appeared only slightly hypertrophic, with minimal signs of onion bulb appearance. This histological picture was consistent with the diagnosis of dermal melanocytosis. According to clinical and histological features we diagnosed a case of DMH. The patient was also affected by a muscle hypotrophy in the forearms and hands, resulting in a claw-like appearance. The distal muscle atrophy of the lower limbs was notable too.

There was no family history of neurological symptoms of this disease. The neurological motor disturbance manifested in the eighth year of life with a limp in the left leg. Symptoms worsened progressively, involving the other limbs. An electromyography and electroneurography showed a sensory-motor neuropathy associated with severe axonopathy. It has not been possible to perform the motor evoked potential because of severe muscular

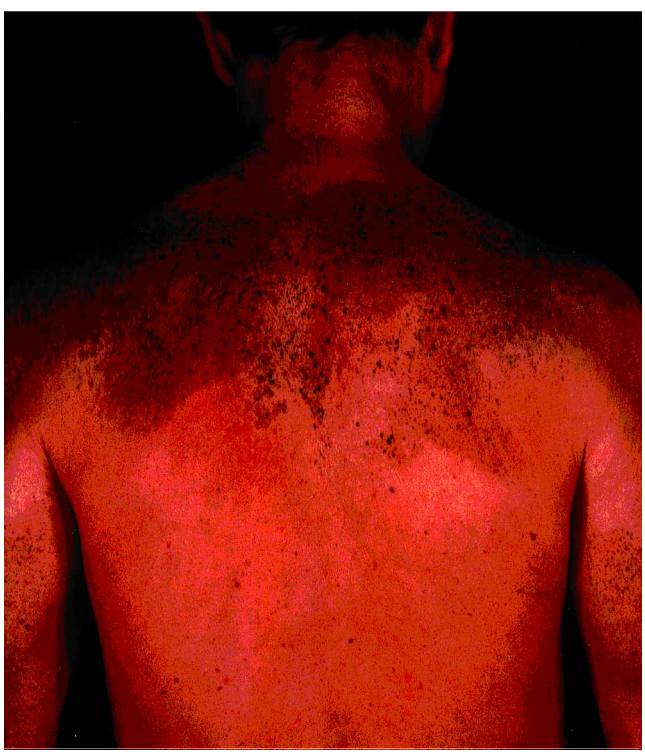

Fig. 1. Dermal melanocyte hamartoma with hyperpigmentation of the skin on the back.

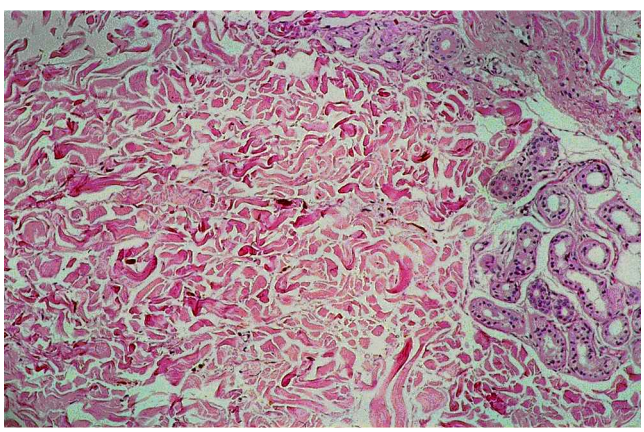

Fig. 2. Scattered pigmented cells along collagen bundles in mid dermis (H&E, original magnification ×250). These cells were S-100 positive.

atrophy, or a nerve biopsy, because of lack of patient consent. A diagnosis of HMSN 2A or Charcot Marie Tooth disease was made in accordance with these data. Based on the Online Mendelian Inheritance in Man, the MacKusick number for this disease is 118210 (11).

DISCUSSION

DMH is a clinico-pathological form of dermal melanocytosis characterized by the presence of ectopic melanocytes in the dermis starting at birth. During the first months of fetal life, melanocytes migrate from the neural crest to the dermo-epidermal junction. The persistence of these cells in the dermis occurs in sites such as the scalp, sacral region, in Negroes on the dorsum of the hand and foot and in pathologies like Mongolian spot, naevus fuscocaeruleus ophthalmo-maxillaris of Ota (12), naevus of Ito and blue naevus. The origin of these conditions is unknown, even though in 1967 Inoue (13) postulated the presence of a fibrous coat which would induce the permanence of the melanocytes in the dermis. There may be a single, very extensive area of grey-blue pigmentation present from birth (2). Sometimes the involvement can be widespread, as in DMH (4). On the contrary, in naevus of Ito it is located only in the supraclavicular, scapular and deltoid regions. In other instances, several coalescing blue macules gradually extend within a circumscribed area (3) or widely scattered blue patches gradually develop during childhood (14).

The histological pattern of DMH differs from that of blue naevus. In fact, in DMH, melanocytes are scattered in the dermis, whereas in blue naevus the cells are arranged together. This complex dysembryoplasia has been correlated with pathologies like pilar neurocristic hamartoma, or phakomatosis pigmentovascularis. Pilar neurocristic hamartoma originates from the neural crest and is characterized by dermal melanocytes and neurosustentacular and fibrogenic components. Both of these components may go into a malignant transformation (15). In phakomatosis pigmentovascularis an extensive blue pigmentation is associated with naevus flammeus (9). We found no report in the literature on associations between DMH and HMSN 2A.

The histological alterations that we have described suggest an anomaly of Schwann cells. It is well known that melanocytes share the same protein pattern as Schwann cells during the premyelinogenetic phase. Several authors have pointed out that Schawnn cells and melanocytes derive from the same stem cell (16). However, the exceptionality of the association we described makes the hypothesis probable that it may be a simple coincidence. Only subsequent similar reports can help our understanding of this association.

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