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Meningioma associated with McCune-Albright syndrome

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Sirs: McCune-Albright syndrome (MAS) is a sporadic syndrome which is characterized by the clinical triad of polyostotic fibrous dysplasia, hyperpigmented macules, and precocious puberty combined with various combinations of other hyperfunctional endocrinopathies. MAS has been suggested to result from an autosomal lethal gene surviving by mosaicism [6]. As a molecular basis of MAS has been found a mutation of the α-unit of the stimulatory guanine nucleotide binding protein ($G_s\alpha$) [2, 8]. In a review by Ringel et al. [8] summarizing the clinical manifestations in 158 individuals the presence of various benign and malignant tumours is described including adenomas of the pituitary gland and in other endocrine organs, myxomas, and osteosarcomas. There is one case report of meningioma in association with MAS [3] and a further case associated with fibrous dysplasia but not the full syndrome [4].

We report a 38-year-old woman who was found to have a spinal meningioma causing myelopathy. Based on the typical history and clinical manifestations the diagnosis of MAS was first made when the patient was admitted for her neurological symptoms. Her symptoms of puberty had already occurred in preschool and menarche in primary school age. The menstrual cycle was irregular. She gave birth to a healthy daughter at age 29 years. Thyroidectomy was necessary because of thyroid hyperfunction at age 32.

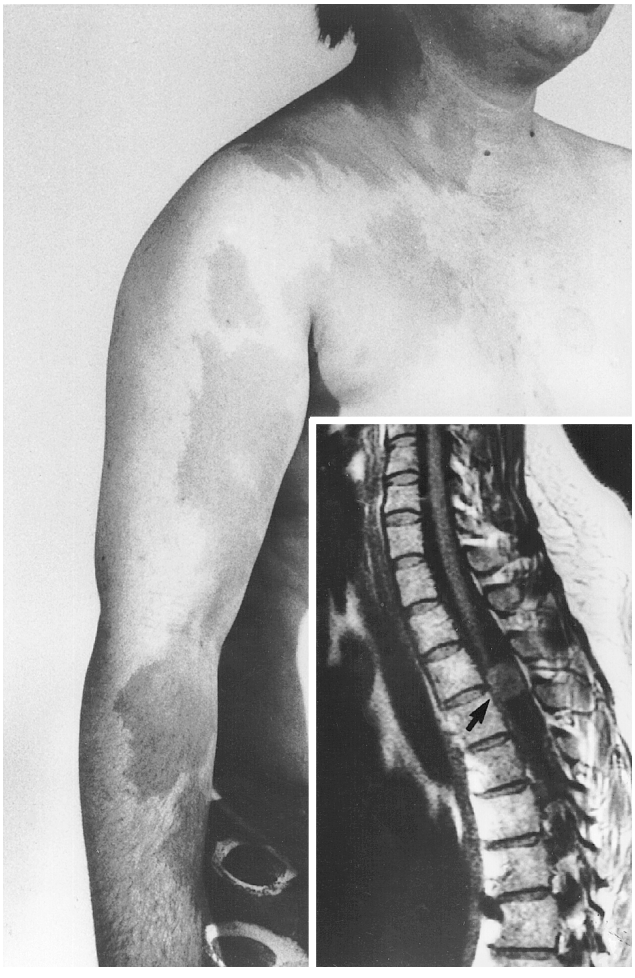

Fig. 1 Typical, unilaterally distributed hyperpigmented macules in McCune-Albright syndrome. *Insert* spinal meningioma (*arrow*) on T1-weighted magnetic resonance imaging

Her skin showed large light-brown macules resembling café-au-lait spots on the right side of the neck, back, sacrum, and arm, with strict midline separation. The shape of the individual macules was irregular, mostly with a ragged margin (Fig. 1). No signs of neurofibromatosis-like cutaneous neurofibromas or axillary freckling were found. Histological examination of the involved skin revealed hyperpigmentation of the basal layer of the epidermis, but the number of melanocytes did not differ from that in normal skin.

Neurological examination showed a spastic-atactic gait disorder and paraparesis with predominant involvement of the left side and hyperactive reflexes in the lower limbs. There was a mild hypesthesia confined to both legs, beginning in the middle of both thighs. Laboratory testing revealed an elevated osteocalcin level as the only pathological finding. Radiologically, dysplastic bone lesions were found in the os frontale, the upper part of the orbita, and the left os sphenoidale. Fibrous dysplasia was seen in the left maxilla, the left ramus, and right corpus mandibulae. Magnetic resonance imaging of the spine showed an intradural, extramedullary mass of 1.5

cm diameter suggestive of a meningioma at T3-T4 on the left side with displacement of the cord (Fig. 1)

The tumor was removed and a psammomatous meningioma was diagnosed by light microscopy. The neurological symptoms and signs improved over the following days after surgery.

This case and the two reports mentioned above [3, 4] suggest that meningiomas may be another feature of MAS. MAS must be differentiated from neurofibromatosis (NF) type 1, a well-known neurocutaneous disorder also presenting with hyperpigmentations, the café-au-lait spots. In contrast to the sporadically occurring MAS, NF-1 is an autosomal dominant condition with occasionally poor prognosis. These syndromes can clinically be differentiated by the different morphology and distribution of the hyperpigmented skin lesions. In NF-1 classical café-au-lait spots typically present as randomly distributed light-brown oval macules with a smooth border. In MAS, however, patients have one or more unilaterally distributed lesions with irregular borders. They often follow the lines of Blaschko, thus reflecting the genetic neuroectodermal mosaicism [7]. However, it should be borne in mind that there is also a segmental variant of NF, probably representing a postzygotic mutation of the NF-1 gene [5]. In these cases café-au-lait spots (and neurofibromas) are confined to one or more segments of the skin and therefore may more easily be mistaken for the melanotic macules of MAS.

While the occurrence of meningiomas is common with NF-2, another type of neurofibromatosis, rare cases with NF-1 have been reported, but these were probably diagnosed before the era of molecular genetics [1]. Since meningiomas may grow for years without clinically overt disease, patients with MAS should be carefully examined for related symptoms.

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