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McCune Albright Syndrome

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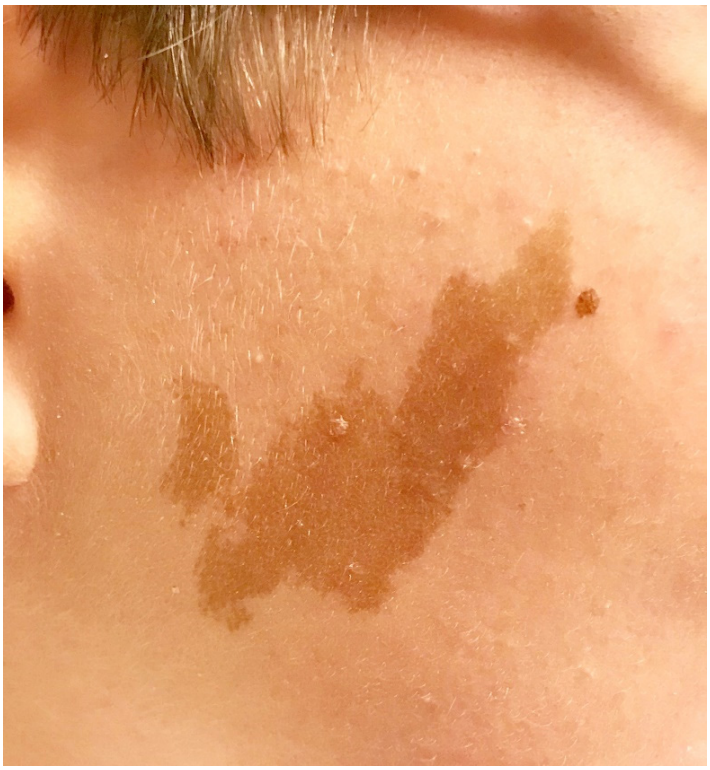

A ten-year-old female presented to our dermatology clinic with her mother, our patient, at which time we incidentally noted a large light brown patch on the daughter's cheek (shown above). The girl was a fifth grader in elementary school. On physical exam, a large brown smooth patch with jagged borders consistent with a café-au-lait patch was noted on the right cheek. The lesion was present since birth, was asymptomatic, and had grown in proportion with her growth overtime.

The girl noted a history of early menses beginning at the age of two for which she follows with endocrinology. She noticed breast enlargement at the age of seven years old. She also noted a history of multiple bone fractures, most recently of the femur after falling in the yard. Musculoskeletal exam revealed asymmetric limb length with the left leg longer than the right. She was ambulating on crutches after fracturing her femur in a fall. Breast exam revealed large breasts relative to height and age. The remainder of the physical exam was non-contributory.

DISCUSSION

Given the clinical manifestations, the patient was diagnosed with McCune Albright Syndrome (MAS), a genetic syndrome characterized by the clinical triad of polyostotic fibrous dysplasia, endocrine abnormalities, most frequently precocious puberty, and a pathognomonic café-au-lait patch.[1] The differential diagnosis of MAS is neurofibromatosis type 1 (NF1), Cutaneous-Skeletal Hypophosphetemia Syndrome, and various fibro-osseous skeletal lesions, such as giant cell tumors of bone, ossifying fibromas, osteofibrous dysplasia, and cherubism.[2] While NF1 shares several features with MAS, such as café-au-lait macules and skeletal deformities, the nature of the café-au-laits (smaller and more numerous) and skeletal deformities (i.e., sphenoid dysplasia and pretibial bowing), along with tumors of the nervous system, distinguish it from MAS. Cutaneous-skeletal hypophosphatemia syndrome presents with epidermal and congenital melanocytic nevi as opposed to café-au-laits and the skeletal development abnormalities are usually that of rickets/osteomalacia rather than polyostotic fibrous dysplasia. Finally, fibrous skeletal lesions, as listed above, are usually solitary and lack the extra-skeletal manifestations seen in MAS.

MAS is a genetic syndrome caused by a post-zygotic somatic activating mutation in GNAS (guanine nucleotide binding protein, alpha stimulating).[2] It initially presents with a unique café-au-lait patch characterized by a light brown patch with jagged, irregular boarders that classically resembles the "coast of Maine". This lesion is typically apparent at or shortly after birth. Often, the café-au-lait patch follows the developmental Blaschko lines.[2] The second clinical feature is that of an endocrine abnormality. The most common endocrine abnormality is precocious puberty seen in approximately 85% of female patients with MAS.[2] Other endocrine abnormalities that can occur are hyperthyroidism, growth hormone excess, hyperprolactemia, and hypercortisolism.[1] Endocrinopathies typically occur in infancy or early childhood and persist into adulthood.[3] In a study of 11 patients with MAS, the average age of gonadotropin-independent precocious puberty onset was around five years with ages of onset ranging from two months to eight years.[4] Precocious puberty in MAS often is referred to as gonadotropin-independent precocious puberty (GIPP). Recurrent ovarian cysts result in episodic estrogen production and intermittent vaginal bleeding.[3] In males, testicular involvement is common, but precocious puberty rarely develops.[5]

Finally, patients with MAS present with polyostotic fibrous dysplasia in which the patient's normal bone and bone marrow are replaced by fibro-osseous tissue, leading to fibrous deposition in bones.[2] This results in an increase in frequency of bone fractures, skeletal deformities, functional impairment, and pain after minimal trauma. Clinicians must have a high suspicion for a diagnosis of MAS when a patient exhibits two or more clinical features described above. Genetic testing for GNAS should be performed to confirm the diagnosis.[2] Managing the manifestations of MAS should be individualized and can be best accomplished by a multidisciplinary team consisting of a primary care physician, endocrinologist, orthopedic surgeon, and physical therapist, with routine follow-up.[2,3,6] Finally, support groups such as the MAGIC Foundation and the Fibrous Dysplasia Foundation also are available for patients and their families.[6]

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