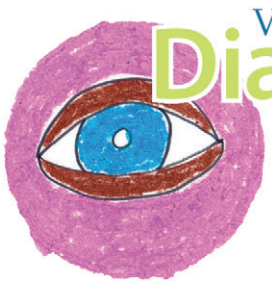

Multiple Falls and a Pigmented Skin Lesion in a 5-year-old Boy

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PRESENTATION

A 5-year old boy is transferred from an outside institution for a radiograph finding of a left femur fracture coursing through a lytic lesion. The boy presented earlier that day with left leg pain and inability to bear weight after tripping and falling. One month previously he was diagnosed as having a left tibia fracture after another child jumped and landed on him in an inflatable bounce house. Before these injuries he had no history of bone pain or muscle weakness. His parents report a long-standing history of poor appetite and hyperactivity. He has no associated fever, weight loss, rash, or night sweats. The medical history includes a recent diagnosis of attention-deficit/hyperactivity disorder (ADHD), a "Mongolian spot" diagnosed in infancy, and 3 hospitalizations in the first 4 months of life for brief resolved unexplained events. An investigation for nonaccidental trauma was initiated at that time and revealed chronic bilateral subdural hemorrhages on magnetic resonance imaging, normal laboratory results, and a normal skeletal survey and ophthalmic examination findings. The boy was temporarily placed in the care of a family friend and eventually placed back into his parents' custody.

On physical examination the boy points to his left thigh as the primary source of pain. He has a posterior long bone splint on the left leg, with an overlying short hard cast that was placed by the outside institution. Range of motion and strength is decreased in the left leg, but he has intact pulses, normal capillary refill, and intact sensation. His previously diagnosed Mongolian spot is a large, flat, hyperpigmented macular lesion with jagged borders that spans his lower back and buttocks (Fig 1).

Radiographs of the left lower extremity reveal a healing fracture of the distal tibia and an acute nondisplaced fracture at the proximal femur (Fig 2). Multiple lucent lesions with cortical thinning are visible throughout the femur, fibula, and tibia (Fig 2). Additional imaging and laboratory evaluation confirm the underlying diagnosis.

DIAGNOSIS

The patient's Mongolian spot has the typical appearance of a café-au-lait skin pigmentation, and the jagged borders mimic the coast of Maine (Fig 1). The lucent lesions on the radiograph are consistent with polyostotic fibrous dysplasia (PFD). Further evaluation in the context of the physical examination findings revealed an elevated testosterone level, suppressed thyrotropin level,

AUTHOR DISCLOSURE Drs Jain and Karaviti have disclosed no financial relationships relevant to this article. This commentary does not contain a discussion of an unapproved/investigative use of a commercial product/device.

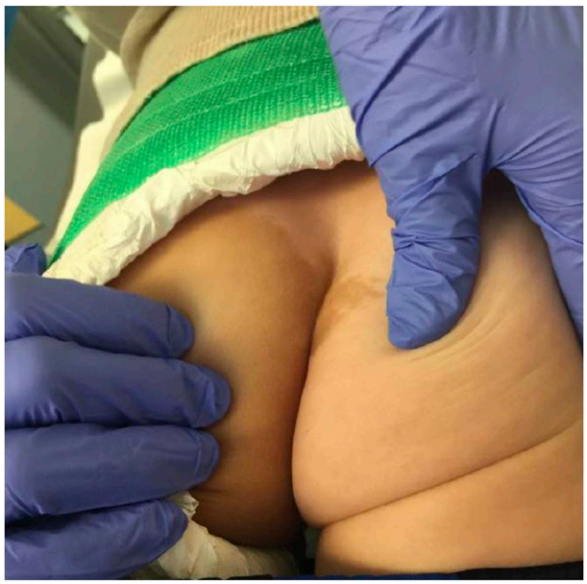

Figure 1. A large, flat, hyperpigmented macular lesion with jagged borders spans the lower back and buttocks.

elevated free thyroid hormone level for his age, and ultrasonographic evidence of Leydig cell hyperplasia. The combination of dermatologic and radiographic findings with evidence of endocrine system hyperfunctionality (testes and thyroid gland) support a diagnosis of McCune-Albright syndrome (MAS).

DISCUSSION

Although congenital dermal melanocytosis, formerly known as a Mongolian spot, is frequently found in the sacral-gluteal region, it differs from a café-au-lait spot in that it has a blue-gray pigmentation and typically fades during the first few years of life. (1) Congenital dermal melanocytosis is also flat and has indefinite borders. Café-au-lait spots seen in MAS can also be confused with those seen in neurofibromatosis (NF), although differences in shape and location can help clinicians distinguish between the 2 conditions. (2) Café-au-lait spots of MAS have jagged borders, similar to the coast of Maine, and generally do not cross the midline, unlike the case presented. In contrast, the spots in NF cross the midline and are smooth, similar to the coast of California. PFD may be an isolated finding or may accompany MAS, which is associated with a spectrum of clinical features. Skeletal findings in NF are uncommon; however, when apparent, they can result in pseudoarthrosis. Malignancy should also be included in the differential diagnosis of bone lesions and pathological fractures.

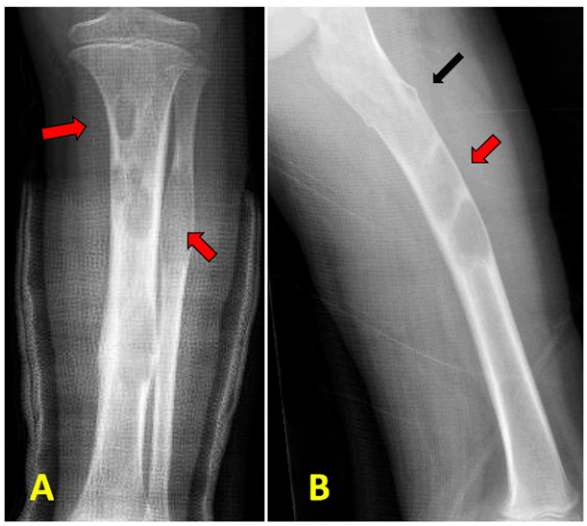

Figure 2. Multiple expansile lucent lesions with cortical thinning (red arrows) are visible throughout the femur, fibula, and tibia (A and B). An acute, nondisplaced pathologic fracture (black arrow) is visible at the proximal femur (B).

MAS is a rare genetic disorder disease, with a predicted prevalence of 1 in 100,000 to 1 in 1,000,000. (2) It is caused by a postzygotic activating mutation of the alpha subunit of the G stimulatory protein that activates adenylyl cyclase. (3) This abnormal G stimulatory protein results in continuous stimulation in tissues with the mutation, which can result in autonomous cell proliferation and/or hyperfunctioning endocrinopathies. (2) A MAS diagnosis can be made clinically when patients present with at least 2 of 3 classical features, ie, polyostic fibrous dysplasia, cafe-au-lait spots, and typical hyperfunctioning endocrinopathies. (2)

Although precocious puberty is a common presenting sign in girls, its incidence in boys is quite low. (4) However, boys have a high prevalence of testicular pathology, predominantly Leydig cell hyperplasia, which can be suggested on testicular ultrasonography by hyperechoic and hypoechoic lesions. (4) Boys are typically referred to urology for long-term observation and serial imaging of testicular lesions; surgery is reserved for those with palpable, invasive, or rapidly enlarging lesions. (4) Café-au-lait spots are often present at birth and are usually the first manifestation of disease. PFD most commonly affects the proximal femur and skull base, and patients with PFD may present with pain, limping, and/or pathological fracture. (5) Several hyperfunctioning endocrinopathies have been described, including peripheral precocious puberty, hyperthyroidism, growth hormone excess, renal phosphate wasting, and Cushing syndrome. (2) Early diagnosis is imperative for detecting and managing disease sequelae. Baseline evaluation may include a nuclear bone scan to delineate PFD

lesions, formal vision and hearing evaluations, testicular ultrasonography in males, laboratory evaluation for precocious puberty, hyperthyroidism, growth hormone excess, renal phosphate wasting/hypophosphatemic rickets, and Cushing syndrome. Management and prognosis depend on the clinical presentation and on the affected tissues. Families should be counseled that MAS is not inherited, and, therefore, patients will not transmit the disease to their own children.

PATIENT COURSE

Our patient underwent closed reduction and spica casting of the left femur by orthopedics. He was referred to our endocrinology clinic and was found to have thyrotropin suppression and an elevated free thyroid hormone level. Thyroid ultrasonography revealed that the right lobe was mostly replaced by nodules, with 2 additional nodules in the left lobe. Thyroid nuclear uptake scan showed asymmetrically decreased uptake in the left thyroid lobe, suggesting that the nodules in the right lobe were hyperfunctioning. The patient's symptoms of hyperactivity and poor appetite were likely secondary to hyperthyroidism; thus, we counseled the family that a definitive diagnosis of ADHD should not be made until his hyperthyroidism is appropriately managed. He will undergo a thyroidectomy for definitive treatment of hyperthyroidism and thyroid nodules in the context of MAS. The boy had a mildly elevated testosterone level for his age and Tanner stage 1 testicles. Testicular ultrasonography revealed patchy hyperechoic foci suggestive of Leydig cell hyperplasia, for which the patient was referred to urology. He underwent formal hearing and vision evaluations, which were normal. He will also undergo a nuclear bone scan to detect any additional lesions of fibrous dysplasia. Notably, the etiology of the patient's chronic bilateral subdural hemorrhages remains unexplained and has no known association with the MAS spectrum.

Summary

- Patients with McCune-Albright syndrome (MAS) often present with 2 of the following: polyostic fibrous dysplasia, cafe-au-lait spots, or hyperfunctioning endocrinopathies. (2)
- Café-au-lait spots, often present at birth, have jagged borders, similar to the coast of Maine, and generally do not cross the midline; in contrast, lesions of neurofibromatosis are smooth, similar to the coast of California, and cross the midline.
- Hyperfunctioning endocrinopathies include precocious puberty, hyperthyroidism, growth hormone excess, renal phosphate wasting, and Cushing syndrome.
- Patients with MAS should undergo a multisystem evaluation and be referred to appropriate specialists in endocrinology, urology, orthopedics, ophthalmology, genetics, and ear, nose, throat/audiology.

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