Secondary aneurysmal bone cyst in McCune-Albright syndrome

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Summary

Polyostotic fibrous dysplasia in combination with café-au-lait macules and hyperfunctioning endocrinopathies consists of a rare clinical condition termed as McCune-Albright syndrome. Aneurysmal bone cysts are tumor-like cystic lesions, composed of blood-filled compartments. They may occur as primary lesions or secondary to other pathologies; most commonly giant cell tumors of bone. However, secondary aneurysmal bone cysts in McCune-Albright syndrome are exceptional.

We present a 28-year-old female with McCune-Albright syndrome. She experienced precocious puberty at age 3 months. In childhood, she experienced multiple long bone fractures, facial deformity and progressive visual and hearing impairment. One year ago, she experienced a painful, gradually enlarging bone lesion involving the right ilium, pubic and ischial bone with ground-glass appearance, septa, marginal sclerosis, endosteal scalloping and blow-out expansion resulting in localized thinning of the cortex. CT-guided needle biopsy of the pelvic lesion showed aneurysmal bone cyst. Selective arterial embolization was recommended, however, the patient and her relatives did not consent to proceed to treatment, and she remained in close surveillance thereafter.

KEY WORDS: fibrous dysplasia; polyostotic; McCune-Albright syndrome; aneurysmal bone cyst; secondary.

Introduction

Fibrous dysplasia (FD) of bone is a rare sporadic congenital disorder that was firstly described by Lichtenstein in 1938. It is a benign condition characterized by abnormal proliferation of fibrous tissue interspersed with normal or immature bone (1). Somatic activating mutations in the cAMP-regulatory protein Gsα, result in osteoblast differentiation deficit, fibrous medullary proliferation and osteoblast hyperactivity. FD may present with monostotic or polyostotic involvement (1). Polyostotic FD combined with cutaneous hyperpigmentation (café-au-lait macules) and hyperfunctioning endocrinopathies (most commonly precocious puberty, hyperthyroidism, acromegaly, and Cushing’s syndrome) is termed as Albright triad or McCune-Albright syndrome (MAS) (1, 2). Aneurysmal bone cyst (ABC) is a benign bone lesion characterized by blood spaces separated by connective tissue septa. ABC is usually a primary lesion; secondary ABC to an underlining condition are rare. The most common entities associated with ABC is giant cell tumor of bone; secondary ABC in FD (3, 4) and MAS (5) is exceptional. This case report presents a female patient with MAS and secondary ABC, and discusses the clinical manifestations and treatment options for this rare entity.

Case report

We present a 28-year-old woman (55 kg weight, 1.40 m height) with café-au-lait macules and a medical history of precocious puberty at age 3 months. At that time, she was treated with testolactone. At age 2.5 years, due to poor response to testolactone she underwent bilateral ovariectomy. Gradually, she developed facial deformity and progressive visual and hearing impairment, due to involvement of the craniofacial region. At age 8 years, she received radioactive iodine (I-131) treatment for hyperthyroidism. At childhood, she experienced multiple long bone fractures, which were mostly re-fractures of both femurs. Currently, at age 28 years, she has hypothyroidism treated with thyroxine, and secondary amenorrhea. Laboratory tests show elevated alkaline phosphatase levels (1662 IU/L; normal range, 40-150 IU/L), normal calcium (9.1 mg/dl) and phosphate (3.1 mg/dl) levels, vitamin D deficiency (14.5 ng/ml; normal range, 20-50 ng/ml), and secondary hyperparathyroidism (PTH, 94.2 pg/ml; normal range, 10-65 pg/ml). Her family medical history is insignificant.

Over the last 1 year, she experienced progressive pain to the right hemipelvis and ipsilateral hip. Radiographs of the pelvis showed a gradually enlarging, expansile lytic lesion involving the right ilium, pubic and ischial bone with ground-glass appearance, septa, marginal sclerosis, endosteal scalloping and blow-out expansion with thinning of the cortex (Figure 1). "Shepherd’s crook" deformity and osteosyntheses of both femurs were evident. Computed tomography (CT)
showed an enlarged trabeculated lesion with fluid-fluid levels (Figure 2). Radiograph of the skull and facial bones showed deformity and a pagetoid pattern including osteolytic lesions and wavy bone sclerosis (Figure 3). CT-guided needle biopsy of the pelvic lesion showed ABC. Selective arterial embolization of the ABC was recommended, however, the patient did not consent to proceed to any treatment, and she remained in close surveillance thereafter.
Discussion

MAS presents a broad phenotype with involvement of any combination of skin, skeleton or endocrine systems. Diagnosis is usually established on clinical grounds, plain radiographs and CT scans (1). GNAS gene testing reveals GNAS activating mutations. Medical history including extraskeletal manifestations is very important. Café-au-lait macules are supposed to be the first manifestation, shortly after birth. Nonetheless, FD lesions usually are not apparent before the first years of life (1, 6). These lesions commonly lead to bone pain and insufficiency fractures (6). Precocious puberty may be the presenting symptom in 80% of girls with MAS (1). Similar manifestations may occur in other entities including monostotic FD, Mazabraud’s syndrome, neurofibromatosis type 1, and Jaffe-Campanacci syndrome. Mazabraud’s syndrome is FD combined with single or multiple soft-tissue myxomas (7). Neurofibromatosis type 1 (von Recklinghausen disease) is an autosomal dominant disorder characterized by multiple peripheral nerve neurofibromas, café-au-lait macules, axillary or inguinal freckling, optic nerve gliomas, iris hamartomas, and bone dysplasia (8). Multiple cafe-au-lait macules and multiple histiocytic fibromas are the prominent features of Jaffe-Campanacci syndrome; however, lesions tend to appear in the metaphysis of long bones (9). Diagnosis of MAS, as in this patient, should be established based on the non-inherited pattern of the disease and the combination of polyostotic FD, café-au-lait macules and hyperfunctioning endocrinopathies (1). Craniofacial bones are involved in 90% of cases, whereas the base of skull in 95% of cases, and the temporal bone in 70% of cases (10). Craniofacial involvement may result in visual and hearing impairment, trigeminal neuralgia, headaches, and epiphora (4). Mechanical stress and repeated fractures result in bowing and deformities of the affected bones, whereas “shepherd’s crook” coxa vara is typical (1).

ABC is a benign, tumor-like bone lesion composed of multiple cystic blood-filled compartments. It occurs more commonly as primary lesions, and rarely as secondary lesions to other entities. Secondary ABC to FD is unusual, whereas secondary ABC to MAS is exceptional (5). FD is thought to be susceptible to bone cyst formation because of the vascularity of the lesion. These cystic lesions can often be filled with an amber fluid that may occasionally be vascular. Radiographically, secondary ABC lesions show an expansile cystic morphology, with a bony shell and fluid or soft tissue center. Fluid-fluid levels are typical but not pathognomonic. In atypical lesions, histological diagnosis is necessary (1-5). Pharmaceutical agents such as bisphosphonates may be administered to inhibit bone resorption in FD, and aromatase inhibitors and tamoxifen citrate may be useful in precocious puberty in MAS (11). Surgical treatment is challenging as there is limited data providing indications or techniques. Therefore, considering that FD lesions in MAS are benign, surgical interventions should be done only when necessary. Asymptomatic lesions may be conservatively followed, if there is no risk for fracture or mass effect. Surgery should be individualized; in general, orthopedic procedures that focus on the prevention or osteosynthesis of fractures and improvement of deformities are considered the mainstay of treatment (1). Similarly, treatment of secondary ABC should be tailored according to the anatomic region involved, extent of lesions, and patients’ needs. As such, there is a wide spectrum of treatment methods for secondary ABC in FD including CT-guided polidocanol sclerotherapy, partial resection of the involved bone, and curettage, local adjuvants, bone grafts and osteosynthesis (12). Above the knee amputation for a secondary ABC in FD of the tibia has also been reported (3, 13). For cranial and skull base secondary ABC in FD, endonasal procedures have been reported (3, 14). Other Authors reported a 14-year-old female with MAS and double secondary ABC in oc-
cipital regions and FD from the skull base to the C2 vertebra with Chiari type 1 malformation treated with complete resection and reconstruction of the calvarial defects with biocompatible cranium grafts (5).

Traditionally, the treatment of choice for ABC included curettage with or without local adjuvants such as acrylic bone cement, argon beam, phenol, or cryotherapy. En bloc resection and radiotherapy are historical therapies that are not recommended because of high morbidity. Current treatment of choice include selective arterial embolization, which may be applied as primary treatment or as adjunct to surgery (15), sclerotherapy that damages the endothelium inducing coagulation cascade and thrombosis, and percutaneous intraluminal doxycyclin administration. Clinical and imaging follow-up is required for persistent or recurrent lesions.

Financial disclosure

All Authors declare that they have no conflicts of interest.

References