

McCune-Albright Syndrome: Report of a Case

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ABSTRACT

A 29- year old female with bone pain and history of precocious puberty was referred for bone scintigraphy. On physical examination café au lait macular spots were noted on her neck, buttocks and left leg. Bone scan showed multiple areas of intense increased activity which was in favour of polyostotic fibrous dysplasia. Considering the presence of polyostotic fibrous dysplasia, precocious puberty and café au lait macular spots, MacCune-Albright syndrome was confirmed in this patient.

Key Words: MacCune-Albright syndrome, Polyostotic fibrous dysplasia, Precocious puberty, Café au lait macular spots

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CASE REPORT

A 29-year-old female with bone pain was referred to nuclear medicine department for bone scintigraphy. She had a history of hyperthyroidism for a few years and spontaneous femoral fracture 6 years previously. Her menarche was at the age of 9. On physical examination café au lait macular spots were noted on her neck, buttocks and left leg (Figure 1).



Figure 1. Café au lait macular spots on neck (A) and left leg (B).

Relevant laboratory data, alkaline phosphatase, growth hormone and insulin growth factor 1 (IGF-1) were 2782, 49.3 and 697; respectively, which were all above the normal level. Radiograph demonstrated an expansile lesion with endosteal scalloping

and thinning of the cortex with a "ground glass" appearance of the intramedullary tissue in the proximal portion of the left tibia (Figure 2).



Figure 2. Radiograph of the left tibia shows an expansile lesion with endosteal scalloping and thinning of the cortex with a "ground glass" appearance of the intramedullary tissue.

Bone scan with Tc -99m methylenediphosphonate (MDP) showed multiple areas of intense increased activity in the skull, mandible, ribs, spine, upper and lower extremities (Figure 3).

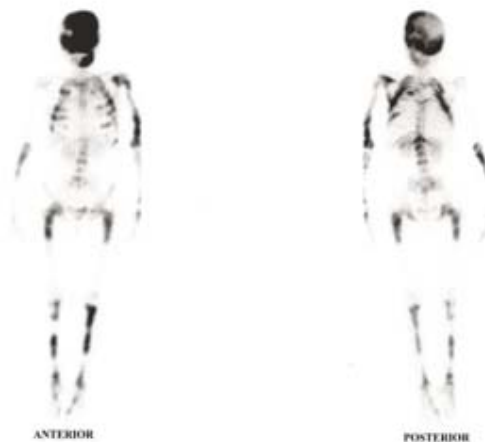


Figure 3. Bone scan with Tc -99m MDP shows multiple areas of intense increased activity in the skull, mandible, ribs, spine, upper and lower extremities.

The scan findings were in favour of polyostotic fibrous dysplasia which was compatible with facial bone biopsy result (fibrous dysplasia, FD). Considering the presence of accompanying findings including precocious puberty and café au lait macular spots, MacCune-Albright syndrome (MAS) was confirmed in this patient. Cranial MRI (T1) image of this patient demonstrated the typical appearance of craniofacial FD, with pressure effect upon the frontotemporal lobes especially on the left side (Figure 4).

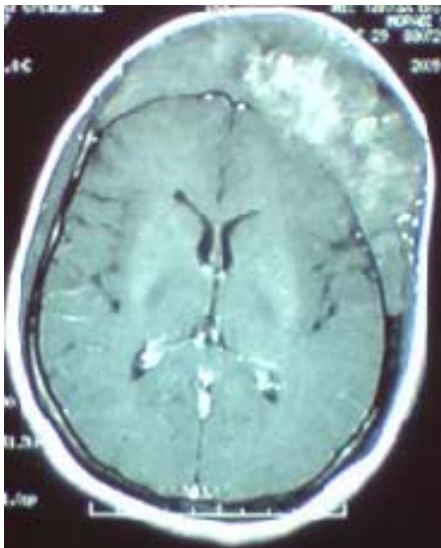


Figure 4. Cranial MRI (T1). Typical appearance of craniofacial FD, with pressure effect upon the frontotemporal lobes, especially on the left side.

DISCUSSION

The MacCune-Albright syndrome is defined by an original triad of polyostotic fibrous dysplasia of bone, *café-au-lait* skin pigmentation, and precocious puberty (PP) (1). It may also be accompanied by other endocrinopathies, including hyperthyroidism (2) and growth hormone (GH) excess (3) (as was the case in our patient). Renal

phosphate wasting with or without rickets/osteomalacia (4) and Cushing syndrome could also be found in association with the original triad (5). Involvement of liver, cardiac, parathyroid, and pancreas might be rarely seen (6). MAS is a rare condition that represents 2% to 3% of the cases of FD (7). FD can be monostotic (MFD) or polyostotic (PFD) (8). Rarely, PP may occur in association with *café-au-lait* skin pigmentation in the absence of FD (about 1% of the cases), but in general, FD is the most common component of MAS. Therefore, a more clinically relevant definition of MAS, broader than the original triad of FD, PP and *café-au-lait* in any possible combination of FD and at least one of the typical hyperfunctioning endocrinopathies and/or *café-au-lait* spots can be seen (8, 9). PP in girls usually appears with vaginal bleeding or spotting, accompanied by development of breast tissue, usually without the development of pubic hair which was also presented in our case. Its appearance in boys can be bilateral (or unilateral) testicular enlargement with penile enlargement, scrotal rugae, body odor, pubic and axillary hair, and precocious sexual behavior. In retrospect, *café-au-lait* spots (Figure 1), which are usually present at birth or shortly thereafter, are the most common but unappreciated "presenting" sign. FD in the long bones usually presents with a limp and/or pain, but occasionally a pathologic fracture may be the presenting sign as in this case. Typical radiographic changes include expansile lesions with endosteal scalloping and thinning of the cortex with the matrix of the intramedullary tissue demonstrating a "ground glass" appearance, as were demonstrated in this case (Figure 2) (9). The weakened osseous structural integrity results in bowing and shepherd's crook deformity of the femur. The expansile multilocular-appearing lesion of the rib may give a soap bubble appearance. FD in the craniofacial bones usually presents as a painless facial-skull

asymmetry, which was seen in our patient (Figure 5), proptosis and cranial nerve deficits might also be seen (7).



Figure 5. Facial-skull asymmetry.

Our patient showed abnormality of femora and skull base which are quite common in this disease. About 90% of the total body skeletal disease burden in FD is usually established by age 15 (10). Hart *et al.* found that lesions in the craniofacial region were established earliest, with 90% of the lesions present by 3.4 years of age. In the extremities, 90% were present by 13.7 yr, and in the axial skeleton, 90% were present by 15.5 yr. It's uncommon in FD that new lesions appear later in life. Most of fractures happen in childhood between the age of 6 and 10 yr, but adulthood fractures also can take place because of intrinsic abnormalities in FD bone (11). Near half of the patients with MAS have renal involvement (9). Malignancies associated with MAS are distinctly uncommon. Malignant transformation of FD lesions occurs in probably less than 1% of the cases of MAS. High dose external beam radiation is a risk factor for sarcomatous transformation (12). Patients who have concomitant GH excess may have a greater tendency for malignant transformation (13). While some have suggested that sarcomatous transformation of skeletal lesions may occur more commonly in patients with Mazabraud's

syndrome (benign intramuscular myxomas in association with long standing FD) (14), this may represent selection bias (9). In addition, the risk of breast cancer may be elevated in patients with MAS (15). Thyroid cancer (16) and testicular cancer are also rare occurrences (9). The disease results from somatic mutations of the *GNAS* gene, specifically mutations in the cAMP regulating protein, Gs alpha. The extent of the disease is determined by the proliferation, migration and survival of the cell in which the mutation spontaneously occurs during embryonic development (9, 17, 18). Diagnosis of MAS is usually clinical. FD often can be diagnosed just with plain radiographs and it can be confirmed by biopsies. To evaluate a patient with MAS we have to know the spectrum of tissues that may be involved, with specific testing for each. Although genetic testing is not routinely available, genetic counseling, however, should be offered. Neurofibromatosis, osteofibrous dysplasia, nonossifying fibromas, idiopathic central precocious puberty, and ovarian neoplasm are in differential diagnoses. Treatment depends on the tissues affected, and the extent to which they are affected. Surgical intervention is recommended in many cases. Bisphosphonates are frequently used in the treatment of FD. To help maintaining the musculature around the FD bone and to minimize the risk for fracture, strengthening exercises are recommended. All endocrinopathies should be treated (9).

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