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MCCUNE ALBRIGHT SYNDROME - ASSOCIATION OF FIBROUS DYSPLASIA, CAFÉ-AU-LAIT SKIN SPOTS AND HYPERTHYROIDISM – CASE REPORT

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Abstract

McCune–Albright syndrome is a rare sporadic disease characterized by bone fibrous dysplasia, café-au-lait skin spots and a variable association of hyperfunctional endocrine disorders. Fibrous dysplasia (FD), which can involve the craniofacial, axial, and appendicular skeleton, may range from an isolated, asymptomatic monostotic lesion to a severe disabling polyostotic disease involving the entire skeleton. A twenty-five-year old male patient presented to our clinic with recently developed heart palpitations. He had also been feeling pain in the right femur since he was younger, without any trauma history, leading to difficulties of ambulation and limping occasionally. His physical examination revealed café-au-lait spots with irregular borders and right testicular agenesis. Laboratory findings identified hyperthyroidism with hyperparathyroidism. Radiographs of the pelvis revealed multiple lytic lesions of the right femur and magnetic resonance imaging (MRI) characterized these lesions as specific to fibrous dysplasia of the bone, without any insufficiency fracture at this level.

The association of café-au-lait skin spots with bone fibrous dysplasia, and hyperthyroidism in this patient suggested the diagnosis of McCune – Albright syndrome.

Keywords: bone fibrous dysplasia, café-au-lait lesions, MRI, hyperthyroidism

Introduction

McCune–Albright syndrome (MAS) is a rare sporadic disease characterized by bone fibrous dysplasia, café-au-lait skin spots and a variable association of hyperfunctional endocrine disorders. The estimated prevalence ranges between 1/100,000 and 1/1,000,000 [1]. Fibrous dysplasia (FD), which can involve any part and combination of the craniofacial, axial, and appendicular skeleton, can range from an isolated, asymptomatic monostotic lesion discovered incidentally to a severe disabling polyostotic disease involving the entire skeleton and leading to progressive scoliosis, facial deformity, and loss of mobility, vision, and hearing. Polyostotic fibrous dysplasia (PFD) is one of the subtypes of fibrous dysplasia, resulted from of an early embryonic postzygotic somatic activating mutation of GNAS (encoding the cAMP pathway-associated G-protein, Gsα), and is characterized by involvement of the skin, skeleton, and endocrine system. This phenotype has the Mendelian Inheritance in Man (MIM) number of 173800 [2]. The proximal femur is often involved associated with Shepherd's deformity, limb shortening, limping and sometimes pathologic fracture [3]. Endocrinopathies include: gonadotropin-independent precocious puberty resulting from recurrent ovarian cysts in girls and autonomous testosterone production in boys; testicular lesions with or without associated gonadotropin-independent precocious puberty; thyroid lesions with or without non-autoimmune hyperthyroidism; growth hormone excess; FGF23-mediated phosphate wasting with or without hypophosphatemia in association with fibrous dysplasia; and neonatal hypercortisolism [4].

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Case-report

A twenty-five-year old male patient presented to our clinic with recently occurring heart palpitations. He reported feeling pain in the right femur from the younger ages, without any trauma history, leading to difficulties with ambulation and limping occasionally. His bone pain occurred in adolescence and progressed into adulthood. The patient was born after a trouble-free pregnancy with a birth weight of 3200 g and a height of 50 cm. He had neonatal jaundice which required phototherapy in the postnatal period. As an infant, the pediatrician suspected him of undescended right testicle for which the patient underwent an exploratory laparotomy at the age of 10 years. None of the commonly ectopic location for undescended testicle was identified.

Physical findings of the patient at presentation were as follows: height: 197 cm, weight: 86 kg and arm span: 200 cm. Cafe-au-lait skin spots with irregular borders, one with diameters of 10x5 cm on the left thigh (Picture 1) and one with diameters of 5x3 cm on the left calf were present (Picture 2). The patient had scoliosis concave to the left. His hearing and vision were normal. He had right testicular agenesis, with a volume of 35 ml of the developed left testicle. His blood pressure was elevated (145/90 mmHg). He had insignificant hypotonia, heart murmur on cardiac auscultation and palpable liver edge 1 cm below the costal margin.

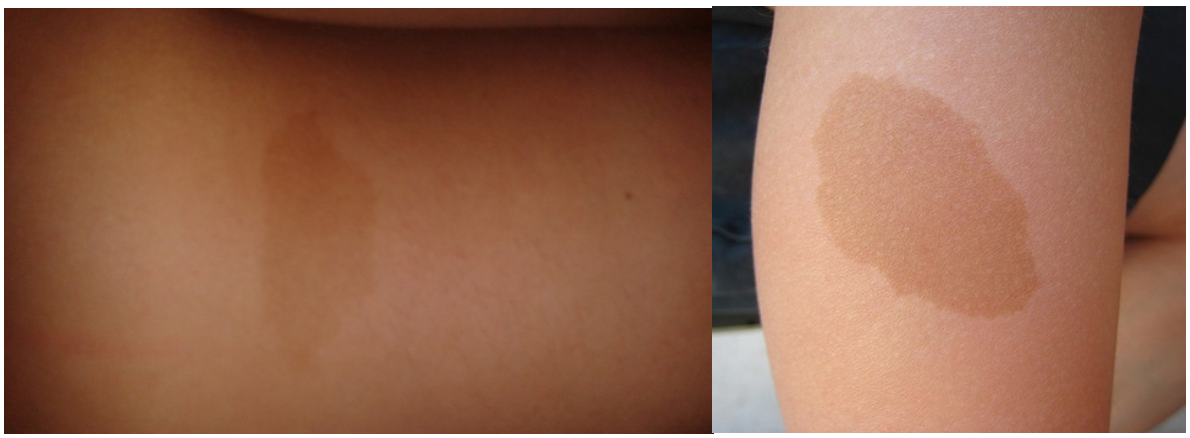
The laboratory findings concerning hormones and electrolytes were as follows: serum prolactin, FSH, LH, cortisol and testosterone with normal values, FT4, PTH, alkaline phosphatase and calcium with elevated serum values, serum phosphate and TSH with decreased value. Hyperthyroidism and hyperparathyroidism were confirmed. Echocardiogram was performed revealing left ventricular hypertrophy, with initial thickness of the interventricular septum. Systemic hypertension (systolic pressures 90 to 145 mmHg, diastolic pressures 55 to 105 mmHg) was confirmed. Primary renal disease was excluded by normal values of plasma renin activity and aldosterone, as well as renal imaging studies. Also his urinary catecholamines were normal.

A pelvis radiograph revealed generalized reduction of bone density at this level, irregular ossification with areas of radiolucency surrounded by sclerosis most evident in his right femur. Also areas of sclerosis of the ilium adjacent to the sacroiliac (SI) joints were found on this X-ray (Image 1). On the right hip-joint X-ray the proximal femur shows a diffusely abnormal irregular trabecular pattern with areas of decreased and increased osseous density and ground-glass opacity (Image 2, 3).

Differential diagnosis of the lesions described should be made with multiple lytic metastases, giant aneurysmal cyst, giant cell tumors of the bone, neurofibromatosis type I, osteofibrous dysplasia, Mazabraud syndrome.

An MRI was performed for a better evaluation of the lesions identified on radiographs. There are some useful but not specific findings for differentiating fibrous dysplasia from other entities, even though there is marked variability in the appearance of the bone lesions, and they can often resemble a tumor [5]. On T1-weighted images there is heterogeneous signal, usually intermediate and high on STIR (Image 4); on T2-weighted images the signal is heterogeneous, usually low, but may have regions of higher signal; on T1 with contrast it can be heterogeneous contrast enhancement (Images 5,6,7).

Until this moment the diagnosis was hyperthyroidism with secondary systemic hypertension, fibrous dysplasia of the right sacrum, ilium and femur, secondary osteitis condensans ilii, cafe-au-lait skin spots and right testicular agenesis. All these entities associated, except testicular agenesis, suggest a diagnosis of McCune Albright syndrome that could be confirmed by genetic analysis.



Picture 1 and 2. Cafe-au-lait skin spots identified on the left thigh with diameters of 10x5 cm and on the left calf with diameters of 5x3 cm.

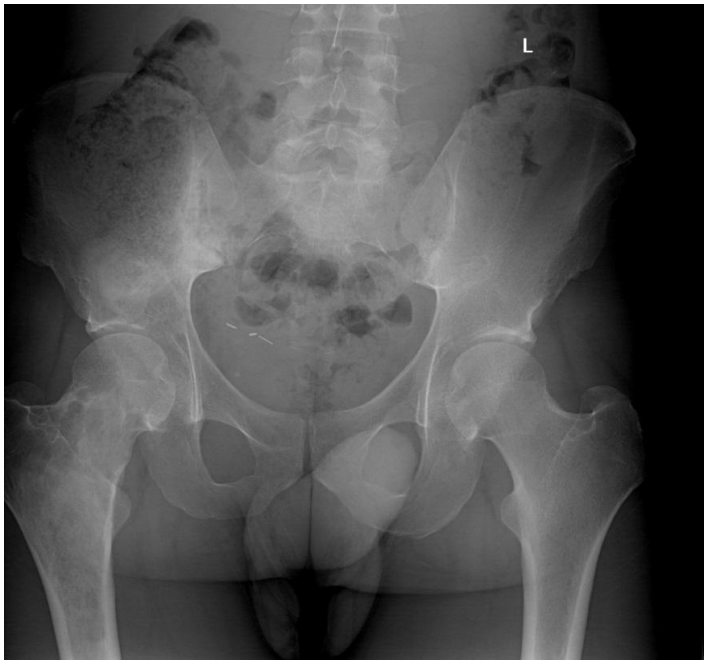


Image 1. Pelvis radiograph shows lesions which cause moderate cortical thinning with endosteal irregularity. There is no associated periosteal reaction or soft-tissue mass. Similar lesions are present within the right ilium in the supra-acetabular region. The right femoral neck demonstrates a focal expansive lytic lesion with important cortical thinning. Sclerosis of the ilium adjacent to the sacroiliac (SI) joints is also identified.

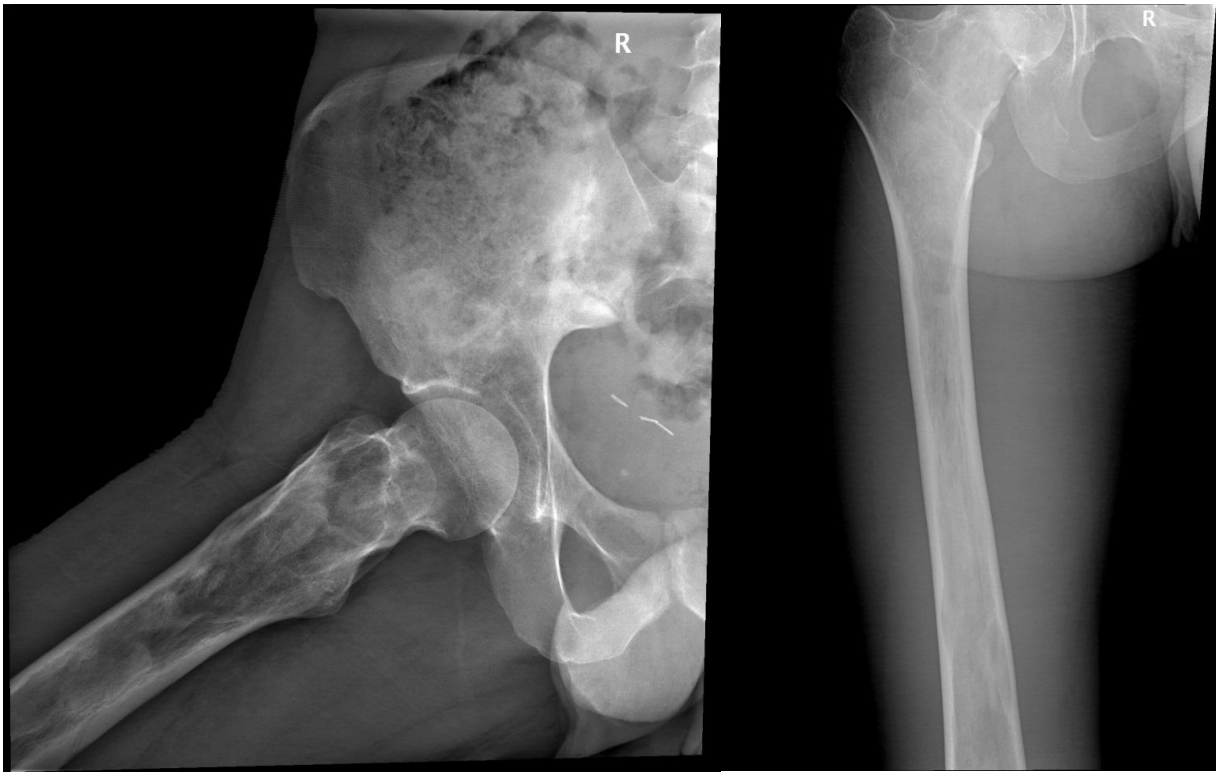


Image 2 and 3. Image 2 represents the femur radiograph in frog leg view, Image 3 represents the femur radiograph in anteroposterior view. In both of them, the cortex along the inferior margin of the right femoral is definitively intact, with multiple well-circumscribed lytic lesions and no periosteal reaction.

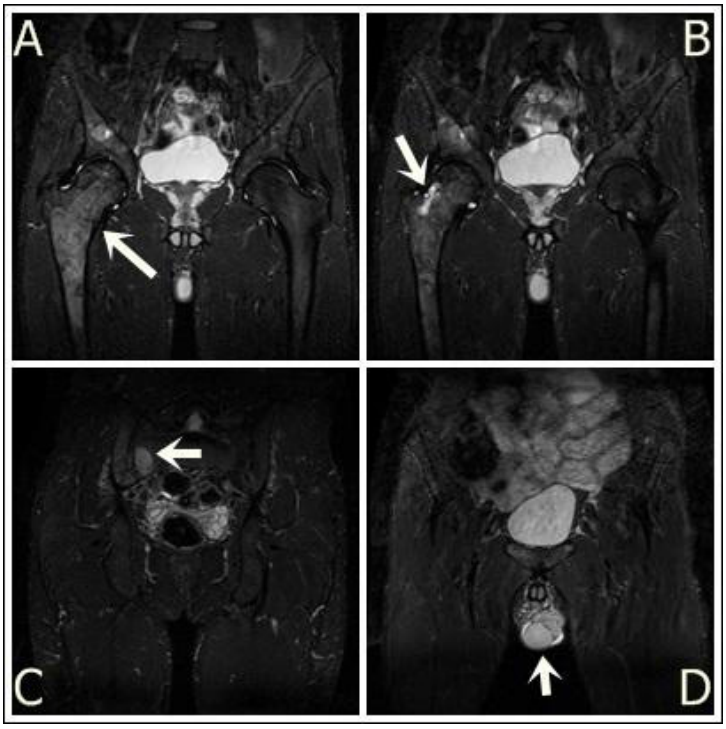


Image 4. Coronal MRI of the pelvis, STIR sequence. There is diffuse intraosseous abnormality characterized by heterogeneously increased signal (frame A,B,C - arrows) involving the right iliac bone, sacrum adjacent to SI joints, anterior acetabulum, femoral head, neck, metaphysis and diaphysis. The cortex is thinned throughout most of the right femur, with several regions of important cortical thinning. Frame D (arrow) is showing right incidental testicular agenesis found on this MRI, confirming the clinical finding at genital organs examination. A large area of cystic degeneration with fluid-fluid levels (Frame B) is present within the right femoral neck. The cortex surrounding this area is severely thinned. However, no displaced fracture is noted at this site.

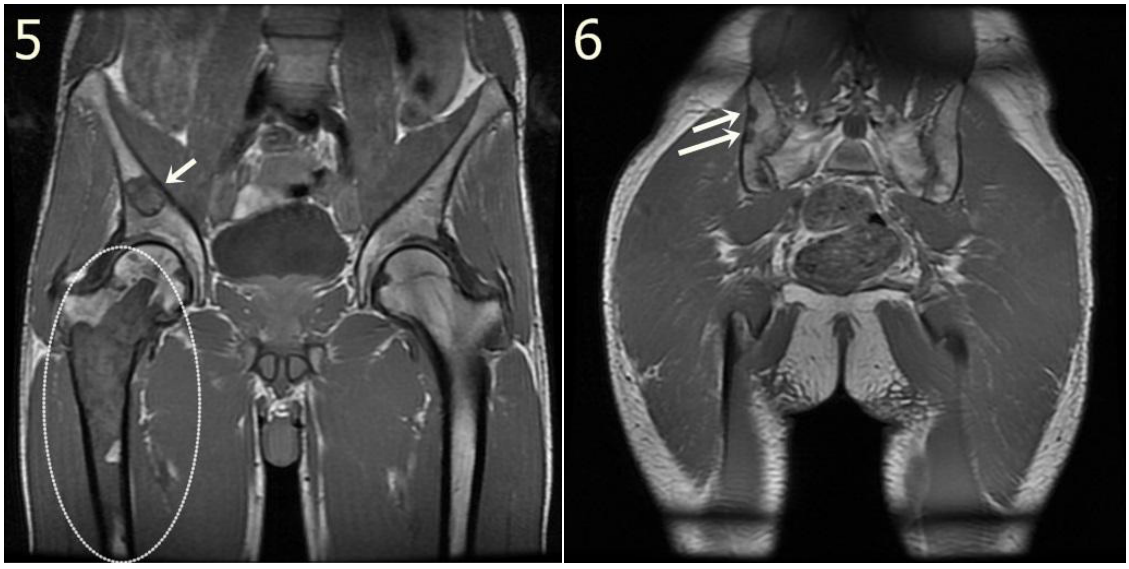


Image 5. Coronal MRI of the pelvis, T1-weighted image. The intraosseous abnormality characterized by intermediate to low signal on T1 involving the right femur (dotted circle) and the right ilium (arrow) represents the fibrous dysplasia lesions of the involved bones.

Image 6. Coronal MRI of the pelvis, T1-weighted image. There are two small rounded lesions (arrows) on the sacrum adjacent to the right SI joint with the same signal as those seen in image 5.

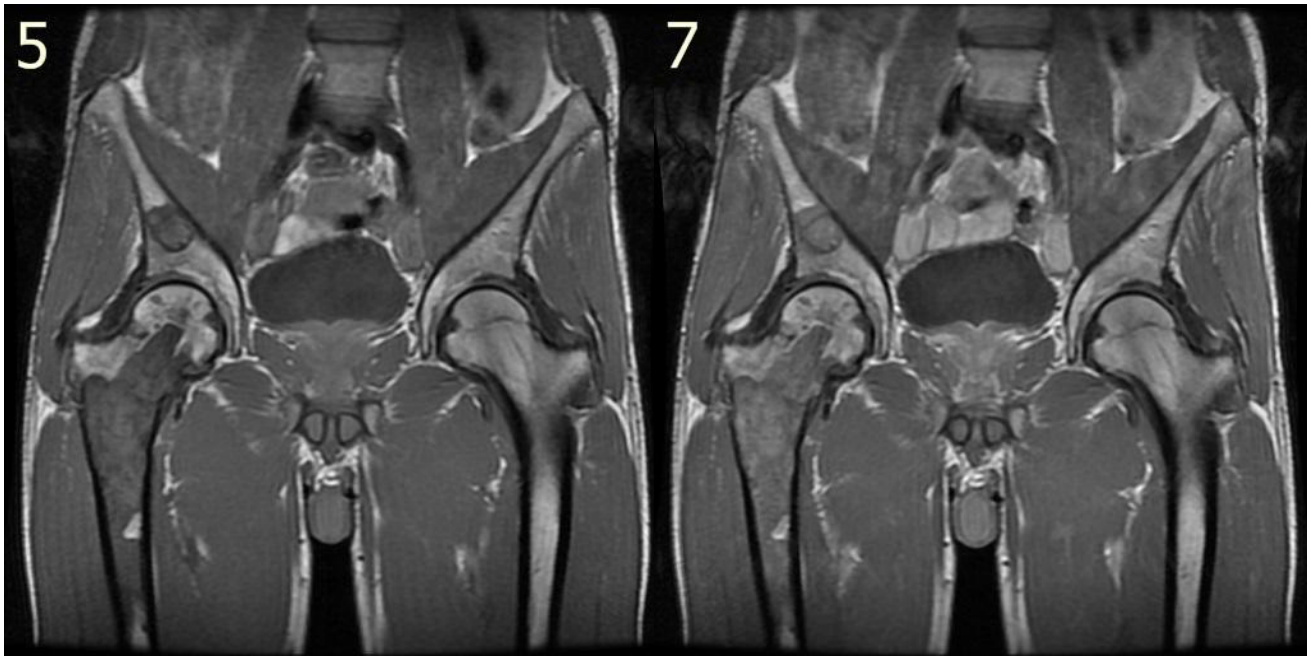


Image 7. Coronal MRI of the pelvis, T1-weighted image with contrast. The diffuse intraosseous lesions present at the right femur and right ilium show minimal contrast enhancement compared with the aspect of these lesions in Image 5.

Discussion

Due to the variability of appearance of fibrous dysplasia the potential differential diagnosis is really complex, but is significantly influenced by the dominant pattern. Giving the clinical presentation of our patient and the laboratory and MRI findings a differential diagnosis should be made with:

Neurofibromatosis type I (NF1) and FD/MAS have several common features, including café-au-lait skin spots and skeletal abnormalities. Skin findings in NF1 include six or more café-au-lait macules, which are generally smooth-bordered as opposed to the irregularly-bordered lesions seen in FD/MAS. Skeletal features of NF1 include kyphoscoliosis, sphenoid dysplasia, cortical thinning of long bones, and dysplasia of the tibia which may result in pseudarthrosis. Distinct features of NF1 include tumors of the nervous system such as neurofibromas and optic gliomas, pigmented iris hamartomas, and axillary freckling [6].

Giant cell tumors of the bone are acquired lesions which have similar histopathological features to fibrous dysplasia, including proliferation of bone marrow stromal cells and the presence of multiple multinucleated giant cells. Giant cell tumors are typically benign, but may result in localized bone destruction [4].

The MRI aspect of bone metastases in T1-weighted images is similar to fibrous dysplasia lesion but after contrast administration there is important enhancement of contrast in case of bone metastases. Furthermore the bone edema, periosteal reaction and soft-tissue mass is usually identified in oncologic patients with bone metastases [7].

Osteitis condensans ilii is represented by the sclerosis of the ilium adjacent to the sacroiliac (SI) joints and develop secondary to antalgic position for protecting the painful femur. The main differential diagnosis is sacroiliitis, but in osteitis condensans ilii the SI joints are normal with no irregularity, erosions or loss of joint space (Image 6). This pathology usually appears in women after multiple births [8].

After the initial diagnosis, all individuals with FD/MAS should be evaluated to determine the extent of disease. Our patient developed systemic hypertension based on chronic hyperthyroidism. He also had chronic osteoporosis determined by hyperparathyroidism, which in addition to fibrous dysplasia of the right femur increases the possibility of insufficiency fractures at any moment. Moreover, to avoid these complications and because there are no available medical therapies capable of altering the disease course in fibrous dysplasia, current management is focused on optimizing function and minimizing morbidity related to fractures and deformity. According to treatment guidelines, hormonal medication and bisphosphonates should be chronically administered [9].

References

1. Lourenço R, Dias P, Gouveia R, Sousa AB and Oliveira G. Neonatal McCune–Albright syndrome with systemic involvement: a case report. J Med Case Rep. 2015 Sep 4;9:189. DOI 10.1186/s13256-015-0689-2

2. McKusick VA. McCune-Albright syndrome; MAS. Mendelian Inheritance in Man [Internet]. USA. Available from: http://www.omim.org/entry/174800
3. Chen F, Wei Y, Xia J, Wu J, Wang S, Huang G, et al. Case Report: Double-level osteotomy and one-stage reconstruction with long intramedullary femoral nail to correct a severe proximal and diaphyseal femur deformity in a patient with polyostotic fibrous dysplasia: case report and literatures review. Int J Clin Exp Med. 2015;8(8):14188-14195.
4. Boyce AM, Collins MT. Fibrous Dysplasia/McCune-Albright Syndrome. In: Pagon RA, Adam MP, Ardinger HH, et al., eds GeneReviews®(2015) . Seattle (WA): University of Washington, Seattle; 1993-2016.
5. Chong VF, Khoo JB, Fan YF. Fibrous dysplasia involving the base of the skull. Am J Roentgenol. 2002;178(3):717-720.
6. Raus I, Coroiu RE, Capusan CS. Neuroimaging in pediatric phakomatoses. An educational review. Clujul Med. 2016;89(1):56-64.
7. Nakanishi K, Kobayashi M, Nakaguchi K, Kyakuno M, Hashimoto N, Onishi H, et al. Whole-body MRI for detecting metastatic bone tumor: diagnostic value of diffusion-weighted images. Magn Reson Med Sci. 2007;6(3):147-155.
8. Cidem M, Capkin E, Karkucak M, Karaca A. Osteitis condensans ilii in differential diagnosis of patients with chronic low back pain: a review of the literature. Mod Rheumatol. 2012;22(3):467-469.
9. Boyce AM, Kelly MH, Brillante BA, Kushner H, Wientroub S, Riminucci M, et al. A randomized, double blind, placebo-controlled trial of alendronate treatment for fibrous dysplasia of bone. J Clin Endocrinol Metab. 2014;99(11):4133-4140.