

A rare cause of acromegaly: McCune-Albright syndrome

Akromegalinin nadir bir nedeni: McCune-Albright sendromu

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ABSTRACT

McCune-Albright syndrome is characterized by polyostotic fibrous dysplasia, brown spots on the skin (café au lait pigmentation) and autonomous endocrine hyperfunction. Early puberty and other endocrinological manifestations, such as acromegaly, gigantism and hypercortisolism are widely observed in the syndrome. Acromegaly is seen in 20% of patients. We report a case of acromegaly accompanied with this syndrome.

Key words: McCune-Albright syndrome; acromegaly; fibrous dysplasia

ÖZET

McCune-Albright sendromu, polioyotik fibröz displazi, deride kahverenginde lekelenme (Cafe au lait lekeleri) ve otonomik endokrin hiperfonksiyon ile karakterize bir sendromdur. Bu sendromda yaygın olarak erken puberte ve diğer endokrinolojik manifestasyonlar örneğin akromegali, jigantizm, hiperkortizolizm görülebilir. Akromegali Mc-Cune-Albriht sendromlu hastaların % 20 sinde görülebilir. Biz bu sendroma eşlik eden bir akromegali vakasını sunduk

Anahtar kelimeler: McCune-Albright sendromu, fibröz displazi, akromegali

INTRODUCTION

McCune-Albright syndrome (MAS) is defined as one or more endocrinopathies accompanied by fibrous dysplastic bone lesions, irregular 'café au lait' skin lesions and any hyper functioning endocrine tumors. Endocrine hyperfunction is independent of the hypothalamic-pituitary axis [1]. Polyostotic fibrous dysplasia is seen in patients who diagnosed with MAS. Fibrous tissue gradually replaces normal bone tissue in these patients. This condition may cause gait impairment, deformity and fractures, particularly in body weight-bearing bone such as the lower extremities. When the skull and jaw bone are affected, unexpected deformities may be seen. Precocious puberty is a common finding in female children. A mutation has been determined in the G protein alpha (Ga) substructure in MAS [2]. Ga is normally responsible for cyclic adenosine mono-

phosphate (cAMP) activation. Increased spontaneous activation of Ga frequently leads to cAMP activation. Autonomously elevated cAMP activation is responsible for endocrine hyperfunctions [2]. Laboratory findings include suppressed gonadotropins, increased estradiol and bone age exceeding chronological age. Other endocrinopathies accompanying with MAS are hyperthyroidism, hypercortisolism, hyperprolactinemia and acromegaly. Acromegaly is seen in approximately 20% of patients with MAS [3]. Excess growth hormone (GH) has been shown to be associated with loss of vision and hearing and with macrocephaly in patients with MAS [3]. Additionally, excess GH can exacerbate craniofacial disease [3-5]. GH and IGF-1 must be investigated in the presence of clinical suspicion of MAS, and the oral glucose suppression test should be performed when necessary. Treatment options are medical, surgical and radiotherapy. Surgical treatment is diffi-

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cult because of fibrous thickening of the skull floor. Effective medical treatment options are; long-acting somatostatin analogues [3,6] and the GH receptor antagonist [7,8]. We present a case of acromegaly accompanied with MAS, who treated with somatostatin analogues.

CASE REPORT

A 20-year-old woman was diagnosed with MAS during tests due to vaginal bleeding at the age of 2.5 years. At the age of 5 she developed difficulty walking, painful bones and swelling. She had been operated due to femur fracture 3 years ago, and a metal fixator had been inserted. The pathology was reported as fibrous dysplasia. She admitted to our clinic due to growth in the hands, feet and jaw in recent months. Difficulty walking, a coarse facial structure, prognathism and facial asymmetry were present. Café au lait skin lesions with irregular margins were present in the right half of the back, in the sacral region and on the right thigh (Figure 1). Weight was 69 kg and height 172 cm. Laboratory analysis revealed that, plasma glucose was 70 mg/dl, and kidney, liver and thyroid function tests were within normal limits. GH level was 19.3 ng/mL (0-8) and IGF 1 was 712 ng/mL (127-424). The lowest GH value at the 30th min after the 75 gram oral glucose tolerance test was 11.5 ng/mL. Acromegaly was diagnosed. Pituitary MR imaging was not available since the metal fixator was attached. Pituitary tomography was therefore performed, and dense lytic, sclerotic expansive lesions were determined in the skull base and cranial bones (Figure 2). Partial erosion was observed in the floor of the sella turcica. The pituitary was visualized within the sella turcica, and no findings in favor of adenoma were determined. Since the lesion was not localized and due to widespread bone involvement in the cranium and sphenoid sinus, surgical treatment was not planned. Lanreotide therapy was started at 90 mg once every 4 weeks. After 3 months, GH was 9.3 ng/mL and IGF-1: 488 ng/mL and therefore lanreotide was increased to 120 mg. At 6th-month follow up with this regimen GH had decreased to 6.2 ng/ml and IGF 1 to 420 ng/mL. The patient is still under monitoring by our clinic, and growth in the hands and feet has stopped.



Figure 1. Café au lait skin lesions with irregular margins in the left half of the back



Figure 2. Pituitary computed tomography shows; dense lytic, sclerotic expansive lesions in the skull base and cranial bones

DISCUSSION

MAS is a rare disease, characterized by the fibrous dysplasia, “café au lait” pigmentation and precocious puberty triad. The syndrome was first described by McCune in 1936 and shortly after redefined by Albright et al. [9]. Estimated prevalence varies between 1/100.000 and 1/1.000.000. Café au lait spots can be differentiated from those in neurofibromatosis by greater irregularity in the margins. Spots are generally on the same side of bone lesions. Precocious puberty is seen commonly in MAS. Multiple endocrine abnormalities includ-

ing hyperthyroidism, hypercortisolism, acromegaly and hyperprolactinemia can also be seen. Hyperthyroidism and acromegaly are the most common endocrine abnormalities in adults. There may be an increase in growth and hormone secretion in the endocrine glands in MAS even in the absence of stimulator hormones. Precocious puberty occurs without excess secretion of gonadotropin. Our patient entered menarche at the age of 2.5 years. The case was considered in terms of endocrine abnormalities other than acromegaly, and no other endocrinopathy was determined. Recently an analysis of 112 cases of acromegaly in combination with MAS was published. Mean age at diagnosis was 24.4 years (3-64). Sixty-five patients were male and 47 were female. Precocious puberty was present in 57% of patients [10]. MRI is superior than CT at pituitary imaging. However, MRI was not available in our case, due to femoral prosthesis. No adenoma was determined at pituitary CT in our case. In the literature, adenoma was determined using CT or MRI in only 54% of cases of acromegaly with MAS, and macroadenoma was determined in more than 2/3 of these patients [10]. The trans-sphenoidal approach is the preferred technique in pituitary surgery, although it is generally impossible due to thickening of the skull floor. The transfrontal approach is also difficult in these patients. Medical treatment is therefore frequently being used [11]. Salenave et al. reported in their review that pituitary surgery was possible in only 25 out of 112 patients, and it is very rarely reported to be curative. Somatostatin analogues improved GH and IGF 1 levels in most cases, although remission was only achieved in 30% of patients. Pegvisomant therapy was employed in 13 patients, and IGF 1 normalization was achieved in 10 [12]. Our patient was treated with 120 mg octreotide but had still not entered into remission after 3 months of treatment.

The GH receptor blocker pegvisomant is also used in patients who do not respond to somatostatin analogues. Radiotherapy is an option when surgery is not possible and medical treatment is insufficient [12,13]. This case is presented because of the rare nature of MAS and accompanying with acromegaly and treatment of acromegaly may differ from standard treatment.

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