

# A Rare Cause of Acromegaly: Short Review of McCune Albright Syndrome

## *Akromegalinin Nadir Bir Sebebi: McCune Albright Sendromu İçin Kısa Literatür Özeti*

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### Abstract

McCune-Albright syndrome (MAS) is characterized by a triad of poly/monostotic fibrous dysplasia, café-au-lait macules, and hyperfunctioning endocrinopathies, including growth hormone (GH) excess. Acromegaly, as a manifestation of endocrine hyperfunction with MAS is uncommon. We report a 34-year-old man with MAS and acromegaly, in whom surgical removal of the pituitary tumour has been technically difficult because of bone deformities. A combination of a long-acting somatostatin analogue (Sandostatin LAR) and external irradiation were therefore used as treatment. Acromegaly associated with MAS is very rarely seen, and has been the subject of approximately 70 published reports. We present a case of acromegaly associated with MAS and a brief survey of relevant literature. *Turk Jem 2009; 13: 13-5*

**Key words:** McCune-Albright syndrome, acromegaly

### Özet

McCune-Albright syndrome (MAS) poli/monoositik fibroz displazi, 'Café au lait' lekeleri, büyüme hormonu (BH) fazlalığı gibi hiperfonsiyone bir endokrinopati ile karakterize çok nadir izlenen bir klinik durumdur. Akromegali MAS ile birlikte çok nadir olarak ortaya çıkmaktadır. Literatürde akromegali ve MAS birlikteliği ile ilgili yaklaşık 70 vaka bildirilmiştir. Hipofiz cerrahisi için kemik deformitelerine bağlı teknik zorlukları olan 34 yaşında MAS ve akromegali birlikteliği olan hastayı sunuyoruz. Hastaya eksternal radyoterapi ve uzun etkili somatostatin analogu tedavisi uygulanmış. Bu vaka aracılığıyla akromegali ve MAS birlikteliği ile ilgili literatür gözden geçirilmiştir. *Turk Jem 2009; 13: 13-5*

**Anahtar kelimeler:** McCune-Albright sendromu, akromegali

### Introduction

The original description of McCune-Albright syndrome (MAS) included diffuse fibrous dysplasia, café-au-lait macules, and precocious puberty (1,2). More recent studies report that polyostotic fibrous dysplasia and café-au-lait macules are invariably present, while monostotic lesions are less common (3). Forms of endocrine hyperfunction reported in association with MAS include precocious puberty, hyperthyroidism, hypercortisolism, hypersomatotropism, and hypophosphatemic rickets (1-3). Hypersomatotropism associated with MAS is rare, and pituitary adenoma is demonstrable in 40% to 50% of these patients (3,4).

Prior to 2002, 51 cases of MAS with acromegaly were reported in English literature (3-5). Since that time, there have been 21

publications regarding MAS in association with acromegaly. Because of the paucity of published information about this association, we report a case of MAS associated with pituitary macroadenoma, resulting in acromegaly.

### Case Report

A 34-year-old man with a 20-year history of McCune Albright syndrome presented to the endocrinology department because of increasing multiple hard swellings over his legs and difficulty walking. He had a history of pathologic fractures of the humerus, femur, tibia, and fibula between 4 and 18 years of age. The diagnosis of polyostotic fibrous dysplasia had been established by radiologic and physical examinations.

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On examination, there were numerous lumps, on the extremities and one on the right side of his forehead. Brown pigmented macules with irregular borders were present on his back and sides. He had facial asymmetry with coarse features and acral enlargement with excessive sweating. He had difficulty walking and was able to walk only with the aid of a crutch. He had no history of precocious puberty.

When he was 18 years of age, he was diagnosed with a pituitary microadenoma causing acromegaly (acral enlargement, coarse and asymmetrical facial features). The pituitary microadenoma was diagnosed by a combination of abnormal hormone levels (growth hormone [GH]: 81.13 ng/mL [0.06-1] and insulin-like growth factor-1 [IGF-1]: 1280 ng/mL [182-680]) and by pituitary magnetic resonance imaging (MRI) (3 cmx1.4 cm pituitary tumor). Pituitary surgery was not performed because of extensive skull involvement caused by the fibrous dysplasia. In our investigation, biochemical values and complete blood count (CBC) were in the normal levels. Radiographs of skull showed radiodense lesions in frontoparietal bone and base of the skull. Pituitary MRI revealed a pituitary microadenoma (30x14 mm) with suprasellar extension and ground-glass appearance (Fig. 1).

After an external irradiation treatment, long-acting octreotide (Sandostatin LAR 30 mg per 28 day) was started in 2002. He received this therapy for approximately 7 years, and his last IGF-1 level while taking this medication was 330 ng/mL (100-494); during glucose-GH suppression test, GH was suppressed to 10.3 ng/mL (0.06-1). Other hormonal results of patient were in table 1 on admission to hospital. Despite receiving the maximum recommended dose

(40 mg) of octreotide LAR for 7 years, we could not achieve ideal metabolic control, so we changed the treatment regimen to 120 mg lanreotide per monthly with cabergoline 0.5 mg twice weekly. After 6 months of this treatment, IGF-1 level was 280 ng/mL and morning GH level was 5.8 ng/mL. GH was suppressed to 3.7 ng/mL during GH-glucose suppression test. These levels represented an improvement from those seen during his previous treatment regimen.

## Discussion

MAS is a rare syndrome, diagnosed by the presence of at least two of three following lesions: poly/monostotic fibrous dysplasia, cutaneous pigmented macules, and hypersecretory endocrinopathies (1,2). Our patient has had polystotic fibrous dysplasia (skull, maxilla, long bones), café-au-lait macules, and hypersecretory endocrinopathy (acromegaly). In our review of the literature, eight of the reported patients had café-au-lait macules, only four of them had monostotic lesions. Fibrodysplasia at the base of the skull is seen in almost all patients with MAS, as is our patient. The course of dysplastic bone disease is independent of time of onset and degree of disease activity (3). Our patient's difficulty walking resulted in inability to perform his daily activities. Chanson et al. reported that in patients with MAS and acromegaly, 34% had precocious puberty, 11% had thyrotoxicosis, and 3% had hypercortisolism (3). No endocrine organ except acromegaly was involved in our patient. Only one patient has been reported to have MAS with acromegaly and hyperthyroidism caused by somatotrophic adenoma (6). GH hypersecretion in MAS differs in several aspects from that observed in classical acromegaly.

MAS patients are generally young (<20 years; our patient was 18 years old) at the onset and diagnosed on the basis of growth acceleration rather than facial dysmorphism (often difficult to assess, as in our patient, because of fibrous dysplasia) (3,4). Only half the patients with acromegaly associated with MAS exhibit radiological evidence of pituitary adenoma, compared with 80% to 90% in classical acromegaly (4). Our patient had a sellar mass with suprasellar extension; this was reported in 3 of 17 (17%) patients in the series of Cuttler et al. (7) and 4 of 12 (33%) 12 in the report of Akintoye et al. (5).

Pituitary surgery in this syndrome is difficult because of problems related to fibrous dysplasia and the resultant thickening of bones (3,4,8,9). Occasional instances of sarcomatous transformation of fibrous dysplastic bones have been reported with radiation therapy (10,11), but radiotherapy may be an option for treatment of acromegaly in patients who have MAS when surgery is impossible and somatostatin analog therapy is ineffective (12). Although no sarcomatous transformation was found within the radiation field in our patient, this risk must be considered. Bromocriptine, cabergoline, and long-acting somatostatin analogs have been used with some success in acromegaly associated with MAS (3,4,9). Our patient received external irradiation treatment and long-acting octreotide therapy (Sandostatin LAR). With this treatment, serum growth hormone and serum IGF-1 levels decreased markedly but not to normal range.

GH excess affects approximately 20% of the patients with MAS, which is caused by sporadic, postzygotic, activating mutations in the GNAS gene that codes for the cAMP-regulating protein, G(s) alpha (gsp oncogene). Akintoye et al. examined efficacy of

Table 1. Hormonal status of patient at the time of admission to hospital

	Patient's results	Normal range
Growth hormone (ng/mL)	9.93	0.06-1
Prolactin (ng/mL)	16.4	2.5-18.1
TSH ( $\mu$ IU/mL)	1.09	0.35-4.2
sT4 (ng/dL)	0.85	0.7-1.48
IGF-1 (insulin-like growth factor-1) (ng/mL)	330	100-494
Cortisol ( $\mu$ g/dL)	12.9	8.7-22.4
25-OH vitamin D (mmol/L)	11.4	10-60

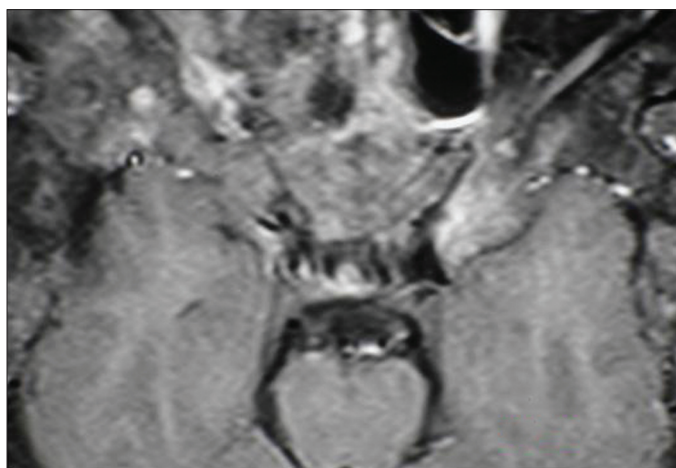


Figure 1. Pituitary MRI of the patient

the GH receptor antagonist pegvisomant, to control gsp oncogene-mediated GH excess and skeletal disease (fibrous dysplasia of bone) associated with MAS. Pegvisomant effectively reduces IGF-1 and IGFBP-3 levels in gsp-mediated GH excess but has no effect on fibrous dysplasia. In severely affected patients, pegvisomant therapy may thus be useful to normalize IGF-1 levels rapidly (12,13). We did not use pegvisomant in our patient, because pegvisomant effectively reduced IGF-1 levels but had no effect on fibrous dysplasia.

As conclusion, we presented this case due to multiple bone involvement of fibrous dysplasia accompanying with acromegaly alone as an endocrinopathy. These severe bone deformities affected the social life of our patient. Although the treatment choice of a large pituitary mass is surgery, surgeons chose not to operate because of the bony involvement of the skull. Nonsurgical treatment choices are somatostatin analogs, radiotherapy, and cabergoline at maximum doses.

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