Endoscopic Decompression for Optic Neuropathy in McCune-Albright Syndrome

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McCune-Albright syndrome (MAS) is characterized by a triad of poly/monostotic fibrous dysplasia, café-au-lait macules and hyperfunctioning endocrinopathies including human growth hormone excess. Acromegaly as a manifestation of endocrine hyperfunction with MAS is uncommon. Surgical excision may be challenging due to the associated severe fibrous dysplasia of the skull base. Through the endoscopic procedures, we treated a case of MAS presenting with compressive optic neuropathy due to fibrous dysplasia and acromegaly caused by growth hormone secreting pituitary adenoma. We reviewed the literature on GH excess in MAS to highlight its surgical and medical challenges.

Key Words: Fibrous dysplasia · McCune-Albright syndrome · Acromegaly.

INTRODUCTION

McCune-Albright syndrome (MAS) is a rare and sporadic disease characterized by a triad of poly/monostotic fibrous dysplasia, café-au-lait macules and hyperfunctioning endocrinopathies\(^1\)\(^-\)\(^8\). The presence of two of the above features is sufficient to make the diagnosis. Polyostotic bone lesions and café-au-lait macules are common, while monostotic bone lesions are rare\(^9\). Endocrinopathies include sexual precocity (most commonly), hyperthyroidism, hypercortisolism, growth hormone (GH) excess and hyperprolactinemia\(^8\).

Approximately 20% of MAS patients have GH excess, which is due to a pituitary adenoma in about one-third of patients. The remaining patients have pituitary hyperplasia of GH and prolactin (PRL) secreting cells\(^3\). Relatively few adenomas from MAS patients have been studied in detail.

The presence of massive, skull-based fibrous dysplasia in some MAS patients with hypersecretory pituitary diseases often precludes the standard transsphenoidal or subfrontal approach to pituitary adenoma resection. Only a few studies have reported successful transsphenoidal approach (TSA) neurosurgical procedure and resection. Thus, this condition presents a significant therapeutic challenge for even the most experienced clinicians\(^3\)\(^-\)\(^5\).

In this case report, we report our surgical, endocrinological experience with a MAS patient with acromegaly who has been followed 3 years and adequately managed by decompression of optic nerve and near-total transsphenoidal resection.

CASE REPORT

First clinical manifestation

A 19-year-old man first visited our medical center when he was 16-years-old because of intermittent headache, dizziness and left eye visual disturbance. He had been assessed using magnetic resonance image (MRI) and electroencephalography (EEG) for these symptoms at a regional hospital. There was no abnormal finding in EEG but MR imaging showed mucoperiosteal thickening in the left maxillary sinus expanded bone in the left frontal, temporal calvarium and body of sphenoid bone with encroachment of the left optic canal. However, MR images did not show abnormal finding of pituitary gland.

On the physical examination, he had prominent left frontotemporal region and no café-au-lait macules. The results of a formal ophthalmologic consultation revealed a left and right visual acuity of 0.6 and 1.2, respectively. His visual fields and ocular fundi were normal. His height was 186 cm, which approached the 3rd percentile for that age in Korea, but there were no other definite acromegaly features. Skeletal long bone X-ray demonstrated no bony abnormality.
Fig. 1. Osteometal unit (OMU) CT scan before and after optic nerve decompression. A: The non-contrast OMU CT scan demonstrates an expanded left basiocciput and greater sphenoid wing, typical for fibrous dysplasia. B: After endoscopic transnasal transsphenoidal and transethmoidal approach, postoperative OMU CT shows relief of left optic canal by removal of the fibrous lesion (arrows).

A non-contrast CT demonstrated an expanded left basiocciput and greater sphenoid wing with "ground glass" appearance, typical for fibrous dysplasia (Fig. 1A). In addition, there was left optic canal narrowing by involvement of fibrous dysplasia in CT scan. Endocrine evaluation demonstrated the following: prolactin (PRL) level 11.8 ng/mL (reference range 3.1–16.5), thyroid-stimulating hormone (TSH) level 0.75 mIU/L (reference range 0.3–6), human GH (hGH) level 3.33 ng/mL (reference range 0.4–4.7), cortisol level 7.2 ug/dL (reference range 5.9–26.1), ACTH level 19.6 pg/mL (reference range 0–60), luteinizing hormone (LH) level 2.1 mIU/mL (reference range 1.4–11.1) and follicle-stimulating hormone (FSH) level 3.9 mIU/mL (reference range 1.6–17.8). Bone scan demonstrated diffuse radioactive uptake in the left temporal, frontal bone, left mandible and left iliac bone that suggested active bone lesions, such as fibrous dysplasia with mild radiouptake in the left tarsal bone and left 2nd metatarsophalangeal joint.

Histological examination of pituitary adenoma. A: Histological examination of pituitary adenoma revealed tumor cells with cytoplasmic, uniformly round, secretory granules (Fig. 3). Immunohistochemistry for growth hormone (GH) with light hematoxylin counterstain, ×400. The majority of adenoma cells manifested GH immunoreactivity.

Second clinical manifestation
During the follow-up period of two years, the patient newly developed prominent supraorbital ridges, prognathism, large spade-like hands and a deep voice.

Sellar magnetic resonance (MR) images revealed slightly prominent posterior pituitary gland with newly developed mass-like lesion on the left side of pituitary gland which is measured about 7 mm, without definite enhancement (red arrow). B: The follow-up sellar MR image 1-year post-operatively demonstrates no residual tumor in the pituitary gland and no significant interval change in polystotic fibrous dysplasia (red arrow).

Hormone evaluation revealed elevation of hGH (10.39 ng/mL) and insulin-like growth factor 1 (IGF-1) [838.3 ng/mL (reference range 49–642)]. The other hormone levels were in the normal range: PRL 7.8 ng/mL, TSH 1.61 mIU/L, cortisol 8.6 ug/dL, ACTH 50.2 pg/mL, LH 3.01 mIU/mL and FSH 3.58 mIU/mL.
For the diagnosis of acromegaly by pituitary adenoma, he underwent endoscopic transsphenoidal tumor removal under navigational guidance (Fig. 3). In the operative field, we found abnormal pituitary mass, which was localized to left side and removed tumor. Postoperatively, hGH and IGH-1 were gradually decreased from 10.39 to 1.65 in hGH and from 838.3 to 704 in IGH-1. The GNAS gene (pseudohyoparathyroidism, type 1a), which is somatic mutations in GNAS, encoding the α-subunit of the heterotrimeric G protein complex (Gαs), occur in fibrous dysplasia and McCune-Albright syndrome b was positive in pituitary tissue and negative in serum specimen.

DISCUSSION

In this case, the patient had polyostotic (skull, left mandible, and left iliac bone in bone scan) and GH secreting pituitary adenoma, but did not display café-au-lait macules compatible with a diagnosis as MAS. In addition, genetic mutation about GNAS gene (pseudohyoparathyroidism, type 1a) in pituitary tissue was positive. In almost every prior case reported the base of the skull was involved, as seen in our patient.

MAS is a genetic abnormality that is an activating mutation in the GNAS1 gene that maps to chromosome 20q13 and encodes a ubiquitously expressed stimulatory (Gsa) subunit of the G protein. Point mutations of Gsa result in constitutive activation of adenylyl cyclase and high cAMP levels with resulting increased mitogenic signaling and autonomous hyperfunction of several endocrine glands. The same activating Gsa mutation is in the bone affected by fibrous dysplasia.

In our case, GNAS gene mutation in pituitary tissue was positive, but negative in serum specimen. However, this was not important for diagnosis because MAS manifests unusual genetics in that it is a postzygotic (non-germline) mutation resulting in both genetically-normal and abnormal cells (mosaicism) being present throughout the body.

Optimal current treatment for GH secreting pituitary adenoma is surgical resection. Even subtotal resection of hypersecretory adenoma is the effective initial therapy to reduce excess hormone levels. In MAS patients, however, even subtotal pituitary adenoma resection is often prohibited by severe skull base fibrous dysplasia. The transfrontal approach or combination of transphenoidal and transfrontal approach has been required in some cases.

There are some differences between our case and other prior reported cases. First, in our case, initial endocrine evaluation was normal finding and only fibrous dysplasia in the skull was evident. However, after 2 years of diagnosis of fibrous dysplasia, the patient had prominent acromegaly feature and showed increased hGH and IGH-1 levels in endocrine evaluation. We did not check the MR images initially because of no acromegaly feature and no abnormalities in hormone evaluation. In some patients with fibrous dysplasia, MR images will be helpful for evaluation of hormone secreting pituitary adenoma.

The first operation was done to decompress the left optic canal for symptom of left eye visual disturbance. The second operation was to remove the hGH secreting pituitary tumor. The second operation, transsphenoidal tumor removal, was complicated by distortion of anatomy by the bony hypertrophy and prior operation. In almost all prior MAS cases, there were remnant tumors after TSA operation. However, in this case the total pituitary tumor was removed and the patient has not experienced any neurologic change.