Transsphenoidal surgery in a patient with acromegaly and McCune–Albright syndrome: application of neuronavigation

Case report

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The McCune–Albright syndrome (MAS) is characterized by a clinical triad of polyostotic fibrous dysplasia, café-au-lait hyperpigmented macules, and hypersecretory endocrinopathies. Acromegaly is an uncommon manifestation of the endocrine disturbance associated with MAS, and the role of surgery in managing these cases has been a topic of debate. The authors present the case of a 35-year-old man with MAS who was also diagnosed with acromegaly, hyperprolactinemia, and pituitary macroadenoma. The patient had an 18-year history of fibrous dysplasia involving the right frontal bone and ribs as well as multiple endocrinopathies, but no cutaneous hyperpigmented macules. An oral glucose tolerance test demonstrated partial suppression of plasma levels of growth hormone (GH). The patient underwent transsphenoidal resection of the pituitary tumor, performed with assistance of neuronavigation, and tolerated the procedure well. After the surgery, both prolactin and GH levels returned to normal. These results suggest that neuronavigation-assisted transsphenoidal surgery can safely remove pituitary adenomas associated with MAS and successfully treat the underlying endocrine abnormalities. (DOI: 10.3171/JNS/2008/108/01/0164)

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Here we report on a patient with polyostotic fibrous dysplasia, acromegaly, and a demonstrable pituitary macroadenoma who underwent neuronavigation-assisted transsphenoidal surgery.

Case Report

History and Presentation. This 35-year-old man presented with an 18-year history of disfiguring facial changes and enlargement of the hands and feet. He reported having had a normal birth and normal childhood development until 17 years of age when his family noticed gradual onset of zygoma bossing, mandible protrusion, face elongation, and lip thickening, which worsened during the next decade. He also reported decreased visual acuity of the right eye since 19 years of age. An MR imaging study of the brain, performed at another hospital, had revealed a pituitary adenoma and prominent fibrous dysplasia. He was thought to have acromegaly and a GH-secreting pituitary tumor and underwent Gamma Knife surgery in December 2004 with a targeted delivery of 36.0 Gy. Postoperatively, however, his serum GH level remained elevated, and he was referred to the Peking Union Medical College Hospital for further care.

Examination. The patient had significant facial asymmetry, with coarse features and acral enlargement, but no café-au-lait hyperpigmented macules. The right nostril was se-

Abbreviations used in this paper: GH = growth hormone; IGF-I = insulin-like growth factor–I; MAS = McCune–Albright syndrome; MR = magnetic resonance; OGTT = oral glucose tolerance test; PRL = prolactin.
Transsphenoidal surgery in McCune–Albright syndrome

revealed reduction of basal serum GH, IGF-I and PRL levels to the reference range (Table 1). Postoperative OGTTs were performed at 2 weeks and 8 months after the operation, and the results were within normal limits (Table 2). Brain MR imaging at 2 weeks and 8 months after the operation demonstrated complete resection of the sellar mass without evidence of stalk deviation (Fig. 4). The patient is currently being followed up by the endocrinological service for management of MAS.

**Discussion**

This report describes a patient with MAS, acromegaly, and a GH-secreting pituitary adenoma who underwent neuronavigation-guided transsphenoidal surgery. More than 60 years ago, McCune and Albright and colleagues identified a syndrome comprising a classic triad of precocious puberty, polyostotic fibrous dysplasia, and café-au-lait cutaneous macules. Although sexual precocity, occurring especially often in female patients, is the most frequently recognized endocrine disturbance associated with MAS, it is now understood that other hypersecretory endocrinopathies may also accompany this disorder, including hyperthyroidism, hyperprolactinemia, and hypophosphatemic osteomalacia. Recent advances revealed that MAS results from sporadic somatic activating mutations of the Gsα subunit of the G protein (Gsa) that stimulates cAMP formation in early development, thus creating a mosaic population of cells that affect multiple organ systems.

Acromegaly is a rare form of endocrinopathy associated with MAS, and less than half of affected patients show radiological evidence of a pituitary adenoma. Sakaki et al. reviewed 8 cases of MAS with acromegaly and immunohistochemical evidence of GH-secreting adenoma and found that more than half of the tumors also secreted growth hormone.

**Table 1**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Preop</th>
<th>Postop</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>GH (ng/ml)</td>
<td>20.4</td>
<td>0.63</td>
<td>0.0–3.0</td>
</tr>
<tr>
<td>PRL (ng/ml)</td>
<td>57.8</td>
<td>1.21</td>
<td>&lt;25.0</td>
</tr>
<tr>
<td>IGF-I (ng/ml)</td>
<td>1252.0</td>
<td>173.7</td>
<td>122.9–570.1</td>
</tr>
<tr>
<td>ALP (U/L)</td>
<td>370</td>
<td>291</td>
<td>27.0–107.0</td>
</tr>
</tbody>
</table>

* ALP = alkaline phosphatase.

**Table 2**

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Glucose (mg/dl)</th>
<th>GH (ng/ml)</th>
<th>Glucose (mg/dl)</th>
<th>GH (ng/ml)</th>
<th>Glucose (mg/dl)</th>
<th>GH (ng/ml)</th>
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<tbody>
<tr>
<td>Preop</td>
<td>0</td>
<td>96</td>
<td>20.4</td>
<td>82</td>
<td>0.63</td>
<td>83</td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>152</td>
<td>18.3</td>
<td>114</td>
<td>0.48</td>
<td>131</td>
</tr>
<tr>
<td></td>
<td>60</td>
<td>193</td>
<td>16.9</td>
<td>113</td>
<td>0.39</td>
<td>149</td>
</tr>
<tr>
<td></td>
<td>120</td>
<td>113</td>
<td>12.5</td>
<td>105</td>
<td>0.38</td>
<td>158</td>
</tr>
<tr>
<td></td>
<td>180</td>
<td>74</td>
<td>14.5</td>
<td>81</td>
<td>0.66</td>
<td>119</td>
</tr>
</tbody>
</table>

**Postoperative Course and Follow-Up.** The patient experienced transient diabetes insipidus for 1–2 days after the operation, but the condition resolved without treatment. His visual acuity remained unchanged and there was no evidence of cerebrospinal fluid leak. Endocrinological testing...
PRL, which suggests frequent occurrence of bimorphous or plurimorphous tumors in MAS patients. This observation is consistent with our findings in the present case.

The management of MAS involves treating fibrous dysplasia and the associated endocrine abnormalities. The goal of treating patients with GH-secreting adenomas is to lower serum GH and IGF-I levels to their respective reference ranges because of the serious comorbidities caused by excessive GH. Moreover, although the natural history of MAS or polyostotic fibrous dysplasia is poorly understood, the potential synergistic effect of elevated serum GH levels on dysplastic bone formation is particularly worrisome. Thus, we believe that when a GH-secreting adenoma occurs in a patient with MAS, treatment should be initially focused on the adenoma and the fibrous dysplasia should be addressed subsequently. We consider endocrinological control to be satisfactory if the serum GH concentration can be reduced to < 1 ng/mL after a loading dose of glucose.

Although surgery is usually the treatment of choice for acromegaly, other treatment modalities, including radiation therapy and administration of a long-acting somatostatin analog, have been reported in the literature. Nevertheless, pharmacological therapy such as octreotide administration has primarily been studied as a secondary treatment, and fractionated radiation therapy may lead to sarcomatous transformation of dysplastic bones and should probably be avoided. Stereotactic radiosurgery allows focal delivery of high doses of radiation and is superior to

Fig. 1. Preoperative neuroimages. A and B: Computed tomography (CT) scans demonstrating significant hyperostosis of the right frontal, zygomatic, sphenoid, and maxillary bones. The sagittal view (A) shows significant protrusion of osseous structure into the anterior cranial space, creating an extra hurdle for a subfrontal approach. The axial view (B) is consistent with a compressed right nasal cavity; the excess bone indicated by the arrowhead was removed during the operation. C: A Gd-enhanced axial T1-weighted MR image of the brain showing a nonenhancing sellar mass displacing the pituitary stalk to the left (arrow). The mass measured 17 × 9 mm.

Fig. 2. Screen images captured from the BrainLAB system at different stages of surgery. A–D: Images captured at the beginning of neuronavigation-guided drilling. The distance between the edge of the obliterated sphenoid sinus to the base of the sella turcica was ~ 60 mm as measured with the BrainLAB software. The 4 sub-images demonstrate the skin overview (A), axial view (B), sagittal view (B), and coronal view (D). E and F: Sagittal (E) and axial (F) images captured near the end of drilling, when the remaining osseous structure in front of the sellar base was measured at only 15 mm.
conventional radiotherapy for recurrent acromegaly after unsuccessful surgery, but its efficacy and application as the primary treatment for GH-secreting adenoma have not yet been established.

Transsphenoidal surgery for acromegaly in MAS patients is complicated by 2 anatomical factors. Fibrous dysplasia in most MAS patients involves the skull base; thus, it is difficult and potentially dangerous to approach the much-thickened sphenoid and ethmoid bones without intraoperative directional guidance. Moreover, many investigators have reported increased vasculature in the osseous structures surrounding the pituitary, further hindering its access. A thorough search of the English literature revealed reports of 10 cases in which patients with MAS and acromegaly had undergone surgical resection, in addition to the present case (Table 3). In 8 out of the 11 reported cases, a more invasive transfrontal or subfrontal approach was used with variable success and usually significant morbidity. Transsphenoidal surgery was attempted in 3 previous cases (twice in 1 of those 3), but no details of the procedures were reported and none achieved satisfactory endocrinological control of the disease.

**Conclusions**

We have reported on a patient with MAS and acromegaly who underwent neuronavigation-guided transsphenoidal surgery. There were no complications during the operation and the short-term outcome was excellent, with radiologically complete resection of the tumor and significant reduction of endocrinological markers to the normal levels. The serum alkaline phosphatase level, which reflects fibrous dysplasia, was slightly reduced as well. Neuronavigation provided important intraoperative anatomical guidance such that the opening of the bone window and the resection of the tumor could be achieved in more prudent fashion. These factors contributed to the good outcome of our case.

![Fig. 3. Photomicrographs showing (left) a section of the pituitary adenoma and (right) a specimen of the resected bone revealing dysplasia. H & E, original magnification: left \( \times 150 \); right \( \times 60 \).](image)

![Fig. 4. Postoperative neuroimages. A: Sagittal reconstruction of a head CT demonstrates the tunnel through the dysplastic anterior skull base that was made to reach the sella turcica. B: Axial MR image obtained 2 weeks after surgery shows the mixed signal consistent with packing material, which is usually absorbed within 3–6 months after an operation. C: Axial MR image obtained 8 months after the operation shows that mixed signal consistent with packing material is no longer present—indicating that the material was absorbed—and there is no evidence of tumor.](image)
Our experience suggests that neuronavigation-guided transsphenoidal resection of pituitary adenoma may provide good outcomes for patients with MAS.

Acknowledgement

Both Dr. Dou and Dr. Lin contributed equally to this manuscript.

References

Transsphenoidal surgery in McCune–Albright syndrome


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