Intraoperative Magnetic Resonance Imaging During Endoscopic Transsphenoidal Surgery of Growth Hormone-Secreting Pituitary Adenomas

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BACKGROUND: **The effect of intraoperative magnetic resonance imaging (iMRI) on the extent of sellar region tumors treated endonasally has been described in previous research. However, the effects of iMRI on endocrinologic outcome of growth hormone-secreting adenomas have been studied in only a few small cohort studies.**

METHODS: **Inclusion criteria were primary transsphenoidal surgery for growth hormone-secreting adenoma from January 2009 to December 2014, a minimum follow-up of 1 year, complete endocrinologic data, at least 1 iMRI, and at least 2 postoperative magnetic resonance images. The cohort consisted of 105 patients (54 females, 51 males) with a mean age of 48.3 years (range, 7–77 years). There were 16 microadenomas and 89 macroadenomas.**

RESULTS: **Endocrinologic remission in the whole cohort was achieved in 64 of the patients (60.9%). Resection after iMRI was attempted in 22 of the cases (20.9%). Resection after iMRI led to hormonal remission in 9 cases (8.6%). Endocrinologic postoperative deficit was observed in 10 cases (12.5%). Postoperative cerebrospinal fluid leakage indicated the necessity to reoperate in 3 cases (3.8%). No neurologic deterioration was observed.**

CONCLUSIONS: **iMRI influences not only the morphologic extent of pituitary adenomas resection but also the endocrinologic results. We encourage the routine application of iMRI in pituitary adenoma surgery, including hormone-secreting pituitary tumors.**

INTRODUCTION

Acromegaly is a rare disease, with an estimated incidence of approximately 4 cases per 1 million persons. Pituitary tumors are the underlying pathologic entity in approximately 99% of the cases of acromegaly and are nearly always benign. Acromegaly is characterized as a chronic disease related to high levels of growth hormone (GH) and insulinlike growth factor I (IGF-I).[1] If excessive outputs of GH are not normalized, severe cardiovascular and metabolic disturbances as well as cosmetic and orthopedic deformities result. Previous studies[2] have shown a 2- to 3-fold increased mortality for treatment-resistant cases compared with successfully treated patients and healthy individuals.

Treatment options for acromegaly include surgery, medical therapy, radiosurgery, and rarely radiotherapy. The development of drug therapy for the control of acromegaly represents an important step toward hormonal control in patients with GH-secreting adenomas. Surgery remains the first line of treatment for GH-secreting adenomas according to recommendations of different endocrinologic societies and pituitary centers.[3-5]

In the past 20 years, endoscopic endonasal surgery has been popularized in the treatment of pituitary adenomas. There is an ongoing debate whether the endoscopic technique can achieve optimal extent of resection consistently across all patients.[6,7]

Several cohort studies have studied the effect of intraoperative magnetic resonance imaging (iMRI) on pituitary surgery.[8-11] In general, these studies confirm a positive effect of iMRI regarding the extent of pituitary adenoma resection. Nevertheless, there are only a few studies on the effect of iMRI in GH-secreting adenomas with respect to not only imaging of residual pituitary adenomas but also endocrinologic remission rates after surgery.[12-14] Accordingly, we share our experiences with iMRI in GH-secreting adenomas treated endonasally.

Key words
- Acromegaly
- Growth hormone
- Intraoperative MRI
- Pituitary adenoma
- Transsphenoidal surgery

Abbreviations and Acronyms
GH: Growth hormone
IGF-I: Insulinlike growth factor I
iMRI: Intraoperative magnetic resonance imaging
MRI: Magnetic resonance imaging
OGTT: Oral glucose tolerance test

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METHODS

The first endonasal procedure in our iMRI suite was performed on 18 April 2008. All the patients' data have been prospectively included into the database of endonasal procedures. The local ethical committee approved the iMRI suite, and signed informed consent was obtained from all patients and legal guardians.

In the current study, all primary transsphenoidal surgeries for GH-secreting adenomas from January 2009 until December 2014 were analyzed. No GH-secreting adenoma surgery was performed without iMRI during the target period. Inclusion criteria were the following: minimum 1 year follow-up, full endocrinologic data, at least 1 iMRI, and at least 2 postoperative magnetic resonance images.

The diagnosis of acromegaly was confirmed clinically and biochemically. Preoperative and follow-up examination after 7–10 days, 3 months, and 12 months included basal hormonal levels and, if indicated, endocrine dynamic testing. Standard ophthalmologic examination was performed preoperatively and postoperatively. Magnetic resonance imaging (MRI) was performed preoperatively, intraoperatively, 1–2 days after surgery, and 3 months postoperatively. Furthermore, in all patients, surgical complications (eg, cerebrospinal fluid fistulas and meningitis) were documented.

For endocrinologic outcome assessment, we used updated consensus criteria from 2010. According to these criteria, disease control is defined as age- and sex-normalized IGF-I and random GH <1 μg/L or nadir GH after an oral glucose tolerance test (OGTT) if <0.4 μg/L. IGF-I was measured using reagents obtained from Diagnostic Systems Laboratories (Webster, Texas, USA). GH was measured using a commercial RIA kit (Cis Bio International, Codolet, France).

Our cohort consists of 105 patients (54 females) with a mean age of 48.3 years (range, 7–77 years). There were 16 microadenomas and 89 macroadenomas. The mean volume of the adenomas was 2838 mm^3 (range, 13.5–29,766 mm^3). The average anterior-posterior size was 15.2 (range, 3–37mm), laterolateral size 16.5 (range, 3–44 mm), and superior-inferior size 14.6 mm (range, 3–41 mm). Fifty-one of the adenomas had a suprasellar component. The Knosp grading system for pituitary adenomas was used to estimate cavernous invasion: Knosp grade 1 and 2 in 19 adenomas, Knosp grade 3 in 10 adenomas, and Knosp grade 4 in 14 adenomas. A preoperative visual deficit was observed in 9 patients.

The intention of the surgical procedure was always established before surgery, which was to attempt radical resection or subtotal/partial resection. Radical resection was the preoperative surgical goal in 80 cases, whereas subtotal/partial resection was the preoperative surgical goal in 25 cases. Subtotal/partial resection was the objective of the surgery in the event of adenoma parasellar growth or in the event of major cavernous sinus invasion laterally to the internal carotid artery or multilobulated giant adenoma. Only 2 of our patients were medically pretreated. In both cases, the treatment proved ineffective.

Mean follow-up was 35 months (range, 13–76 months).

Technique

The bilateral endoscopic endonasal approach was used for all procedures. An MRI-compatible head-holder was applied after induction of general anesthesia. The head of the patient was registered to a frameless navigation system that is used obligatorily. The patient is undraped after tumor resection and immediately transferred to the MRI scanner. All MRI sequences are analyzed for pituitary adenoma remnants or any other kind of surgical complication. At this point, a decision is taken either to continue the surgical resection or to check the operative field to perform closure of the sella if needed. Our MRI protocol comprises preoperative 3.0-T MRI scanning followed by iMRI on the same scanner. Six channel intraoperative coils are used for iMRI. iMRI is performed both in T1-weighted images with and without gadolinium and in T2-weighted images. Next, MRI is performed on the first or second postoperative day. All images are used to evaluate the extent of surgical resection. Further MRI is performed at 3–4 months after surgery and later each 6–12 months.

RESULTS

Endocrinologic remission in the whole cohort was achieved in 64 patients (60.9%). Resection after iMRI was performed in 22 surgeries (20.9%).

When radical resection was the object of the surgery (80 patients), endocrinologic remission was achieved in 62 patients (77.5%). Resection after iMRI was continued in 12 cases (15%). MRI radical resection and endocrinologic remission were achieved in 9 of these cases (11.3%), implicating that resection after iMRI led to MRI radical resection and endocrinologic remission in 75% of the cases when iMRI confirmed residual adenoma. A case of successful hormonal remission as a result of resection after iMRI is shown in Figure 1. Results are summarized in Figure 2.

Endocrinologic remission could not be achieved in 18 cases (22.5%) when radical resection was planned. Reanalysis of these cases was performed by 2 neurosurgeons (M.M. and V.B.) and by a neuroradiologist (T.B.). All 3 were blinded to the endocrinologic results. Neither iMRI nor postoperative MRI disclosed any obvious residual adenomas in 8 cases (10%). iMRI showed residual adenomas in 6 cases (7.5%), which were not resected after iMRI. Postoperative MRI showed the same extent of residual adenoma as iMRI. All these residual adenomas were located in the cavernous sinus. An attempt to resect this part of the adenoma using surgical resection was performed in 3 cases but the surgeon failed to achieve radical resection (Figure 3). In 3 cases, a surgeon deemed further resection too risky, with little chance for radical resection. Therefore, no further resection was performed on these 3 cases. iMRI was negative for any residual adenoma in 4 cases (5%) but postoperative MRI showed a small residuum. In 2 of these cases, the initial iMRI analysis proved incorrect, and a reanalysis indicated a residual adenoma on iMRI. In the remaining 2 cases, reanalysis of iMRI came to the same interpretation as the initial analysis (ie, there was no indication of a residual tumor according to the iMRI). Failures to achieve endocrinologic remission are summarized in Figure 4.

Endocrinologic postoperative deficits indicated that hormonal substitution was observed in 10 cases (12.5%), hypocortisolism in 5 (6.3%), hypothyroidism in 4 (5%), hypogonadism in 3 (3.8%), panhypopituitarism without diabetes insipidus in 1 (1.3%), and diabetes insipidus in 1 (1.3%). Postoperative cerebrospinal fluid