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Case Report

The Role of Endoscopic Endonasal Approach in the Multimodal Management of Giant Pituitary Adenoma: Case Report and Literature Review

Abstract

Giant pituitary adenomas (GPAs) are defined as pituitary lesions larger than 40 mm of diameter. Surgical resection remains the gold standard to decompress the optic apparatus, reduce lesion load, and preserve hormonal function. The endoscopic endonasal approach (EEA) has been increasingly used for the treatment of pituitary adenomas and skull base tumors due to the wide angle of view and exposure. Through the description of an exemplificative case of EEA resection of a nonsecreting GPA in the setting of a multimodal treatment, the authors discuss the advantages and disadvantages of this management strategy and provide a detailed review of the literature.

Keywords: *Endoscopic endonasal approach, giant pituitary adenoma, radiosurgery, transcranial route*

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Introduction

Giant pituitary adenomas (GPAs) are defined as pituitary adenomas larger than 40 mm of diameter; depending on the patient neurological status, hormonal profile, and lesion boundaries, the management options available include pharmacological treatment in functional GPA and surgical resection with or without radiotherapy/radiosurgery for nonfunctional ones.[1,2]

Surgical removal of GPA is challenging due to their size and the proximity of neurovascular structures, which are commonly invaded by these lesions.[3] Microsurgical and endoscopic approaches as standalone options or combinations of the two are available and chosen on a case by case basis. The endoscopic endonasal approach (EEA) generally allows visualization of neurovascular structures, lesion boundaries, and its suprasellar extension;[4,5] it certainly offers a series of advantages in the multimodal management of patients harboring GPA.

This article describes an exemplificative case of EEA resection of a nonfunctional GPA in the setting of a multimodal treatment, highlights the advantages and disadvantages of this management strategy, and provides a detailed review of the literature.

Case Report

A 62-year-old woman presented with an 18-month history of progressive headache, generalized weakness, and bilateral exophthalmus more relevant on the right. Neurological examination demonstrated diplopia on the right lateral gaze and bilateral decrease of visual acuity, especially in the right eye, without visual field deficit. Endocrine workup revealed hypocortisolism (cortisol: 49.3 µg/l, normal: 70–250 µg/l; ACTH: 8.3 ng/l, normal: 9–60 ng/l) and hypothyroidism (TSH: 0.84 mUI/l, normal: 0.270–4.20 mUI/l; T4: 5.1 ng/l, normal: 9.5–18 ng/l). Computer tomography (CT) and magnetic resonance imaging (MRI) scans showed a large (62 mm) extradural lesion invading sphenoid, right maxillary sinus, both cavernous sinuses (CSs), anterior and posterior ethmoid bone, orbits, and anterior and middle skull base with bone invasion extending to the clivus [Figure 1]. The patient was initially managed with a 15-day course of steroids (prednisolone 80 mg twice a day): bilateral exophthalmus remarkably improved, and a MRI (1 week after steroid interruption) showed a

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significant volume reduction (44 mm) [Figure 2]. At our skull base meeting, it was decided to proceed with Stage I EEA for tissue biopsy that suggested the diagnosis of a pituitary adenoma and therefore induced to offer a Stage II EEA surgical resection to the patient. Surprisingly, the MRI realized for navigation protocols the day before surgery (6 weeks after discontinuing steroids) showed a dramatic volumetric increase of the lesion. Surgery was undertaken using image-guided surgery with MRI and CT imaging fusion. The first step consisted in making a nasoseptal flap.[6] The lesion consistency was quite soft in its upper and superficial-anterior part, whereas the lower and deeper posterior portion involving the clivus, the internal carotid artery (ICA), and the CS was firmer, oozy, and fairly adherent. The tumor invaded and eroded the petrous bone; the ICAs were uncovered and identified with the help of a micro-Doppler probe. At the end, the resection was subtotal and the nasoseptal flap was lined over tuberculum sellae, sellar floor, clival recess, and ICAs and sealed with fibrin glue. The postoperative course was uneventful, and the patient was discharged after 3 days. The histopathology of the lesion confirmed a GPA with a Ki-67 of 1%. Immunohistochemistry analysis showed that cells had an epithelial phenotype with positivity of anti-pan-keratin staining and neuroendocrine differentiation with positive anti-chromogranin A, synaptophysin, CD56, and NSE antibodies. PS100, vimentin, GFAP, and TTF1 were absent. Furthermore, there was a positivity of 5%–10% of the cells to anti-ACTH antibodies (polyclonal) and negativity for all other hormones.

Early postoperative MRI confirmed residues in the right orbit, the right frontobasal region as well as the lower clivus, and both CSs [Figure 3]. At 6-week follow-up, the clinical examination showed the resolution of diplopia and exophthalmus, with improvement of the visual acuity; hydrocortisone and thyroid replacement therapy were weaned off after 6 months due to normal hormonal assessment. At 6 months, MRI showed once again a limited progression of the residue. The case was discussed at our neuro-oncology meeting and given the lesion's aggressive behavior despite a Ki-67 of 1%, and it was decided to start a radiotherapy treatment. No further progression of the residue was seen at the 12-, 24-, 36-, and 48-month follow-up, and the patient remained asymptomatic with a normal pituitary function.

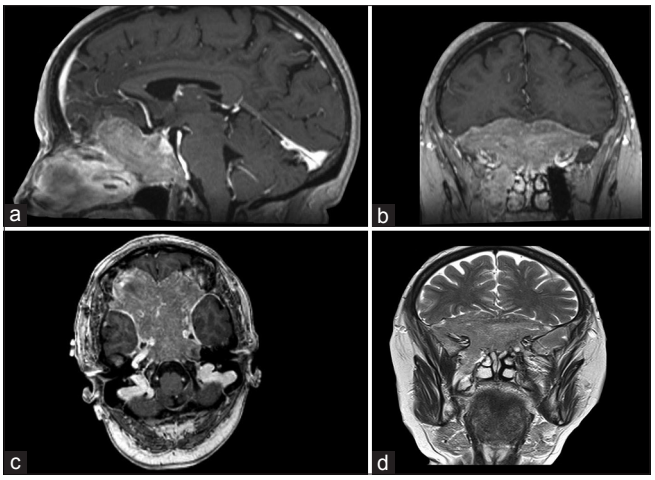

Figure 1: Preoperative sagittal (a), coronal (b), and axial (c) T1-magnetic resonance imaging showing slightly hyperintense and preoperative coronal (d) T2-magnetic resonance imaging showing isointense: anterior and middle skull base lesion with suprasellar extension, invading sphenoid sinus, clivus, ethmoid bone, anterior cranial fossa, and cavernous sinus extending in the right masticator space and encasing internal carotid artery

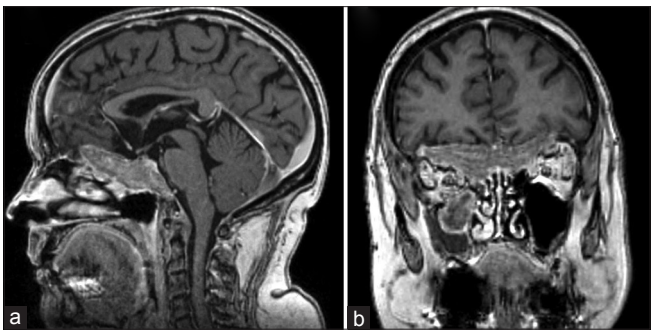

Figure 2: T1-magnetic resonance imaging ([a], sagittal, [b], coronal) showing the consistent lesion volume reduction after steroid treatment

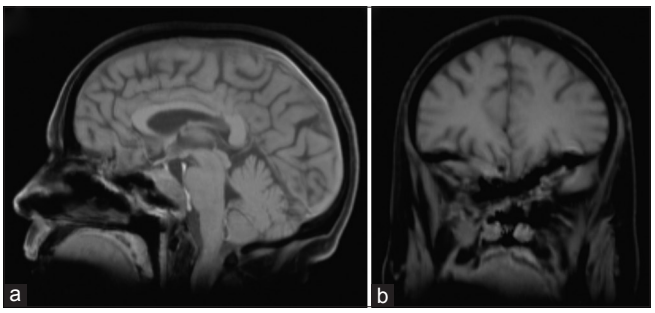

Figure 3: Postoperative T1-magnetic resonance imaging ([a], sagittal, [b], coronal) after an early injection of gadolinium showing large lesion debulking with residual mass in the clival, right subfrontal area, and the right orbit

Discussion

In the present article, we describe a case of GPA invading sphenoid, right maxillary sinus, CSs, anterior and posterior ethmoid bone, orbits, and anterior and middle skull base, in which EEA followed by the administration of adjuvant radiotherapy allowed a long-term (48-month) clinical remission with lesion control and normal pituitary function. Management of GPA is challenging because of their size, their consistency, their vascularization, and tendency to encase ICA and optic nerves as well as to invade the CSs.[7-10] The most common surgical routes used to address these lesions have been the transsphenoidal microscope-assisted approach (TSMA) (a.k.a. Hardy procedure)[11] and transcranial approaches (TCAs).[6,12,13] Since the introduction of EEA, the management of GPA has significantly improved;[14] multiple advantages such as reduction of surgical time and intraoperative risks will

probably make this the standard treatment for Stages I and II (biopsy and excision) of most GPA in the near future. On the other hand, surgeons possessing only training in conventional microsurgery (TSMA or TCA) may find the learning curve very steep.[14-16] The most recent literature[17-20] highlights that EEA could be considered a valid alternative to more traditional TSMA and TCA, especially in the context of a multimodal management. The different surgical approaches with their anatomical, technical limitations and complications are summarized in Table 1. In general, the main goals for GPA management are reversal of the visual field deficits, improvement of the endocrine deficits, and neurological recovery. Preoperative visual field deficit can improve in up to 80% of patients;[6,21] nonetheless, postoperative visual worsening can also occur in up to 22% of cases, being more frequent following TCA (especially for lesions extending to the CS) than transsphenoidal surgery.[6,22] Improvement of pituitary function after surgery for GPA has not been explored in detail; although the reported improvement rate for hormonal function in patients with macroadenomas ranges between 35% and 50%, this might not be consistent in GPA given that the long-standing hypopituitarism is more unlikely to recover.[23,24] Transient or permanent hypopituitarism is a relatively common complication of EEA although its rate is similar to that of TSMA; nevertheless, due to the greater respect of pituitary stalk, decreased hormonal function following transsphenoidal approaches (either EEA or TSMA) remains lower than of TCA.[7,6,21] Postoperative diabetes insipidus (DI) is also more common after TCA than transsphenoidal surgery for GPA;[6,21] in TSMA series, the reported incidence of permanent postoperative DI ranges between 8.2%[6] and 10.4%.[8] The most common complication encountered in multistaged EEA is postoperative rhinorrhea (16.7%); great attention should be paid during reconstruction using multilevel grafts (fascia lata, fat, bone, glue, etc.). Nevertheless, in the last years, the cerebrospinal fluid (CSF) leak rate has dramatically improved thanks to the implementation of pedicled nasoseptal flap.[25-27] In the existing literature, a gross total removal of GPA is described in only 50% of cases;[6,12] because subtotal resection may be associated with early postoperative hemorrhages, acute hydrocephalus, and persistent optic nerve compression, a multimodal approach is warranted in most cases which can lead to a control of the disease as happened in this case report. In fact, the concomitant use of pharmacological therapy and radiotherapy or radiosurgery could become more relevant in the future thanks to advances obtained with the introduction of radioenhancers and radiosensitizers.[28,29] Finally, one of the interesting aspects of the present case is the initial lesion shrinkage after steroid therapy. Giant lesion may present an inflammatory component on which steroids could have acted, obtaining a volumetric reduction. Furthermore, the

Table 1: Surgical approaches with their anatomical and technical limitations and complications

Surgical approach	Endoscopic endonasal approach	Transsphenoidal microscope-assisted approach	Transcranial approach
Anatomical and technical limitations	Cavernous sinus invasion (relative contraindication) except when tumor invasion of the lateral wall of the cavernous sinus (especially if extending to the temporal lobe)	Cavernous sinus invasion	Cavernous sinus invasion (formal contraindication)
	Tumor extending into planum sphenoidale (relative contraindication)	Retrochiasmatic extension of the tumor and expansion into the ventricular system	Temporal lobe invasion suitable for transcranial approach
	Formal limitation is tumor extension laterally to the supraclinoid part of the ICA		Formal indication for very large or dumbbell-shaped tumors (usually more than 50 mm) extending into the planum sphenoidale, middle fossa, or retrochiasmatic region, especially in case of a shallow sella and/or narrow intercarotid space
Complications			
Visual deterioration	↓		↑
Postoperative cranial nerve dysfunction	↓		↑
Pituitary function amelioration	↑		↓
Diabetes insipidus	↓		↑
Cerebrospinal fluid leak	↑		↓
Meningitis	↓		↑
Mortality	↔		↔

"↓" – Decrease; "↑" – Increase; "↔" – Equal; ICA – Internal carotid artery

histopathology examination revealed, in 5%–10% of the cells, positivity to anti-ACTH antibodies (polyclonal) and negativity for all other hormones. Therefore, this GPA may have been a silent corticotroph adenoma, very well known for its aggressive behavior and tendency to recur, thus explaining its regrowth after steroid therapy suspension.[13,30]

Conclusion

Many factors affect the outcome of patients with GPA, and the management of these lesions should, therefore, be tailored on a case-by-case basis. Although long-term disease control requires adjuvant treatment, its initial treatment consists in maximal surgical resection. Multistaged EEA allows good resection of lesions extending into the CS, ventricular, and clival regions. This approach is more difficult in case of fibrous lesions, with adherent and multilobular configurations, and/or extension beyond the lateral wall of CS. With the exception of CSF leak, the complication rate of EEA remains nearly the same or even lower than that reported for other approaches. The EEA represents a safe and effective treatment for GPA in a setting of multimodal management since surgery alone cures <60% of patients with GPA. Depending on the presence of a surgical residue and the histology/immunohistochemistry characteristics of the lesion, the remaining 40% will require medical therapy and most likely adjuvant radiosurgery/radiotherapy to achieve disease control.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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