ORIGINAL ARTICLE

Results of cerebral cavernous malformation surgery in patients with cavernoma-associated epilepsy

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Abstract

Objective: To evaluate the outcomes of surgical resection of cerebral cavernous malformations (CCMs) in patients with cavernoma-associated epilepsy and to identify risk factors for adverse outcomes.

Methods: A retrospective analysis was performed on 50 patients diagnosed with supratentorial CCMs who presented with epileptic seizures. CCM resection, including excision of the hemosiderin rim, was performed in all cases except those with CCMs located in eloquent brain regions. Postoperative brain MRI was performed within 24 hours and reviewed by two independent radiologists to assess the completeness of CCM and hemosiderin rim resection. Long-term outcomes were assessed using the Engel Surgical Outcome Scale.

Results: The duration of the follow-up period was 36.5/33 (21.2; 47.8) months, range:11.2-70.6 months. Forty-four patients (88%) were seizure-free postoperatively. Of these, 30 (60%) completely discontinued anticonvulsant medication. Four patients (8%) had infrequent seizures (Engel class 2), and two (4%) had no change in seizure frequency. Complete hemosiderin rim resection was significantly associated with seizure freedom (p = 0.043). Among seizure-free patients, complete hemosiderin rim resection was achieved in 27 of 38 (71%), compared with only one of five (20%) in those with unsatisfactory outcomes. Gender, age, seizure type, and CCM location did not significantly affect postoperative epilepsy outcomes.

Conclusions: Surgical resection of CCMs is an effective treatment for CCM-associated epilepsy with a low risk of surgical complications. Complete excision of the hemosiderin rim is a favorable prognostic factor for seizure control in this patient population.

Keywords: cavernoma; cavernous malformation; epilepsy surgery; seizure; hemosiderin

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Introduction

Cavernous malformations (CCMs) are vascular developmental anomalies characterized by clusters of endothelium-lined cavities lacking a mature vascular wall. CCMs are typically discovered incidentally on brain MRI; however, epileptic seizures are frequently the initial clinical presentation in over 25% of cases (1).

Surgical resection of supratentorial CCMs is routinely performed by both experienced and novice neurosurgeons due to the relative ease of resection, attributed to well-defined anatomical boundaries and low vascularity. The primary challenge lies in determining appropriate surgical indications and the extent of surgical intervention. Currently, there is no clearly established consensus regarding the optimal timing of surgery. According to the International League Against Epilepsy (ILAE) clinical practice recommendations, pharmacoresistant cavernoma-associated structural epilepsy is an absolute indication for surgical intervention (1). However, some surgeons

advocate for earlier microsurgical resection (2). The extent of excision during surgery remains debated. In cases of cavernoma-associated structural epilepsy, various resection volumes and strategies have been described. These include isolated CCM resection, resection of the CCM with the adjacent hemosiderin rim, and, when the CCM is located in the temporal lobe, a combined approach involving CCM resection with amygdalohippocampectomy or extended temporal lobe resection (1, 3–9). Different surgical timings and extents have been proposed based on identified risk factors, complications, and predictors of adverse outcomes. In this paper, we present our study findings on surgical treatment outcomes for CCMs in patients with a history of seizures. We assessed both short-term and long-term results, as well as risk factors for adverse outcomes following microsurgical procedures.

Materials and methods

This study evaluated treatment outcomes in 50 of 60 patients who underwent surgery for CCMs with epileptic seizures between 2014 and 2020. Ten patients were excluded from the study due to loss to follow-up. The cohort included patients with sporadic seizures (up to two seizures) and those with structural epilepsy (three or more seizures). All patients underwent preoperative electroencephalography (EEG), supplemented by ictal video-EEG when clinically indicated. Preoperative magnetic resonance imaging (MRI) and neurological examination were also performed.

During surgery, the surgeon aimed to resect the CCM and the surrounding hemosiderin rim (visible as yellow or gliotic tissue), unless the CCM was located in an eloquent brain region. All procedures were performed using a surgical microscope and frameless stereotactic neuronavigation, with intraoperative ultrasonography used as needed.

Postoperative brain MRI was routinely performed within 24 hours to assess the completeness of resection. Brain MRI was performed using 1.5 and 3 Tesla MR systems according to a standard protocol. Images were reviewed by two independent radiologists.

Postoperatively, all patients received anticonvulsant medication under the supervision of a clinical epileptologist. Patients were typically discharged within 4–6 days postoperatively and remained under the care of an epileptologist, with consideration for antiepileptic medication tapering no sooner than six months after surgery.

Long-term outcomes were assessed via in-person clinic visits or telephone interviews. Surgical effectiveness for epilepsy was evaluated using the Engel Surgical Outcome Scale. Due to limited sample size, Engel class subgroups were not analyzed separately. Patients with Engel class 1 outcomes were categorized as having satisfactory outcomes, while those with Engel classes 2 – 4 were categorized as having unsatisfactory outcomes.

Statistical analysis

Since most of the data were not normally distributed, the following format was used to describe the numerical data: M/Me (Q1; Q3), where M is the arithmetic mean, Me is the median, Q1 and Q3 are the first and third quartiles. Group comparisons were conducted using the two-tailed Fisher's exact test and the two-tailed Mann–Whitney *U* test, with statistical significance set at $p < 0.05$. Statistical analyses were performed using R Statistical Software (version 4.3.1) (10).

Results

Postoperative seizure control

Long-term outcomes were evaluated in 50 of 60 patients (83.3%). The follow-up duration was 36.5/33 (21.2; 47.8) months (range: 11.2 - 70.6 months). During the follow-up period, 44 patients (88%) remained seizure-free. Of these, 30 patients (60%) were able to discontinue anticonvulsant medication completely. Four patients (8%) experienced infrequent seizures (Engel class II), and two patients (4%) reported no reduction in seizure frequency.

Demographic distribution

Of the 50 patients included in this study, 27 (54%) were male. The age of the patients at the time of surgery was 41/38 (32.2; 48.5) years (range: 19 - 70 years old). No statistically significant association was found between demographic factors and intervention outcomes (Table 1).

Clinical data

The duration of the disease before surgery ranged from 1 to 437 months. The mean/median duration was 83.4/24 (8.2; 144) months. In the Engel class 1 group, the median duration was 13.5 months (7; 144), while in the Engel classes 2-4 group, it was 108 months (90; 144). Although no statistically significant difference was observed between these groups ($p = 0.1$) (Table 1), earlier intervention appears to be associated with a more favorable outcome.

Rare episodic seizures (up to three) occurred in 13 patients (26%), epilepsy was present in 36 patients (72%), and one patient (2%) presented with status epilepticus.

Case report

A 53-year-old male presented with a history of prolactinoma managed with cabergoline therapy for 4 years. After three years, the patient developed with gradual visual deterioration with prolactin levels within the normal range. Neuroophtalmological examination revealed bitemporal visual field defects. Follow-up magnetic resonance imaging (MRI) demonstrated a reduction in prolactinoma volume with development of symptomatic secondary empty sella, and significant dislocation of the optic system (***Figures 1***).

Surgical Procedure

The patient was positioned supine. Under general anesthesia, the patient underwent endoscopic transnasal transsphenoidal surgery providing access to the sphenoid sinus. During the approach, parts of nasal septum bone and cartilage were harvested. A bony opening in the floor of sella turcica was made using a high-speed drill preventing the injury to the dura and CSF leak. Gently dissection followed with mobilization and elevation of the dura of the sellar floor to diminish the displacement of optic nerves, chiasm and tracts. To ensure the extradural fixation of the construction, attainable autologous

grafts were used. The cartilage was trimmed to the appropriate size and shape, while the septal bone was shaped to fit the bony defect of the sellar floor. These grafts were precisely tailored to fit and provide support to the repositioned optical system.

Postoperative course was uneventful. On follow-up patient showed improvement of visual impairment (***Figure 2***).

Postoperative MRI image demonstrated a sellar packing with autologous material with optic chiasm elevation with no signs of compression (***Figure 3***). Hormonal checkup revealed hormonal levels within normal range. No CSF leak or infections were observed during the postoperative period.

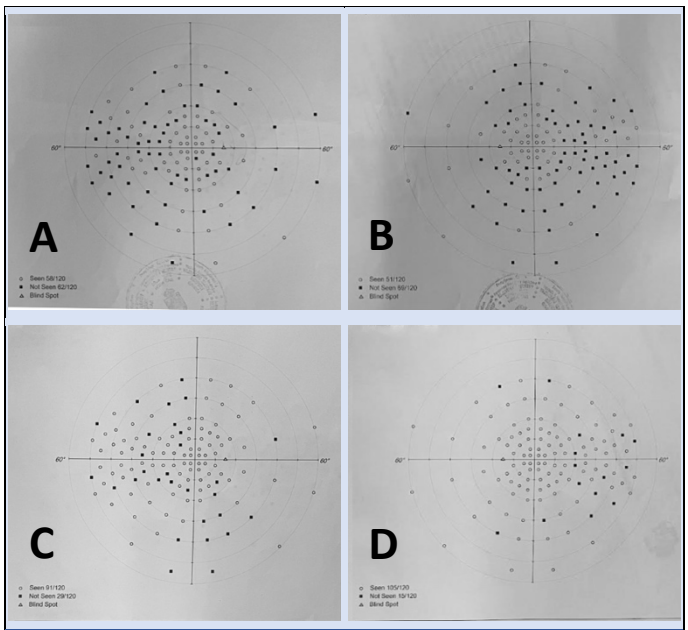
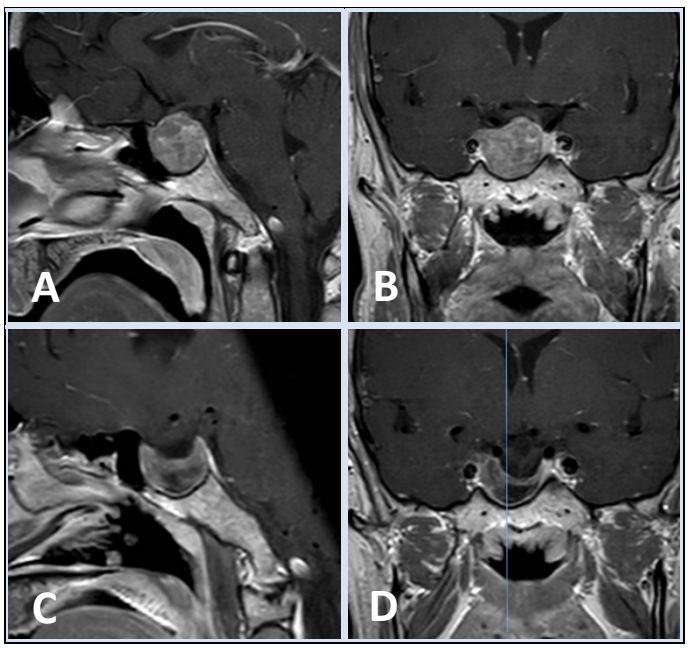


Figure 2. Visual field computerized perimetry **A and B**. prior to surgical treatment;**C and D.** after surgical treatment chiasmopexy



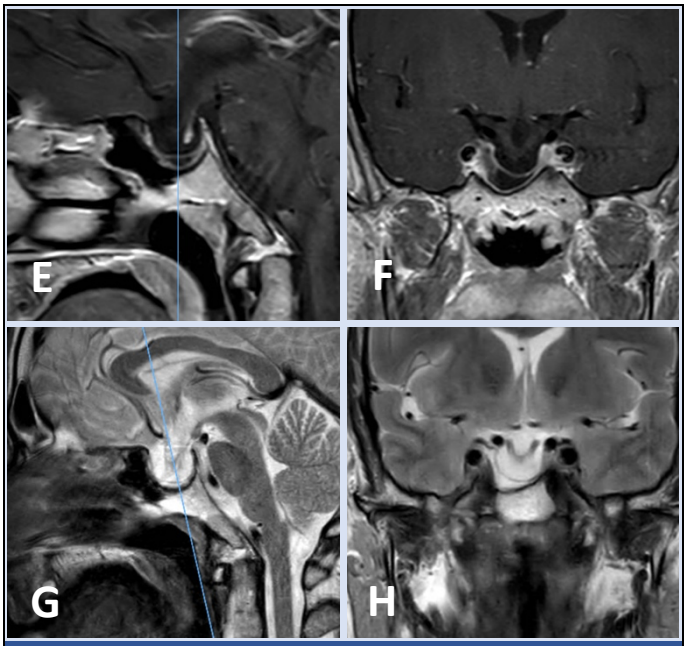


Figure 1. MRI of sellar region (sagittal and coronal): **A and B**. prior to medical management of prolactinoma; **C and D.** 8 months after the initiation of cabergoline treatement; **E and F.** 21 months after the initiation of cabergoline treatement; **G and H.** 4 years after the initiation of cabergoline treatement;

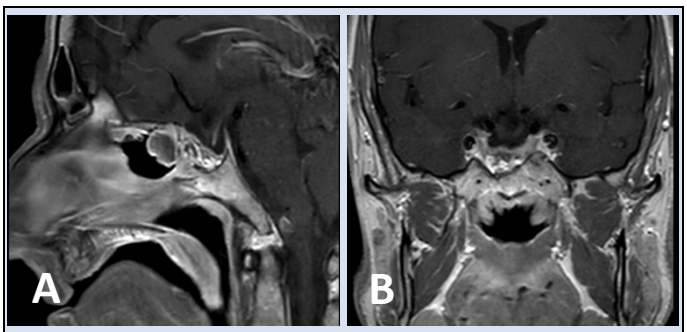


Figure 3. Postoperative MRI imaging of sellar region.

Discussion

Symptomatic SESS after cabergoline treatment for prolactinoma is a rare but challenging complication. The surgical management with chiasmopexy aims to elevate the optic nerves and the chiasm to relieve traction and improve patient symptoms. Over the years, chiasmopexy was performed utilizing different surgical approaches, both intra and extradural, with the use of various materials to stabilize the reposition of the optic system.[8,9,10] Our case demonstrates successful use of attainable autologous material harvested from the septal bone and cartilage during the endoscopic transnasal transsphenoidal extradural chiasmopexy. The nasal septum provides an easily accessible autologous graft site with suitable biomechanical properties of bone and cartilage for stabilizing the optic chiasm.[2,3,11,12] Additionally, the autologous material eliminates the risk of graft rejection and reduces the possibility of postoperative complications.[7,12].

Conclusion

Endoscopic transnasal transsphenoidal extradural chiasmopexy is an effective surgical procedure in terms of visual field improvement of patients with symptomatic SESS after medical treatment of pituitary adenoma. The use of easily attainable autologous grafts excludes the need for synthetic materials, reduces the risk of graft rejection additional donor-site surgeries, and postoperative complications.

Disclosures

Conflict of Interest: All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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