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Clinico-Surgical Outcomes of Giant Intracranial Epidermoids: Gross Total Resection vs Subtotal Resection Which is Better?

Manish BALDIA, Edmond GANDHAM, Krishna PRABHU

Christian Medical College, Vellore, Department of Neurological Sciences, Vellore, India

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Corresponding author: Krishna PRABHU ✉ krishnaprabhu@cmcvellore.ac.in

ABSTRACT

AIM: To analyze the clinical and surgical outcomes following gross total resection (GTR) and planned subtotal resection (STR) of giant intracranial epidermoid tumors.

MATERIAL and METHODS: In this retrospective cohort study, all patients who were diagnosed with and operated for giant intracranial epidermoid tumors between January 2007 and May 2016 were included. The demographics, clinical outcomes, and surgical outcomes of these patients were analyzed.

RESULTS: Forty-eight patients were enrolled in this study, and multicompartmental epidermoid tumors were observed in 23% of the patients. The mean size of the tumors was 6.2 cm (range, 4.0–9.0 cm). GTR and near-total resection (NTR) were performed in 34 (71%) patients. Fourteen patients (29%) underwent STR. Most patients (89%) had Glasgow Outcome Scale (GOS) of 5, whereas 8% had GOS of 4. The GTR/NTR group (23.5%) had more permanent complications than the STR group (7.1%). The mean follow-up period was 5.2 years (range, eight months to nine years). In the STR group, four patients (29%) showed an increase in the residual tumor, and only one patient (7%) was symptomatic and required reoperation.

CONCLUSION: STR of giant intracranial epidermoid tumors is a safe surgical strategy with good surgical outcome. The requirement for reoperation is usually late and seldom required but can be done safely. The average time to recurrence was more than seven years.

KEYWORDS: Giant epidermoid tumor, Gross total resection, Subtotal resection

INTRODUCTION

Intracranial epidermoid tumor is a benign lesion comprising 1% of brain tumors and contains stratified squamous epithelium with keratin deposition (8). Epidermoid tumors can occur in the anterior, middle, and posterior cranial fossae, with the latter being the commonest location. Among all epidermoid tumors, 40%–50% occur in the cerebellopontine angle cistern (8,18,32). In addition, an epidermoid tumor can occur in the suprasellar, interpeduncular, prepontine, and ambient cisterns, interhemispheric fissure, and fourth ventricle. The age distribution of epidermoid tumors is wide, and they can occur at any age but are commonly seen in the middle age group (7). Giant intracranial epidermoid tumors tend to extend into various cisternal spaces and encase major neurovascular bundles. Total excision offers surgical cure but is often difficult due to encasement of neurovascular bundles, brainstem invasion, or proximity to the eloquent cortex (2,15, 18,19,28,31). Many surgeons perform adventurous excisions at the risk of functional outcome. As available literature (1) on outcomes following excision of giant intracranial epidermoid tumors is limited, this study will help us understand the long-term outcomes of subtotal resection (STR).

MATERIAL and METHODS

In this retrospective study, all patients who underwent surgery for a giant intracranial epidermoid tumor (size $\geq$4 cm) between

Manish BALDIA : 0000-0001-8470-0589 Edmond GANDHAM : 0000-0003-1326-4892 Krishna PRABHU : 0000-0002-2644-7201

January 2007 and December 2016 were included. Their demographic data, preoperative clinical signs and symptoms, radiological findings, and distribution were analyzed. Patients who were operated elsewhere and came to our institution for surgery were not included in this study. Gross total resection (GTR)/near-total resection (NTR) involved the removal of 95% of the tumor volume, whereas any excision less than 95% of the tumor volume corresponds to STR. All patients received steroids (4-mg dexamethasone every six hours) postoperatively for three days followed by tapering doses (2 mg every six hours) for another two days, which was stopped thereafter.

Surgical outcomes were assessed using the Glasgow Outcome Scale (GOS) and Karnofsky Performance Scale (KPS). The recurrence and reoperation rates and complications were analyzed. Complications were divided into transient (up to two months) and permanent (more than two months). Follow-up data were obtained from the electronic database and telephonic follow up.

RESULTS

Forty-eight patients were recruited in the study. The mean age of the patients at presentation was 38 years (range, 18–64 years), with the male–female ratio being 1:1. The age distribution is summarized in Figure 1.

Site and size

Among the 48 patients, 19 (40%) had their tumors located in the posterior fossa, 13 (27%) in the middle cranial fossa, five (10%) in the anterior cranial fossa, and 11 (23%) had multicompartmental tumors. The commonest tumor site was the posterior fossa, and the cerebellopontine angle (CPA) cistern was the most common location within the posterior fossa (Figure 2). The mean size of the tumors was 6.2 cm (range, 4.0–9.0 cm).

Clinical Features

The most common presentation was headache, which was experienced by 28 patients (58.3%). Seizures were observed in 15 patients (31.2%). Cerebellar signs were seen in 18 patients (37.5%). Seventh nerve paresis was observed in 11 patients (22.9%) in the posterior fossa group. The clinical features differ among patients based upon the location of the tumors. The signs and symptoms are tabulated in Table I.

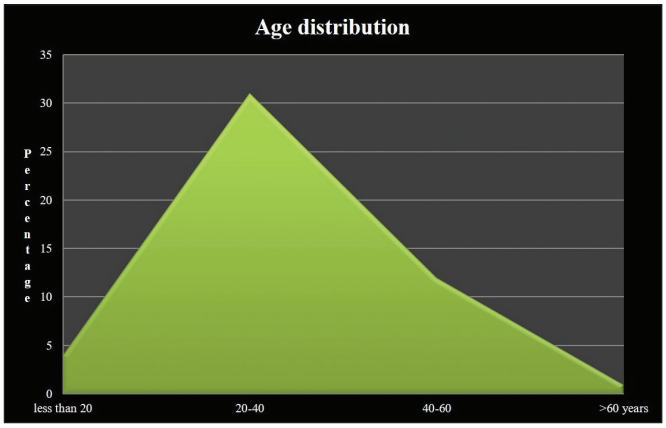

Figure 1: Showing graph of age distribution in our series with the peak incidence in middle age group.

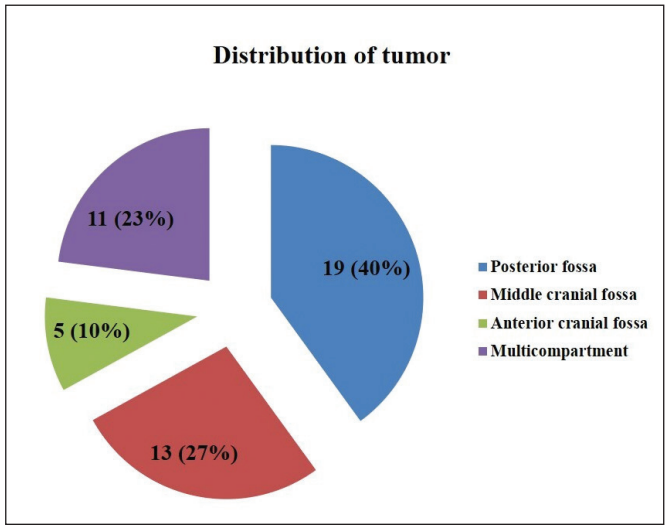

Figure 2: Pie diagram demonstrating the various sites of involvement with posterior fossa being the most common site.

Table I: Showing the Distribution of Symptoms and Signs

Symptoms	No. of patients (n) (%)	Signs	No. of patients (n) (%)
Trigeminal neuralgia	4 (8.3)	5th nerve deficit	9 (18.7)
Double vision	5 (10.4)	Motor deficit	1 (2.1)
Decreased vision	6 (12.5)	Optic nerve deficit	7 (14.6)
Decreased hearing	8 (16.6)	8th nerve deficit	9 (18.7)
Seizures	15 (31.2)	9th and 10th deficit	1 (2.1)
Facial weakness	10 (20.8)	7th nerve deficit	11 (22.9)
Imbalance while walking	10 (20.8)	Cerebellar signs	18 (37.5)
Headache	28 (58.3)		

Radiology

All patients were evaluated preoperatively using brain gadolinium MRI with driven equilibrium radio frequency reset pulse (DRIVE) sequences. The tumors showed the classical features of an epidermoid tumor with diffusion restriction but did not show enhancement. During the immediate postoperative period, the patients underwent plain CT to rule out hematoma. At follow up, all patients underwent plain brain MRI. A representative image from our series is illustrated in Figure 3A-K.

Operative Procedure

Among the 48 patients operated, retromastoid suboccipital craniectomy/craniotomy was the most common surgical procedure for the infratentorial group of tumors. Frontotemporal craniotomy was the most common surgical procedure used in the supratentorial group of tumors. The surgical approaches are summarized in Table II. Standard microsurgical techniques were followed. Peeling the capsule was attempted if it was not adherent to the vital neurovascular structures; if peeling the capsule failed, STR was performed. Cranial nerve monitoring was performed while operating on CPA lesions. We had always found a good arachnoid plane between the capsule and surrounding brain parenchyma in patients who underwent GTR/NTR. The poor arachnoid plane between the capsule and surrounding brain was a deterrent for GTR. No second-stage surgery was performed in our series.

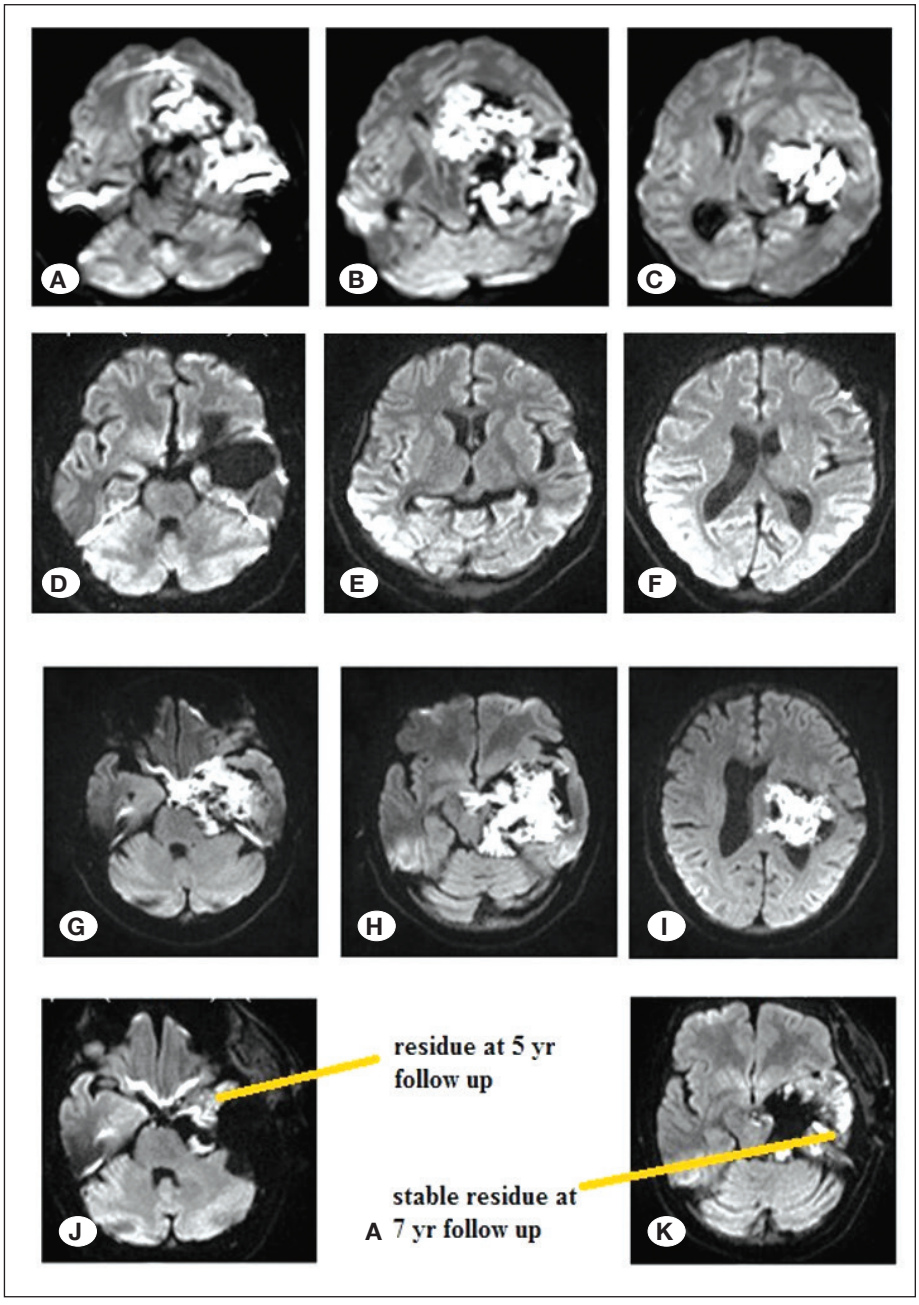

Figure 3: A-C) Demonstrates giant intracranial epidermoids involving middle cranial fossa, **D-F)** 6 year follow-up MRI with DWI sequence showing no residue, **G-I)** preoperative MRI showing giant intracranial epidermoids involving the middle cranial fossa and posterior fossa, **(J)** stable residue at 5 year follow up after STR, **(K)** MRI brain with DWI showing a stable residue at 7 year follow up following STR.

Extent of Resection

Among the 48 patients, 34 (71%) underwent GTR and NTR, whereas 14 (29%) underwent STR. In the STR group, the various reasons that deterred GTR/NTR are summarized in Table III.

Follow up and Outcomes

We had 38 patients (79.2%) on regular follow-ups, and 10 (20.8%) were lost to follow up. The mean duration of follow up was 5.2 years and ranged from 8 months to 9 years. Thirty-four patients (89%) had a GOS of 5. Three patients (8%) had GOS of 4. One patient had a GOS of 3. Among the 27 patients in the GTR group, 24 had GOS of 5 and KPS of 90–100. Ten (91%) of the 11 patients in the STR group had a GOS of 5 and KPS of 90–100. Lesser morbidity was seen in patients who underwent STR, which was not statistically significant (p=0.85). These outcomes are summarized in Table IV.

Table II: Operative Techniques Used in Our Series

Operative procedure	Number of cases (n)
FTOZ	1
Frontoparietal	2
Frontal	5
Frontotemporal	10
Temporal	5
Temporoparietal	3
RMSOC	16
MSOC	5
Occipital	1

FTOZ: *Fronto temporo orbitozygomatic approach,* ***RMSOC:*** *Retromastoid sub-occipital approach,* ***MSOC:*** *Midline suboccipital approach.*

Recurrence and Increase in Residual Size

Six patients had an increase in the residual tumor size; among them, four were in the STR group and two were in the GTR/NTR group. The median time taken for the residual tumor size to increase was seven years (range, 5.5–8.3). Only one patient (7.1%) from the STR group required reoperation as the patient was symptomatic eight years after the first surgery (Table V).

Complications

In this study, among the 48 patients, 19 (39.5%) developed transient postoperative complications, whereas 9 (18.7%) had permanent complications. Postoperative hydrocephalus and seventh nerve paresis along with sixth nerve paresis constituted permanent complications. Worsening of preexisting seventh nerve paresis (n=3) and new-onset sixth nerve paresis were the most common cranial nerve deficits in this study, and there were transient in two patients. Aseptic meningitis was seen in five patients, who improved with the administration of steroids. Cerebrospinal fluid (CSF) diversion was required in 11 (23%) patients, and among them, four (8.3%) and seven (14.5%) were shunted preoperatively and postoperatively, respectively. Transient motor deficits were seen in two patients in the GTR group. The details of the complications are listed in Table VI. We found that the STR group had lesser total complication rates than the GTR/NTR group (42.8% vs. 64.7%, respectively), which was statistically significant (p=0.02).

DISCUSSION

Epidermoid tumor, a benign lesion also known as pearly white tumor of the brain, is composed of stratified squamous

Table III: Tumour Location and Reason for Patients with Subtotal Excision

Site	No. of patients	Excision	Reason
Supratentorial	8	Subtotal	Adherent to neurovascular structures and poor plane with brain, near eloquent cortex
Infratentorial	6	Subtotal	Adherent to neurovascular structures and brain stem

Table IV: Surgical Outcomes of 38 Follow up Patients as Measured by Glasgow Outcome Scale (GOS) and Karnofsky Performance Score (KPS)

GOS and KPS score	No. of patients 38 (79.2%)	GTR/NTR 27 (71%)	STR 11 (29%)
5 (Good, able to return for work) KPS 90-100	34 (89)	24 (89)	10 (91)
4 (Mild disability, independent of daily work but, not able to return for work) KPS -80	3 (8)	2 (7)	1 (9)
3 (Moderate disability- dependent on daily activities) KPS -70	1 (3)	1 (4)	0

GTR: *Gross total resection,* ***STR:*** *Subtotal resection,* ***NTR:*** *Near total resection.*

epithelium (23). Total excision of the tumor offers a complete cure; however, when it is giant and involves various compartments, achieving GTR is difficult. Other than the series of Aboud et al. (1), no studies in the literature have focused on multicompartmental giant epidermoid tumors. This study is the largest series (n=48) of patients with giant epidermoid tumors with (n=38; 79.2%) long-term outcomes. Surgical nuances, the usage of neuronavigation, and endoscopy-assisted microsurgery have been used to achieve GTR; however, encasement of neurovascular structures, adherence to the brainstem, and proximity to the eloquent cortex prevent GTR (8,13,25,26,28,32). Therefore, many authors have considered leaving behind the adherent capsule to preserve them functionally and follow up. Recurrence is possible when leaving behind a capsule, and these cases need long-term follow up (5,14,21,24). However, in the literature, few case reports have focused on the malignant transformation of residual tumors, though the occurrence of malignancy is unusual and rare (4,10,12,20).

Surgical Resection and Recurrence

In our series, 71% of the cases had GTR and NTR, which was comparable to the rates described in the literature (1,9,15,26,33). The remaining 29% underwent STR due to encasement of neurovascular structures, a poor plane with the brainstem, and close proximity to the eloquent cortex. Long-term outcomes of STR were determined by reviewing the literature on STR that had an average follow-up duration of more than four years (Table VII) (1,6,11,15,18,24,26,27, 30-32). A recent meta-analysis on extent of resection and the risk of recurrence by Shear et al. showed a higher recurrence rate (17.4%) for an average follow-up duration of more than 4.4 years than follow-up duration of less than 4.4 years (5.7%). However, in this meta-analysis, they could not delineate symptomatic recurrences and reoperation cases (29). In our literature review, following STR, no reoperations were performed for recurrences in four series with follow-up durations ranging from 4.5 years to 5.7 years (6,11,15,26). In the series of Tancredi et al., seven cases (77.8%) had STR and three (42.8%) of them required reoperation for symptomatic

Table V: Outcomes in 38 Follow up Patients

Type of excision	Increase in residue	Clinically symptomatic	Re-surgery	Outcome (GOS)
GTR/NTR	2	0	0	5
STR	4	1	1	5

GOS: *Glasgow Outcome Scale,* ***GTR:*** *Gross total resection,* ***STR:*** *Subtotal resection,* ***NTR:*** *Near total resection.*

Table VI: Transient and Permanent Postoperative Complication Rates in GTR/NTR and STR

Complications	Overall no. of patients, n=48 (%)	GTR/NTR, n=34 (71%)	STR, n=14 (29%)
Transient			
Cranial nerve deficit	4	2	2
CN VI	2	1	1
CN VII	2	1	1
Aseptic meningitis	5	3	2
CSF leak from the wound	3	2	1
Bacterial meningitis	4	4	0
Motor deficit	2	2	0
Subdural hygroma	1	1	0
Total transient complications	19 (39.5)	14 (41.2)	5 (35.7)
Permanent			
Hydrocephalus	7	6	1
Cranial nerve deficits	2	2	0
CN VI	1	1	0
CN VII	1	1	0
Total permanent complications	9 (18.7)	8 (23.5)	1 (7.1)
Total complications	28 (58.3)	22 (64.7)	6 (42.8)

Table VII: Literature Review of Series with Subtotal Excision and Minimum Follow up of 4 Years

Author and year	No. of sub- total resection (%)	Mean follow up (years)	Recurrence (%)	Re-operation, n (%)	Outcome KPS
Berger and Wilson 1985 (6)	13 (100)	4.5	0	0	NA
Sabin et al. 1987 (24)	23 (91.4)	6	21.73	4 (17)	80-100
Yamakawa et al. 1989 (32)	33 (63.6)	8.83	24.13	6 (18)	NA
Souza et al. 1989 (30)	27 (81.5)	5	14.81	2 (7.4)	NA
Samii et al. 1996 (26)	40 (25)	5.7	7.5	0	90-100
Kobata et al. 2002 (18)	30 (43.3)	11.5	6.6	2 (6.6)	NA
Tancredi et al. 2003 (31)	7 (77.8)	14.5	33.3	3 (42.8)	90-100
Goel et al. 2006 (15)	13 (13.5)	4.3	2	0	90-100
Desai et al. 2006 (11)	24 (75)	5.2	4.2	0	NA
Schiefer and Link 2008 (27)	11 (45.8)	6.2	27	3 (27)	NA
Aboud et al. 2015 (1)	7 (27)	9.2	15.4	4 (57)	80-90
Our series 2020	14 (29)	7	28.6	1 (7.1)	KPS >90-91% KPS 80 -9%
Mean values	51.7%	7.3	16.6	15.3%	

KPS: *Karnofsky Performance Score,* ***NA:*** *Not available.*

recurrence between 10 and 17 years after the first surgery (31). Another series by Aboud et al. reported that seven (27%) cases underwent STR, of them four (57%) had reoperation after a mean recurrence-free period of 10.2 years (1). Similarly, in our series, the reoperation rate was as low as 7.1% with symptomatic recurrence eight years after the first surgery. In the literature review (Table VII), the mean reoperation rate for patients who underwent STR was 15.3% with average follow-up duration of 7.3 years. However, in this study, the mean follow-up duration was only 5.2 years, which might explain the low reoperation rate.

A long asymptomatic recurrence-free period can be explained by the theory that the time taken for a tumor to increase to its initial size is calculated by the patient's age at initial surgery plus nine months, which justifies that STR is a safe surgical option in cases where GTR is unfeasible (3). Patients who underwent STR had good functional outcomes with a mean KPS of 91%, which is comparable to other published series in the literature. These findings favor STR over GTR/NTR. However, the meta-analysis by Shear et al. showed that patients who underwent STR had seven times higher recurrence rate than those who underwent GTR (29). These findings should be kept in mind while operating *de novo* cases. It is important to remember that these tumors are benign and do not raise intracranial pressure and that symptomatic recurrence is late. Knowing the natural history of these tumors and complications associated with GTR, STR would be enough for elderly patients with symptomatic recurrence. Therefore, the decision to perform GTR or STR should be taken from case to case, keeping in mind the natural history of this tumor and seniority of the operating surgeon.

Complications

Most of us attempt to perform GTR as epidermoid tumors are insensitive to radiation and chemotherapy. Evaluating whether GTR has more complications than STR is essential. Lunardi et al. have concluded that STR was associated with no mortality and improved functional outcomes with delayed recurrence (19). Similarly, Samii et al. concluded in their series that GTR for giant and multicompartmental lesions can cause severe neurological deficits (26). We have noticed lesser total complication rates in patients who underwent STR (42.8%) than those who underwent GTR/NTR (64.7%). Moreover, permanent complications were higher in patients who underwent GTR (n=8, 23.5%) than those who underwent STR (n=1, 7.1%). In a recent meta-analysis, Shear et al. also had a higher number of permanent complications in patients who underwent GTR (n=11, 15.5%) than those who underwent STR (n=6, 8.4%). However, they did not look into motor deficits in their meta-analysis, which is mainly observed in patients who underwent GTR as seen in our series (29). Complications such as cranial nerve deficits were observed more in patients who underwent GTR than those who underwent STR (17 vs. 11, respectively) in Shear et al.'s meta-analysis as these deficits usually occur while attempting total tumor removal along with the capsule (29). This clearly demonstrates that the morbidity associated with STR is minimal, making STR a safe strategy for giant epidermoid tumors.

As mentioned in the literature, the occurrence rate of aseptic meningitis is higher in patients who underwent STR (1). In our series, the incidence of aseptic meningitis was approximately 7%, which was comparatively lower than those in other series described in the literature (0%–33.3%) (1,15,19,24,31–33). Aseptic meningitis can be reduced by intraoperative hydrocortisone wash and preventing blood/tumor spillage in the postoperative field. In addition, giving a tapering dose of dexamethasone for five days postoperatively could help prevent aseptic meningitis.

In this study, the most common postoperative complications were postoperative new-onset hydrocephalus, which was observed in seven patients (14.6%), and cranial nerve deficits, which was seen in six patients (12.5%). Four patients (8%) required CSF diversion preoperatively, and seven patients (14%) required shunt surgery postoperatively. Yasargil et al. have performed shunt surgery in 19% of the cases postoperatively, whereas Aboud et al. have performed shunt surgery in 17% of the patients in their series (1,33). In our series, 14% required shunt surgery postoperatively, which was comparable with that in the literature (29). Aseptic meningitis predisposes the patients to secondary hydrocephalus. The incidence of multiple cranial nerve paresis postoperatively was 12.5% in our series, which was dramatically lower than those in other giant tumor series (20%–50%) (1,9,21,29,33).

Malignant Transformation

When performing STR of tumors, surgeons often worry about recurrences and malignant transformation. However, the incidence of malignant transformation in residual epidermoid tumors is low. The first malignant transformation of a epidermoid tumor was reported in 1912 (16). Among the 26 malignant transformations reviewed by Hao et al., 12 were operated and 11 were primarily malignant (17). No mechanism could describe how these tumors undergo malignant transformation (17,19,34). The possible mechanism noted in few residual lesions that turned malignant is the repeated inflammation sustained due to repeated surgeries; however, this does not explain the pathophysiology behind primary malignant epidermoid tumors. Further long-term studies are warranted to study the natural history of these subtotally excised tumors. The treatment recommended for malignant transformation is GTR followed by adjuvant radiation therapy and chemotherapy (22).

Limitations

The main limitation of this study was its retrospective design, and the mean follow-up duration was 5.2 years. This study was a large series of giant epidermoid tumors; however, long-term follow-up data were obtained only in 79.2% of the cases.

CONCLUSION

Giant multicompartmental epidermoid tumors are difficult to totally excise, and STR is acknowledged as an alternative treatment modality for these tumors in the perspective of functional preservation as the symptomatic recurrence rate is low and late. An average duration for symptomatic recurrence is greater than seven years.

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