Turk Neurosurg 30(2):171-177, 2020

Original Investigation

DOI: 10.5137/1019-5149.JTN.24341-18.3

Received: 24.07.2018
Accepted: 07.11.2018
Published Online: 15.04.2019

Clinicopathological Features and Microsurgical Management of Lesions Located in the Cavernous Sinus: Analysis of 66 Cases

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ABSTRACT

AIM: To investigate the clinicopathological features and related factors affecting microsurgical resection of lesions in the cavernous sinus.

MATERIAL and METHODS: Clinical data of 66 patients undergoing microsurgery for lesions located in the cavernous sinus from January 2011 to December 2017 were retrospectively reviewed.

RESULTS: Histopathological examination revealed benign lesions in 60 (90.9%) patients, the most common histopathological types were meningiomas, schwannomas, and cavernous hemangiomas. Only six (9.1%) patients had malignant lesions. The gross total resection rate was 33%, subtotal resection rate was 21%, substantial partial resection rate was 26%, and partial resection rate was 20%. Factors influencing the extent of lesion resection included the presence of cavernous sinus syndrome prior to surgery, the size of the lesion, the site of origin, and the surrounding of the internal carotid artery, all of which detrimentally influenced total excision ($p<0.05$).

CONCLUSION: Most lesions involving the cavernous sinus are histopathologically benign. Preoperative cavernous sinus syndrome, the size of the lesion, the site of origin, and the surrounding of the internal carotid artery all detrimentally influence the extent of lesion resection.

KEYWORDS: Cavernous sinus, Pathological features, Microsurgery

ABBREVIATIONS: CS: Cavernous sinus, **ICA:** Internal carotid artery

INTRODUCTION

The cavernous sinus (CS) is located on both sides of the cranial fossa and is a relatively large and irregular lacuna situated between two layers of dura mater. The CS contains venous blood; the internal carotid artery; and cranial nerves III, IV, V, and VI. It is a major site of intracranial lesions. The CS is considered to be a risky site to operate due to its complex anatomical structure (13,15). In an early study, not only was the mortality rate associated with CS hemangiomas 5% following microsurgery, but also cranial neuropathies at discharge worsened in 76.9% and 83.3% of patients who underwent treatment with the epidural and intradural approaches, respectively (14). A recent report described four (1.71%) patients with an internal carotid artery injury and one (0.4%) patient who died from a tumor of the CS that had been treated by advanced endoscopic endonasal surgery (4). Consequently, tumors involving the CS continue to pose a formidable challenge for skull base surgeons due to the confluence of critical neurovascular structures surrounded by the complex bony topography in these closely associated anatomical areas (8,12). In this study, we investigated a series

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of 66 patients with lesions involving the CS. We retrospectively analyzed the clinicopathological features and related factors affecting the extent of microsurgical resection of the lesions.

MATERIAL and METHODS

Clinical Manifestations

From January 2011 to December 2017, a total of 66 patients with CS lesions who underwent surgery were enrolled in this study (26 male and 40 female patients; age range: 6–68 years; mean age: 47 years). During this period, another 8 patients (3 male and 5 female patients; age range: 31-65 years; mean age: 49 years) with CS lesions were treated by gamma knife alone due to small lesions and inconspicuous symptoms of CS syndrome, and were therefore not enrolled in the study.

Prior to surgery, all patients provided written informed consent to undergo the surgery and for to have their data and samples used for research purposes. The present study was approved by the Ethics Committee of Zhengzhou University and conducted in accordance with the Helsinki Declaration.

Among all patients, 36 had CS syndrome and 30 had nonspecific symptoms. Details of the patients' clinical symptoms are shown in Table I. All patients underwent conventional 3.0T enhanced magnetic resonance imaging. The lesions were located on the left side in 37 patients and on the right side in 29 patients. Lesion diameters ranged from 1.7 to 7.7 cm, averaging 3.5 cm. Moreover, 48 patients had lesions that originated and grew within the CS, 14 patients had lesions that originated in the lateral wall of the CS and grew to the middle cranial fossa, and 4 patients had lesions that originated in the saddle and developed into unilateral CS tumors. The internal carotid artery was surrounded by the lesion in 40 patients but was only compressed by the lesion in 26 patients.

Surgical Methods

One of five potential surgical approaches was selected based on the site of origin and surgeon's experience. These include the pterion approach, subtemporal (hook incision) approach, modified subtemporal approach (approximately 8-cm oblique incision starting from the lower edge of the zygomatic arch midpoint), transnasal sphenoidal approach, or breaking of the zygomatic pterion (Figure 1). Based on the criteria described in previous literature (7), resection via an intradural approach was mainly used for lesions that involved the lateral compartment of the CS, lesions that had crossed the CS to involve the middle fossa floor, or for lesions that had secondarily involved the CS. The epidural approach was used in 6 patients while the intradural approach was used in 55 patients. In addition, five patients underwent an extended transnasal sphenoidal approach.

Follow-Up

Follow-up neurological examination and enhanced magnetic resonance imaging were performed at 3 months postoperatively and every year thereafter. The follow-up duration ranged from 1 to 84 months (average: 36 months).

Statistical Analyses

The presence of CS syndrome, lesion site of origin, lesion

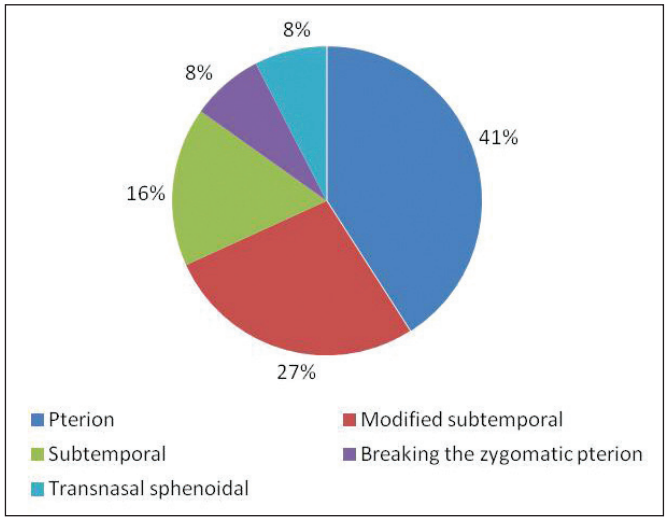

Figure 1: Distribution as percentages of different surgical approaches.

Table I: Clinical Manifestations in 66 Cases Involved in Cavernous Sinus

Cavernous Sinus Syndrome (+) n=36	Cranial nerve symptoms: 34 cases	III:	Ptosis,Eyeball fixed
		IV:	Diplopia
		V:	Facial numbness Sensation diminished
		VI:	Exterior disorders, Diplopia
	Ocular venous reflux disorder: 7 cases		Orbital pain Eyeball congestion Eyeball prominent
Cavernous Sinus Syndrome (-) n=30			Headache Eyesight decreased Dizziness

size, lesion texture, whether the internal carotid artery was surrounded, surgical approach, and extent of successful lesion removal were assessed by univariate analysis using SPSS 22.0 statistical software (IBM Corp., Armonk, NY, USA). A Mann–Whitney U test or Kruskal–Wallis one-way analysis of variance was performed, with lesion sizes classified as ordinal (using quartiles for the four categories). The linear chi-square test for trend was also used. Statistical significance was set at $p<0.05$.

RESULTS

Postoperative Pathology

Benign lesions were observed in 60 patients, including 20 meningiomas, 14 schwannomas, 14 cavernous hemangiomas, 5 pituitary adenomas, 3 epidermoid cysts, 1 dermoid cyst, 1 chondroma, 1 mature teratoma, and 1 aneurysm. Malignant lesions were observed in six patients, including five brain metastases (from the lung in four patients and from the kidney in one) and one chordoma (Figures 2A-H; 3A-H; 4A-H, Table II).

Extent of Surgical Removal and Related Factors

Five different surgical approaches were adopted for the CS lesions (Figure 5). The gross total resection rate was 33%, subtotal resection rate was 21%, substantial partial resection rate was 26%, and partial resection rate was 20%. In this series of patients, 12 patients with partial resection received gamma

Table II: The Percentage of Pathological Features of Cavernous Sinus Lesions in all 66 Cases

Benign cases	**n (%)**
Meningiomas	20 (30.3)
Schwannomas	14 (21.2)
Cavernous hemangiomas	14 (21.2)
Pituitary adenomas	5 (7.5)
Epidermoid cysts	3 (4.5)
Dermoid cysts	1 (1.5)
Chondroma	1 (1.5)
Mature teratoma	1 (1.5)
Aneurysm	1 (1.5)
Malignant cases	**n (%)**
Brain metastases	5 (7.5)
From Lung	4 (6.0)
From Kidney	1 (1.5)
Chordoma	1 (1.5)

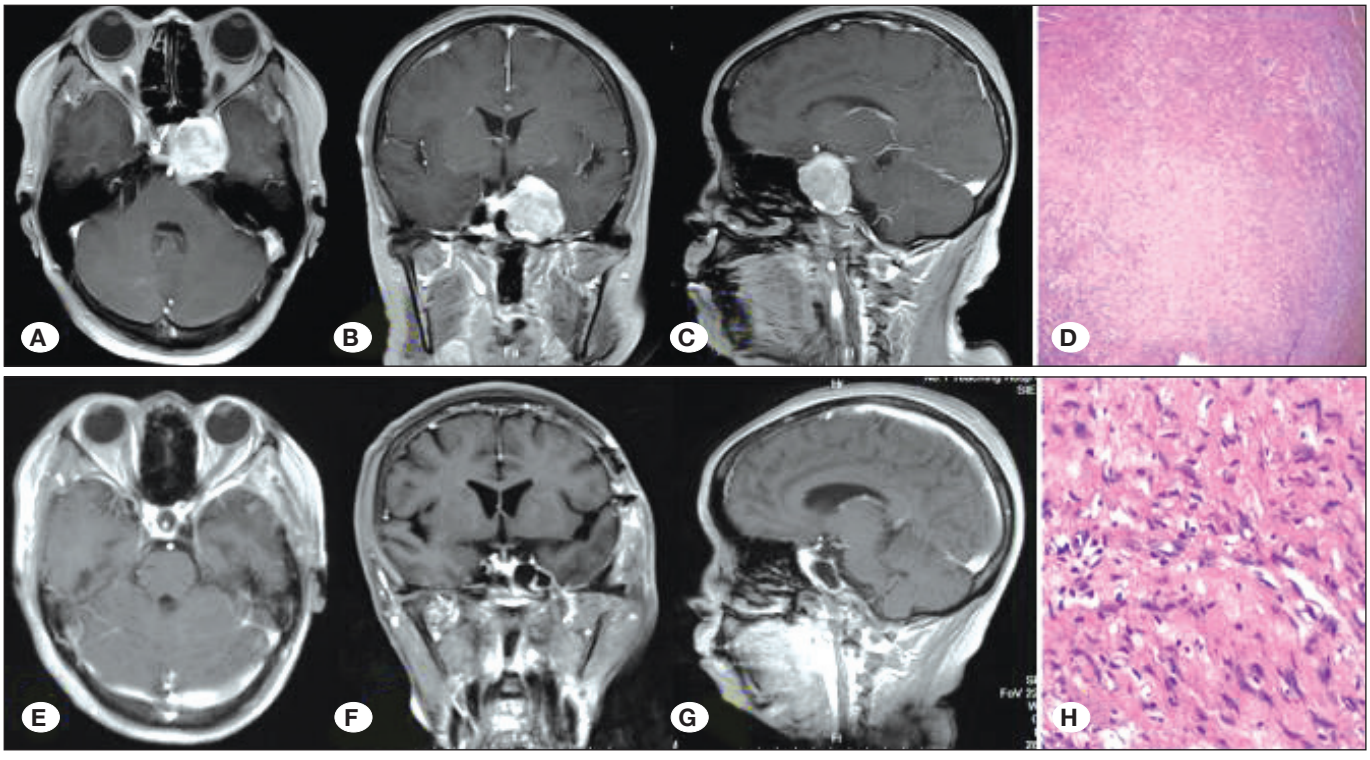

Figure 2: Preoperative contrast enhanced MRI showed, in axial **(A)**, coronal **(B)** and sagittal **(C)** images, that the cavernous sinus lesion was significantly uniform and enhanced. Three months after surgery, MRI with contrast showed that the lesion had grossly been totally resected **(E-G)**. Hematoxylin Eosin staining (Light Microscopy) (**D:** x200, **H:** x400) suggested the presence of a schwannoma.

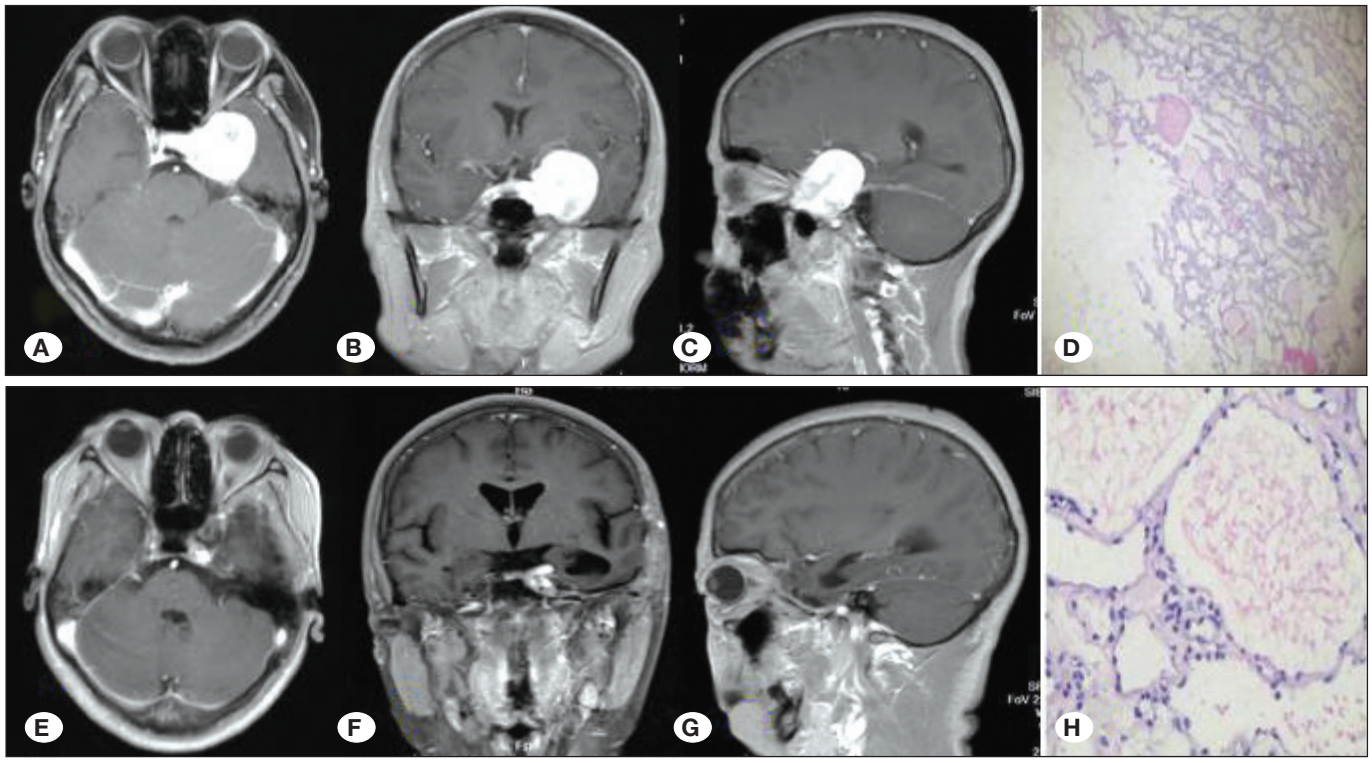

Figure 3: Preoperative contrast enhanced MRI showed, in axial **(A)**, coronal **(B)** and sagittal **(C)** images, that the cavernous sinus lesion was significantly uniform and enhanced. Three months after surgery, MRI with contrast showed that the lesion had been grossly totally resected **(E-G)**. Hematoxylin Eosin staining (Light Microscopy) (**D:** x200, **H:** x400) suggested the presence of a cavernous hemangioma.

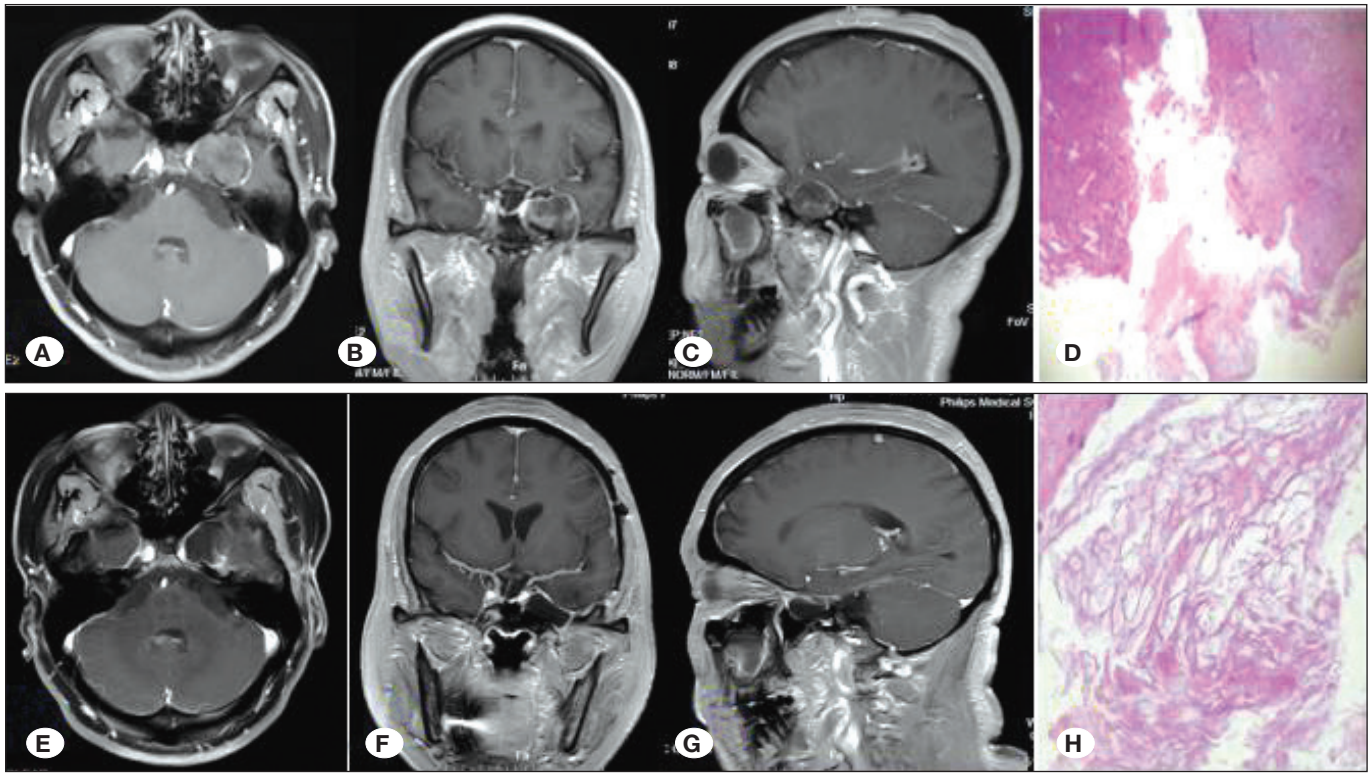

Figure 4: Preoperative contrast enhanced MRI showed, in axial **(A)**, coronal **(B)** and sagittal **(C)** images, that the cavernous sinus lesion was not enhanced. Three months after surgery, MRI with contrast showed that the lesion had been grossly totally resected **(E-G)**. Hematoxylin Eosin staining (Light Microscopy) (**D:** x200, **H:** x400) suggested the presence of epidermoid cysts.

knife adjuvant radiotherapy 3 months after surgery. These included 4 meningioma cases, 3 schwannoma cases, 2 cases cavernous hemangioma cases, 2 invasive pituitary adenoma cases, and 1 chordoma case. During the follow-up period, all residual tumors showed no significant progression, and all showed stable or reduced size. Two residual meningioma patients developed a headache and cerebral edema after receiving gamma knife treatment and were relieved with corticosteroid drugs and mannitol. None of the 12 cases showed any deterioration in cranial nerve dysfunction.

The factors influencing the extent of lesion resection included the presence of CS syndrome before surgery, size of the lesion, site of origin, and the surrounding of the internal carotid artery, all of which detrimentally affected total excision ($p<0.05$). However, there was no difference based on lesion consistency or surgical approach ($p>0.05$; Table III).

Postoperative Complications

No death or serious complications occurred postoperatively. However, postoperative complications occurred in 19 patients, 18 of whom showed postoperative cranial nerve function defects mainly due to oculomotor nerve damage causing ptosis and abductor nerve damage causing ocular motility disorders. Another patient had one seizure occurrence following surgery.

Follow-up Results

All patients underwent a regular follow-up every 3 months for the first 12 months and about once a year thereafter. Postoperative CS syndrome was significantly improved compared to preoperative conditions (28/36, 77.8%). Postoperative complications were reduced or had disappeared after the 6-month follow-up. Twelve patients underwent postoperative gamma

Table III: Related Factors Influencing Resection Degree of Cavernous Sinus

Factors	PR	SPR	STR	GTR	Z/c2	p
CS syndrome					-2.225/-	**0.026**
Presence	9	13	6	9		
Absence	4	4	8	13		
Lesion diameter (mm)					-/4.127	**0.042**
<28.6	0	4	3	9		
28.6-32.2	5	4	4	3		
32.2-40.1	3	5	4	7		
>40.1	5	4	3	3		
Site of origin					2.302/-	**0.021**
CS internal	12	14	12	13		
CS lateral wall	1	3	2	9		
Lesion consistency					0.014/-	0.993
Hard	3	2	2	4		
Medium	6	14	10	13		
Soft	4	1	2	5		
Surgical approach					5.724/-	0.221
Pterion	6	9	7	5		
Modified subtemporal	3	5	1	9		
Subtemporal	3	3	1	4		
Breaking the zygomatic	0	0	2	3		
Transnasal sphenoidal	1	0	3	1		
ICA surrounded					-6.107/-	**0.000**
Presence	13	16	9	2		
Absence	0	1	5	20		

PR: *Partial resection,* ***SPR:*** *Substantial partial resection,* ***STR:*** *Sub-total resection,* ***GTR:*** *Gross-total resection,* ***CS:*** *Cavernous sinus,* ***ICA:*** *Internal carotid artery.*

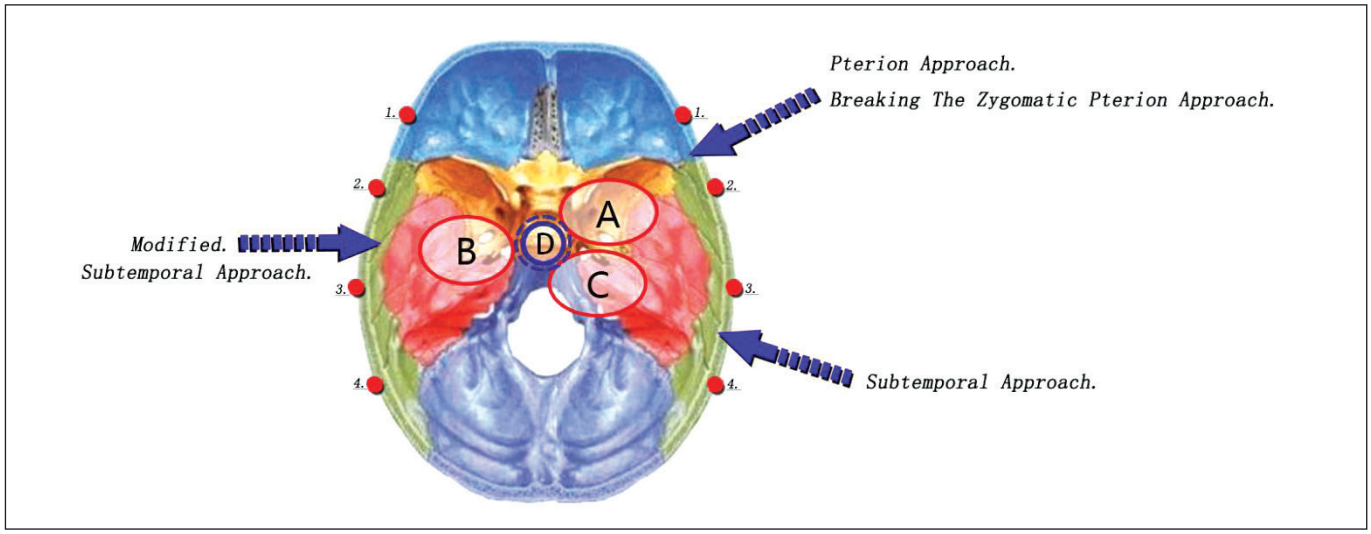

Figure 5: Diverse surgical approaches used for lesion resection. **Lesion A:** Adopt "Pterion Approach" or "Breaking the Zygomatic Pterion Approach". **Lesion B:** "Modified Subtemporal Approach". **Lesion C:** Adopt "Subtemporal Approach". **Lesion D:** Adopt "Transnasal Sphenoidal Approach".

knife irradiation but showed no signs of significant residual tumor progression.

DISCUSSION

The CS, a pentahedral structure, is located on both sides of the cranial fossa. The outer wall consists of the outer dura, and the inner layer is formed from the sheath of cranial nerves III and IV. The lower wall is lined by periosteum, and the other walls are formed by dura mater. The CS contains venous blood; the internal carotid artery; and cranial nerves III, IV, V, and VI (15). Not only can CS lesions compress or surround the internal carotid artery and cranial nerves, but they can also invade adjacent anatomical structures in different directions. CS lesions can grow through the lateral wall toward the middle cranial fossa, invade the orbit through the superior orbital fissure, extend beyond the petrous apex into the petroclival and cerebellopontine angle areas, invade the sella, and move inward into the sphenoid sinus cavity (9). Microsurgery of lesions involving the CS is therefore very risky due to this complex anatomical structure. However, evaluation of this series of 66 CS lesions revealed several striking features. First, the clinical manifestations of CS lesions involved CS syndrome in 36 (54.5%) patients. Second, the pathological examination revealed benign lesions in 60 (90.9%) patients, the most common histopathological types being meningiomas, schwannomas, and cavernous hemangiomas. Third, five different surgical approaches were adopted in this study and the optimal surgical approach was selected based on the origin and direction of growth of the lesion as well as the surgeon's experience. Consequently, no death or serious complications occurred following operation in our patients. Finally, we identified four factors that detrimentally affected the extent of lesion resection, including preoperative CS syndrome, the size of the lesion, the site of origin, and the surrounding of the internal carotid artery.

Many types of lesions may affect the CS, the predominant histopathological category being benign lesions (3,5,10). Benign lesions accounted for 90.9% of all lesions in our study. The most benign types were meningiomas (30%), schwannomas (21%), and cavernous hemangiomas (21%), followed by invasive pituitary adenomas, epidermoid cysts, dermoid cysts, chondromas, mature teratomas, and aneurysms. Metastases are the most common malignant lesions in the CS, and most originate from the lungs (2). Few reports to date have described CS metastases. Six patients in this study had malignant lesions. With the exception of one chordoma, the remaining five lesions were brain metastases (four of which originated in the lung and one of which originated in the kidney).

In addition, our results indicated that preoperative CS syndrome, the size of the lesion, the site of origin, and the surrounding of the internal carotid artery all detrimentally influence the extent of lesion resection. CS syndrome mostly manifests as cranial nerve dysfunction and ocular venous reflux obstruction (6). In this study, cranial nerve dysfunction occurred in 34 (53%) patients, while exophthalmos, eyeball congestion, and ocular pain caused by ocular venous reflux obstruction affected 7 (11%) patients. If the lesion is small and only present within the CS, function of a single cranial nerve may be disrupted, but when the lesion is larger or shows extensive invasive growth, the function of multiple cranial nerves may be affected. Larger tumors often affect sinus reflux, causing orbital venous reflux disorders and intracranial hypertension. If the tumor originates from the lateral wall of the CS or if the tumor has a tough texture (e.g. meningioma or schwannoma), it will often pass and squeeze the cranial nerves and internal carotid artery. However, if the lesion originates in the sinus or has a soft texture (e.g. epidermoid cyst or pituitary adenoma), it will often invade and surround the cranial nerve and internal carotid artery (1,11). Therefore, preoperative CS syndrome, lesion size, the origin in the CS, and the surrounding of the

internal carotid artery are interrelated factors affecting the extent of CS lesion resection. Surgery should be performed to remove the lesion while safely retaining the nerve function.

CS lesions should be individually approached through several different avenues . Nanda et al. described four approaches to CS meningiomas: frontotemporal orbitozygomatic, frontotemporal craniotomy with orbital osteotomy, frontotemporal, and extended middle fossa transpetrous approaches (7). Based on our experience, the appropriate approach should be selected mainly based on the extent and characteristics of involvement of adjacent structures. In brief, the surgical approach should consider not only the surgeon's experience but also the location of the lesion, direction of growth, type of tissue, and other factors to minimize brain damage and ensure adequate exposure. To this end, five surgical approaches were used in our series based on the craniotomy location: pterion, breaking of the zygomatic pterion, modified subtemporal, subtemporal, and transnasal sphenoidal approaches. When the lesion is located in the CS and extends into the sphenoid ridge and middle cranial fossa, both the pterion approach or breaking of the zygomatic pterion are appropriate. When the lesion is located in the middle cranial fossa and invades the petroclival or cerebellopontine angle area, both the modified subtemporal approach or subtemporal approach are suitable; the tentorium cerebelli can be simultaneously cut to obtain good surgical exposure. If the lesion originates in the saddle, invades the bilateral CS, and grows into the sphenoid sinus, the transnasal sphenoidal approach should be prioritized.

For CS lesions that have a rough texture and adhere closely to the cranial nerve and internal carotid artery, radical excision is dangerous and associated with unacceptable morbidity and mortality. Since a conservative surgical approach with adjuvant radiotherapy for residual lesions is already effective, we do not encourage gross-total resection to sacrifice cranial nerve function. We do encourage, however, removing most of the lesion according to a deliberately selected individualized surgical approach, sufficiently exposing the lesion while retaining small pieces of the lesion closely adhering to the cranial nerve and internal carotid artery. Residual lesions could be treated with gamma knife adjuvant radiotherapy 3 months after surgery to control tumor progression and improve patient quality of life.

CONCLUSION

Most CS lesions are benign, and our findings suggest that the most common histopathological categories are meningiomas, schwannomas, and cavernous hemangiomas. Preoperative CS syndrome, lesion size, site of origin, and the surrounding of the internal carotid artery all significantly contribute to poor total resection. In the presence of such compromising factors, a balance between neuroprotective features and maximum tumor removal needs to be carefully optimized. This study suggests that both an individual selection of the most appropriate surgical approach and a precise assessment of the negative factors affecting the extent of resection play vital roles in the surgical results of CS lesions.

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