

Original Article

Clinical features and prognosis of cerebellopontine angle cholesteatoma in 54 patients

Yong Deng*, Yanming Ren*, Chenghong Wang, Yuekang Zhang

Department of Neurosurgery, West China Hospital of Sichuan University, Chengdu, Sichuan Province, PR China.

*Equal contributors and co-first authors.

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Abstract: Objective: To summarize our experience with clinical features and prognosis of cerebellopontine angle (CPA) cholesteatoma and to explore the optimal surgical strategy. Patients and Methods: We performed a retrospective review of all patients (N = 54) diagnosed with CPA cholesteatoma from January 2014 to January 2018 at West China Hospital of Sichuan University. The clinical characteristics of the patients, surgical consequences, and follow-up results were analyzed. Results: The mean time span from initial symptoms to surgery was 2.9 years. Before surgery, there were 44 cases of cranial nerve (CN) dysfunction, 10 cases of headache, 5 cases of gait instability, and 1 case of epilepsy. Total removal was achieved in 27 patients, and the other 27 patients experienced near/subtotal removal. In 13 patients, new/aggravated CN dysfunction occurred, and 6 of these patients developed permanent CN dysfunction. New/aggravated CN dysfunction was associated with total removal (χ^2 , $P = 0.011$, respectively). During the mean 32-month follow-up period, no patients developed recurrence. Conclusion: Cholesteatoma in CPA is a disease mainly characterized by CN dysfunction, especially trigeminal neuralgia. Aggressive total resection may increase postoperative neurological dysfunction. Therefore, near/subtotal resection is a more optimal choice, especially for those tumor capsules closely adhering to nearby nerves and vessels.

Keywords: Cholesteatoma, cerebellopontine angle, clinical features, cranial nerve dysfunction, risk factors

Introduction

Cholesteatoma, also known as an epidermoid cyst, it is a rare lesion of ectodermal origin, accounting for approximately 0.2% to 1% of all intracranial tumors [1, 2].

Among intracranial cholesteatomas, about 40% occur in the cerebellopontine angle (CPA), an area containing cranial nerves (CNs), brain stem, cerebellum, and arteriovenous vessels [3-5]. Because cholesteatomas are insensitive to radiation and chemotherapy, surgical resection is the current treatment standard [6]. However, it is extremely difficult for neurosurgeons to completely remove the tumor without any impairment to the neurovascular structures because the tumors are usually involved in these vital neurovascular structures, especially the capsules of the tumors, which adhere densely. Although there have been some reports on CPA cholesteatoma, the main clinical manifestations and prognosis detailed in the

literature have not been exactly consistent, especially in terms of the effect of the different extent of resection on postoperative CN function [2-4, 7, 8]. The purpose of this study is to report our experience of the clinical features and prognosis of CPA cholesteatoma.

Materials and methods

Patients

We collected data from all patients who had a postoperative pathological diagnosis of cholesteatoma located in the CPA at the West China Hospital of Sichuan University from January 2014 to January 2018. All perioperative information of the cholesteatoma patients was collected from the medical records.

Neuroimaging

All patients underwent preoperative head magnetic resonance imaging (MRI) or head computed tomography (CT) [9]. On CT scan, choles-

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teatoma often presents as a hypodense lesion without enhancement. Moreover, a cholesteatoma typically exhibits a hypodense signal on T1-weighted MRI and a hyperintense signal on T2-weighted MRI, which is similar to the signal of the cerebrospinal fluid. Because the tumor lacks blood vessels, there is usually no enhancement on contrast-enhanced T1 images or with only slight edge enhancement. On diffusion-weighted imaging, the tumor presents a distinct hyperintense signal, which is different from the cyst signal, and it is used to differentiate the tumor from an arachnoid cyst but not routinely before surgery.

Surgical management

The subtemporal approach or the retrosigmoid approach was performed for CPA cholesteatoma. When the CPA area was exposed, the tumor capsule was then cut open, and the contents in the capsule were removed alternately by aspiration and washing. Finally, the tumor capsule was removed according to the degree of adhesion between the capsule and the neurovascular structures. Total resection was defined as the removal of the entire capsule and the keratin inside the capsule. If all the keratin was removed and some of the capsules adhered to the neurovascular remains, it was considered to be a near total resection. If the capsule and the contents of the capsule were partially residual, it was considered to be subtotal resection.

During resection, patients were under intraoperative neurophysiological monitoring: somatosensory evoked potentials, motor evoked potentials, auditory evoked potentials, as well as the functions of CNs V, VII, and X to XII.

All patients were treated with dehydrating agents to relieve postoperative cerebral edema and with glucocorticoids to prevent aseptic meningitis.

Follow-up

We completed the postoperative follow-up by reexamination of neuroimaging or by telephone. MRI was carried out in patients without contraindications at 2 days, 3 months, and 1 year after surgery, respectively, and then once a year was recommended. A CT scan was performed when MRI was not available. The postoperative complications of the patients were

based on the pre-discharge results. Preoperative symptom relief and postoperative permanent neurological dysfunction were observed 1 year after operation. According to the results of postoperative CN function, we classified all patients into 4 grades with excellent/good/fair/poor outcome scales. The patient was classified as excellent if the postoperative symptoms were significantly relieved after operation or there was no postoperative CN dysfunction, good if moderately relieved, fair if mildly relieved or no remission, and poor if aggravated or patients developed new CN dysfunction.

Data collection and analysis

The following patient information was collected: age, gender, hemisphere of tumor, tumor size, brainstem compression or not, hydrocephalus, the extent of resection, surgical approach, presence of preoperative CN (III-XII) dysfunction, duration of symptoms, and duration of surgery. We also extracted any other postoperative complications, including hematoma, acute hydrocephalus, and recurrence.

Patients who developed new/aggravated CN dysfunction were defined as group A, and the others who did not develop new/aggravated CN dysfunction were defined as group B. We used chi-squared test or Fisher's exact test to analyze whether new/aggravated CN dysfunction was associated with age, gender, diabetes, presence of preoperative CN dysfunction, side of operation, tumor size, surgical approach, extension (CPA alone or extension to other areas), duration of surgery, compression of brainstem, hydrocephalus, and the extent of resection. Statistical analysis was performed with SPSS software, version 24.0. Continuous variables were described by the mean (range), and classified variables were described by percentages. When the two-sided *P* values were <0.05, the difference was considered significant.

Results

Baseline characteristics

From January 2014 to January 2018, 54 patients were diagnosed with cholesteatoma by postoperative pathological examination in our institute, including 36 females and 18 males, with a female/male ratio of 2:1. Their ages at symptom onset ranged from 5 to 75 years

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Table 1. Patient characteristics

Features	Patients (N = 54)
Age at surgery (years)	43
Gender	
Male	18
Female	36
Side of tumor	
Left	28
Right	24
Left + right	2
Duration of symptom (years)	2.9
Brainstem compression	38
Hydrocephalus	12
Surgery approach	
Retrosigmoid approach	49
Subtemporal approach	5
Extension of tumor	
Unilateral CPA	26
CPA + slope expansion	16
CPA + foramen magnum expansion	5
CPA + supratentorial expansion	5
Bilateral CPA	2

CPA, Cerebellopontine Angle.

(mean 37.9 years), with onset in 48% of patients (n = 26) occurring during their third to fifth decades of life. Patient age at surgery ranged from 18 to 78 years (mean 40.8 years). The mean duration of symptoms from onset to operation was 2.9 years (range, 1 month to 50 years). There were 24 cases of right-sided tumor, 28 cases of left-sided tumors, and 2 cases of bilateral CPA tumors. The general characteristics of the patients are summarized in **Table 1**.

Neuroimaging and approach

All patients underwent preoperative head MRI, except one patient who had undergone head CT due to internal fixation of the tibiofibular fracture. There were 26 cases of unilateral CPA cholesteatoma, 16 cases of slope expansion, 5 cases of foramen magnum expansion, 5 cases of supratentorial expansion, and 2 cases of expansion to the contralateral CPA. Brainstem compression (defined as brainstem compression by one-third or more) due to the tumor mass effect was observed in 38 patients. Twelve patients developed obstructive hydrocephalus preoperatively.

Table 2. Preoperative presentations

Presentation	Patients (N = 54)
Headache	10
CN dysfunction (III, IV, VI)	5
Double vision	5
CN dysfunction (V)	
Trigeminal neuralgia	27
Facial numbness	6
CN dysfunction (VII)	
Facial spasm	2
Facial weakness	4
CN dysfunction (VIII)	
Tinnitus	5
Hearing deficit	13
Lower CN dysfunction	2
Gait instability	5
Seizures	1

CN, cranial nerve.

According to the extension of tumor in radiologic examinations, 5 cases of supratentorial expansion were removed via the subtemporal approach and the rest via the retrosigmoid approach. Bilateral CPA cholesteatoma was operated in stages, with priority given to the side with more severe symptom. The above information is contained in **Table 1**.

Clinical features

Details of preoperative clinical manifestations are shown in **Table 2**. Among the 54 patients, 44 (81.5%) presented with CN dysfunction before surgery, which was the most common presenting symptom. Of the 44 patients there was a total of 64 CN impairments; 33 patients (51.6%) had trigeminal nerve dysfunction, 18 patients (28.1%) had tinnitus or hearing loss, 6 patients (9.4%) had facial palsy or spasm, 5 patients (7.8%) had diplopia, 2 patients (3.1%) had lower CN dysfunction, and 12 patients had more than one CN impairment. Other clinical manifestations included headache (n = 10), gait instability (n = 5), and seizures (n = 1).

Prognosis and recurrence

Of the 54 patients, 27 (50.0%) achieved total resection, and near or subtotal resection was performed in the others. Close adhesion of tumor capsules to neurovascular structures usually resulted in failure of total resection.

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Table 3. Surgical outcomes

Surgical outcome	Before discharge	1 year after surgery
Excellent	33	41
Good	4	5
Fair	4	1
Poor	13	7

Table 4. Postoperative complications

Complication	Patients (N = 13)
Temporarily new/aggravated CN deficits	
CN V	
Hypoesthesia	5
Mastication weakness	1
CN VI	2
CN VII	
Facial paralysis	5
CN VIII	
Hearing deficit	3
Tinnitus	1
CN IX-XII	2
Permanent CN deficits	
CN VII	
Facial paralysis	4
CN VIII	
Hearing deficit	1
Lower CN dysfunction	1
Hematoma	2
Aseptic meningitis	2
Recurrence	0

CN, cranial nerve.

Before discharge, 33 patients (61.1%) were classified as excellent, 4 patients (7.4%) as good, 4 patients (7.4%) as fair, and 13 patients (24.1%; including 11 patients with new neurological dysfunctions after surgery and 2 patients with aggravated CN dysfunctions) as poor (**Table 3**). Among the 13 patients, 6 had facial hypoesthesia, 5 had facial paralysis (House-Brackmann II-IV), 4 had hearing loss or tinnitus, 2 had exceptional abductor palsy, and 2 had lower CN dysfunction (**Table 4**). Temporarily new/aggravated CN dysfunction was associated with total removal (χ^2 , $P = 0.011$, respectively). There were no significant differences in age, gender, diabetes status, presence of preoperative CN dysfunction, side of tumor, tumor size, surgical approach, location

(CPA alone or extension to other areas), duration of surgery, compression of brainstem, and hydrocephalus between patients with and without temporarily new/aggravated CN dysfunction (**Table 5**).

Postoperative neurological dysfunction was usually temporary. After 1 year, 41 patients (75.9%) were classified as excellent, 5 patients (9.3%) as good, 1 patient (1.9%) as fair, and 7 patients (12.9%) as poor. Six patients developed permanent neurological dysfunction. Among the 6 patients, 4 had facial paralysis (House-Brackmann II), 1 had hearing loss, and 1 had lower CN dysfunction (**Table 3**).

In addition, 2 patients developed postoperative hematoma. In 1 patient, hematoma clearance was carried out, and conservative treatment after evaluation was implemented in the other patient. Both patients recovered well (MRS scores = 1). Two patients developed aseptic meningitis despite the use of prophylactic steroid. There was no death, acute hydrocephalus, or intracranial infection in the patients after surgery. No recurrence was observed during the follow-up period (**Table 4**).

Discussion

The incidence of cholesteatoma had been reported to be 9.2 per 100,000 in adults [9]. CPA cholesteatoma is the third most common tumor in the CPA, secondary to acoustic neuroma and meningioma, but it accounts for only about 4% to 8.2% of tumors in this region [2, 10]. To our knowledge, this is one of the largest sample sizes for CPA cholesteatoma. This study retrospectively analyzed our experience with clinical features and surgical outcomes of 54 patients with CPA cholesteatoma at our center.

Clinical features

Consistent with our results, trigeminal neuralgia is considered the most common form of CN dysfunction before operation in most of the literature [2, 4, 7, 11]. However, in a meta-analysis of 263 patients, it was reported that hearing loss was the most common symptom of CN dysfunction, followed by trigeminal neuralgia, which was different from our findings [3]. This discrepancy may be explained by the following reasons. First, as indicated by Koichi Iwasaki, race may play a role in this difference [3, 12].

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Table 5. Univariate analysis of risk factors for new/aggravated CN dysfunction

Variable	Patients with new/aggravated CN dysfunction		P value
	Yes (n = 13)	No (n = 41)	
Gender			0.910 ^a
Male	4	14	
Female	9	27	
Age (years)			0.321 ^b
≥ 60	0	5	
< 60	13	36	
Diabetes mellitus			1 ^b
Present	0	1	
Absent	13	40	
Tumor size (cm)			0.150 ^a
≥ 3	7	13	
< 3	6	28	
Preoperative CN dysfunction			0.939 ^a
Present	11	33	
Absent	2	8	
Brainstem compression			1 ^a
Yes	9	29	
No	4	12	
Hydrocephalus			0.640 ^a
Yes	4	8	
No	9	33	
Side of operation			0.991 ^a
Right	6	19	
left	7	22	
Surgery approach			1 ^a
Subtemporal approach	1	4	
Retrosigmoid approach	12	37	
Extension of tumor			0.429 ^a
Unilateral CPA alone	8	18	
CPA + expansion	5	23	
Duration of operation (hours)			0.457 ^a
≥ 3	12	32	
< 3	1	9	
Extent of removal			0.011 ^a
Total removal	11	16	
Near/subtotal removal	2	25	

CN, cranial nerve; CPA, Cerebellopontine Angle. ^aChi-square test. ^bFisher's exact test.

From this perspective, our result was similar to those of other Asian studies [2, 3, 13], and different from those of Caucasians [4]. Second, there is a difference in the length of the root entry zone, a vulnerable area of the CN. Anatomical study confirmed that the trigeminal nerve has a longer REZ, which means that the trigeminal nerve is more susceptible to violation [14]. In addition, as reported by Guidetti,

Dandy who believed that trigeminal neuralgia was the typical symptom of CPA cholesteatoma compared with hearing impairment [11].

As for the etiological factors of CN dysfunction caused by CPA cholesteatoma, the following three may account for it: (1) Many authors disclosed that the tumor mass effect results in distortion of the REZ and ischemia because of

compression of the neurotrophic vessels. (2) In cases in which the tumor completely encloses the nerve, local irritation of cholesterol exudate is assumed to be the cause of pain. (3) The tumor may have pushed nerves toward the blood vessels of REZ because of strong adhesion or compression [3]. In addition, permanent neurological impairment was attributed to neurological ischemia caused by extensive adhesions of the tumor [6, 7]. Therefore, microvascular decompression prior to the ischemic events may improve clinical outcomes [15].

Surgical outcomes of CNs

The rate of improvement of neurological function after surgery varies from 54% to 97% among studies in the literature [2, 4, 16, 17]. The difference is not only among the different centers but also among different CNs. Sam-Safavi-Abbasi believed that the function of the trigeminal nerve could recover well after decompression, while the functional recovery of CN VIII was not obvious, which was consistent with our result [17]. This difference may be attributed to the shorter duration from symptoms onset to surgery in patients with trigeminal nerve dysfunction. Trigeminal nerve dysfunction mostly manifests as trigeminal neuralgia. This unbearable pain shortens the duration from symptom onset to surgery to even 1.5 years, which is associated with better surgical outcomes [2, 18, 19].

The extent of removal and new/aggravated CN dysfunctions

Although most patients usually obtain relief from preoperative symptoms after surgery, a few patients developed aggravated primary symptoms and even experienced new postoperative complications after the operation [4, 13, 17, 20, 21]. Among these postoperative complications, CN dysfunction is the predominant one [5]. The relationship between the extent of resection and postoperative new/aggravated CN dysfunction is still controversial. On one hand, some authors have deemed this to be related to aggressive total resection of the tumor, especially resection of the part of the tumor capsule that is compact and adhered to the nerve [4, 7, 10, 19]. On the other hand, some others have suggested that total resection could reduce postoperative aseptic meningitis and the recurrence rate without increasing

postoperative mortality or disability [13, 22]. The following two points may provide an explanation for this difference. First, there are differences in the level of surgery as a result of different hospitals, surgeons, and long time spans in these studies. Second, the rarity of cholesteatoma makes it quite difficult for most studies in the literature to obtain a sufficient sample size. Thus, it is difficult to reach a final conclusion. Although most of the postoperative neurological impairments can recover spontaneously, some patients still develop permanent neurological dysfunctions. Therefore, we believe that radical total resection still needs prudent consideration, especially for tumors that are tightly attached to nearby nerves and vessels.

Perioperative risk factors for postoperative new/aggravated CN dysfunctions

Aside from total excision, which was thought to increase the incidence of postoperative new/aggravated CN dysfunctions, the strong adhesion between the tumor capsule wall and the nerve may also be one of the risk factors that results in the inevitable nerve injury and even permanent neurological dysfunction during surgical resection of the capsule wall [6]. This conclusion is also supported by the fact that cystic acoustic neuromas have poorer neurological function than solid acoustic neuromas [23, 24].

The presence of preoperative neurological dysfunction was also regarded as one of the causes of CN dysfunction [10]. However, different CNs have different responses to surgical decompression, leading to confounding factors in research that may differ from our results. A more scientific design may be necessary.

It was reported that a history of radiation therapy was a risk factor for postoperative CN dysfunction after surgery for pituitary adenoma [25]. For CPA cholesteatoma, however, with the popularization of MRI, few patients are misdiagnosed and treated with radiotherapy, so we could not collect enough cases to analyze this topic.

Other postoperative complications

The recurrence rate of cholesteatoma ranges from 0% to 34% in the literature [3, 16, 20]. No recurrence was observed during the follow-up period in our study. This may be related to our

short follow-up period. The relationship between the extent of resection and the recurrence rate remains controversial. A 20-year experience revealed that there was no evident difference between the two in the recurrence rate [4]. It was reported that partial removal increased the rate of recurrence after a long follow-up period because the tumors are slow growing [26]. Thus, they thought that total excision was a better option because it did not increase the rate of disability and it could reduce the rate of recurrence. On the contrary, some centers believed that it is extremely difficult to remove the tumor completely without causing any damage to the surrounding neurovascular structures. Therefore, aggressive subtotal resection, including the nonadherent portion of the capsule, may be a better approach [16, 22]. Combined with our findings, the latter approach may be more satisfactory after weighing the advantages and disadvantages.

Two patients with postoperative hemorrhage may have been related to active removal of the capsule from the blood vessel. Postoperative observation and timely treatment resulted in no new disability due to hematoma.

Aseptic meningitis is a common complication after cholesteatoma resection, which is caused by the entry of highly irritating residual cyst contents into the arachnoid space. Preventive measures for acute aseptic meningitis include removal of the capsule as much as possible, washing the CPA with hydrocortisone solution, and prolonged use of steroids postoperatively [5, 10, 11, 27].

Study limitations

Because of the small sample size, it is difficult for us to stratify the data in detail to reduce confounding or complete multivariate regression analysis to further identify the risk factors. Hearing tests are not routinely performed on all patients unless they report hearing impairment or physical examination reveals hearing impairment. This raises the risk of missed diagnosis. In addition, because of the different postoperative rehabilitation management styles of patients and relatively good outcomes, the risk factors of permanent neurological dysfunction were not discussed in this paper. A multicenter prospective study with a larger sample size and a longer follow-up period is necessary to confirm our conclusions.

Conclusion

We found that cholesteatoma in CPA is a disease mainly characterized by CN dysfunction, especially trigeminal neuralgia. Most patients usually achieve relief from preoperative symptoms after surgery, and the function of CN V is easier to recover than that of other CNs. Total resection may increase postoperative neurological dysfunction. Therefore, aggressive near/subtotal resection, including the nonadherent portion of the capsule, is a more optimal choice, especially for those tumor capsules closely adhering to nearby nerves and vessels.

Disclosure of conflict of interest

None.

Address correspondence to: Yuekang Zhang, Department of Neurosurgery, West China Hospital of Sichuan University, 37 Guoxue Alley, Chengdu 610041, Sichuan Province, PR China. Tel: +86-010-88659000; E-mail: 2012zykyx@sina.cn

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