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Epidermoid cysts of the cerebellopontine angle: Clinical features and treatment outcomes

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ABSTRACT

Objective: To report clinical characteristics, treatment outcomes and risk of recurrence in patients with surgically treated cerebellopontine angle epidermoids.
Methods: In 1994–2013, we operated 17 patients, including 7 with tumor limited to the cerebellopontine angle, 7 with cerebellopontine angle tumor penetrating supratentorially, and 3 with cerebellopontine angle tumor extending along skull base to contralateral cerebellopontine angle. All patients were followed-up for the mean duration of 126 months.
Results: On admission cranial nerve symptoms predominated. Total tumor removal was achieved in 5 patients, and incomplete removal (with small tumor remnants left on vessels, nerves, or brainstem) in 12 patients. Postoperatively, preoperative deficits worsened in 2 and new postoperative deficits occurred in 10 patients. The extent of tumor expansion had no effect on postoperative morbidity and risk of recurrence. During long-term follow-up, improvement or resolution of preoperative deficits was seen in 11 of 17 patients, and new postoperative deficits in 8 of 10 patients. Symptomatic recurrences after an average of more than 9 years were noted in 5 patients, 3 of whom were reoperated. Recurrences occurred in some younger patients and always in area of primary tumor. No effect of extent of tumor removal on risk of recurrence was found.
Conclusions: The extent of tumor removal had no effect on the risk of recurrence, and thus it may be acceptable to leave tumor capsule fragments adhering closely to nerves, vessels, or brainstem. During long-term follow-up, resolution or improvement of present preoperatively and new postoperative neurological deficits may be expected in most patients.

1. Introduction

Epidermoid cysts are benign, usually congenital brain tumors, that are formed between 3 and 5 weeks of fetal life due to abnormal trapping of ectodermal cells, later developing into the epidermis, within the nervous tissue during neural tube closure. During the same period of embryogenesis, the otic and optic vesicles are also being formed, and inclusion of ectodermal cells within these structures results in the most

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common intracranial location of epidermoids, i.e. in the cerebellopontine angle and in the parasellar region [1,2]. It is suspected, that cysts located within the fourth ventricle result from ectodermal cell misplacement before neural tube closure, and cysts located epidurally or within the diploe are formed after neural tube closure [1]. The incidence of epidermoid cysts has been estimated at about 1% of all brain tumors [1,3]. Nearly half of them occur in the cerebellopontine angle and they are the third most common brain tumors in this location after schwannomas and meningiomas, comprising 5–7% of tumors in this region [1–4].

Epidermoid cysts are lined with stratified squamous epithelium overlying a connective tissue lamina that closely adheres to the pia mater and is anatomically indistinguishable from the latter. These tumors, being located in the subarachnoid space, when they grow and spread, fill subarachnoid cisterns, encompassing the nerves and vessels, much less frequently displacing them. Only after the all available spaces like cisterns, fissures, ventricles are filled, a space-occupying lesion effect ensues. Tumor growth results mostly from desquamation of epithelial cells inside the cyst, forming pearly, shiny debris, and also cholesterol and keratin secretion into the cyst [1,2,4,5]. These tumors grow very slowly, and hence the duration of symptoms often spans many years [3,4,6,7].

In computed tomography (CT), epidermoid cysts are difficult to distinguish from normal spaces with cerebrospinal fluid, and their presence may be suspected based on a finding of an abnormal space-occupying non-enhancing mass with signal density slightly higher compared to that of the cerebrospinal fluid [1–5]. Identification of calcifications within the tumor, which are present in 10–25% of cases, may be helpful in diagnosis [1–3,5]. Hyperdense epidermoid cysts are seen in 3% of cases, related to previous intracystic hemorrhage, high protein content, or saponification of keratinized debris to calcium soaps [1]. However, the imaging method of choice is magnetic resonance imaging (MRI) with diffusion-weighted imaging (DWI) sequence [2,4,8,9]. In most cases, epidermoid cysts are hypointense in T1-weighted images, with a signal intensity intermediate between the cerebrospinal fluid and the brain, and are markedly hyperintense in T2-weighted images, iso- or slightly hyperintense relative to the cerebrospinal fluid signal [3–6,8–10]. In FLAIR sequence, their signal does not attenuate completely, unlike the cerebrospinal fluid signal. DWI is most important for the diagnosis and differentiation from other lesions, mostly arachnoid cysts, as the content of the epidermoid cysts show prominent diffusion restriction (i.e. they are markedly hyperintense in DWI) due to layered microstructure of the debris [2,4,6,8]. The CISS sequence is also useful, clearly showing nerves and vessels within the tumor [1]. Previously heavy-T2-weighted images were used for this purpose [2,9]. Minimal contrast enhancement within the cyst capsule is seen in one fourth of epidermoids [1,9].

2. Material and methods

Between 1994 and 2013, 17 patients were operated due to an epidermoid cyst of the cerebellopontine angle, including 11 women and 6 men. In all cases, preoperative brain MRI was performed, in the recent years also using the DWI sequence. Tumor size was assessed based on their largest dimension in MRI, which ranged from 30 to 83 mm (mean 54.3 mm, median 50 mm). Based on MRI and intraoperative findings, cerebellopontine angle epidermoids were divided into three groups: tumors limited to the cerebellopontine angle ($n = 7$) (Fig. 1), tumors located in the cerebellopontine angle and extending supratentorially ($n = 7$) (Fig. 2), tumors located in the cerebellopontine angle and extending along the skull base to the contralateral cerebellopontine angle ($n = 3$) (Fig. 3). Clinical condition of the patients before the surgery and at discharge was evaluated based on the presence of neurological deficits, whereas long-term outcomes were evaluated based on both: the presence of neurological deficits and the modified Rankin scale [11]. As some patients, mostly those operated many years ago, did not undergo early postoperative MRI, evaluation of the completeness of tumor removal was based mostly on the assessment by the operating surgeon. Long-term follow-up data were obtained in all patients. Duration of follow-up ranged from 16 to 184 months, with mean 126 months. A long-term follow-up MRI was performed in all patients. Recurrence was defined as meeting both conditions: tumor recurrence or progression of residual tumor in neuroimaging studies and at the same time exacerbation of preexisting or occurrence of the new neurological deficits.

The aim of the study was evaluation of treatment outcomes in patients with cerebellopontine angle epidermoids, taking into account preoperative patient's condition and evolution of new postoperative neurological deficits, and evaluation of the risk of recurrence.

Statistical analysis was performed using the Statistica, ver. 12.0 (StatSoft) including basic descriptive statistics, the Student t-test and contingency tables with the Pearson Chi-square test and the exact Fisher test. $p \leq 0.05$ was considered statistically significant.

3. Results

3.1. *Patient symptoms*

Patient age on admission ranged from 17 to 60 years, with mean 39 years. Duration of symptoms ranged from 50 days to 11 years, with mean 3 years, and was longer than one year in half of patients. All operated tumor were symptomatic, and vertigo was the most common initial symptom (Table 1).

On admission, cranial nerve symptoms predominated, including hearing impairment ($n = 10$), vertigo ($n = 8$), facial nerve paresis ($n = 7$), lower cranial nerve paresis ($n = 7$). Table 3 shows all symptoms and signs present on admission along with their changes at discharge from hospital and during long-term follow-up.

3.2. *Surgical treatment*

The goal of surgical treatment was complete removal of the tumor with its capsule. However, if it was difficult to separate the capsule in places where it adhered closely to nerves, vessels or the brainstem, small fragments of the capsule were left to avoid the risk of serious neurological deficits due to

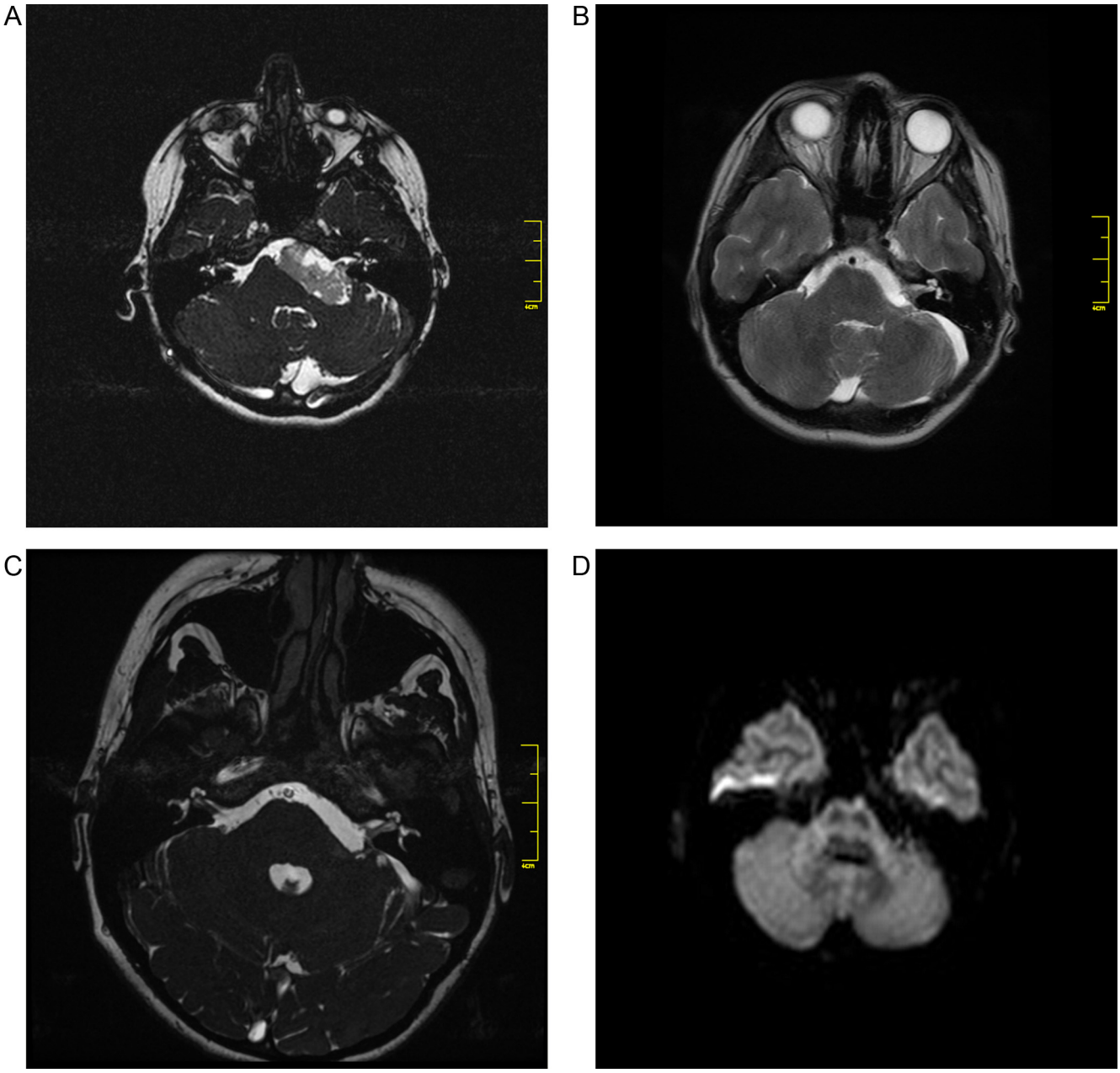

Fig. 1 – Preoperative axial MR examination in CISS sequence (A) demonstrating epidermoid cyst limited to the left cerebellopontine angle. Last follow-up MR examination obtained after complete resection shows no recurrence in T2-weighted image (B), 3D-FIESTA (C) and DWI (D) sequences.

inadvertent damage to these structures. During the surgery all arachnoid cisterns, which had been filled by growing tumor, were sequentially opened and tumor was removed successively from these spaces. The operative field was repeatedly flushed with Ringer solution at the end of the operation. Tumors were removed completely in 5 patients (29.4%), while excision was not complete, i.e. with tumor remnants left on vital structures, in the remaining patients. No effect of the extent of tumor removal on the risk of recurrence was found (p = ns).

In case of tumors limited to the cerebellopontine angle, a retrosigmoid suboccipital approach was used. In patients with supratentorial tumor extension, retrosigmoid suboccipital approach was performed in 3 cases, and a one-stage combined supra- and infratentorial approach was used in the other 4 patients. In patients with tumor spreading to the contralateral cerebellopontine angle, two-stage surgery was planned, with retrosigmoid craniotomy on the site of the major tumor mass as the first stage, and contralateral surgery as the second stage. However, contralateral retrosigmoid suboccipital approach was ultimately performed in only one of the 3 patients with the tumor extending to the contralateral cerebellopontine angle. One patient did not consent to the second stage of surgical treatment and the tumor was stable

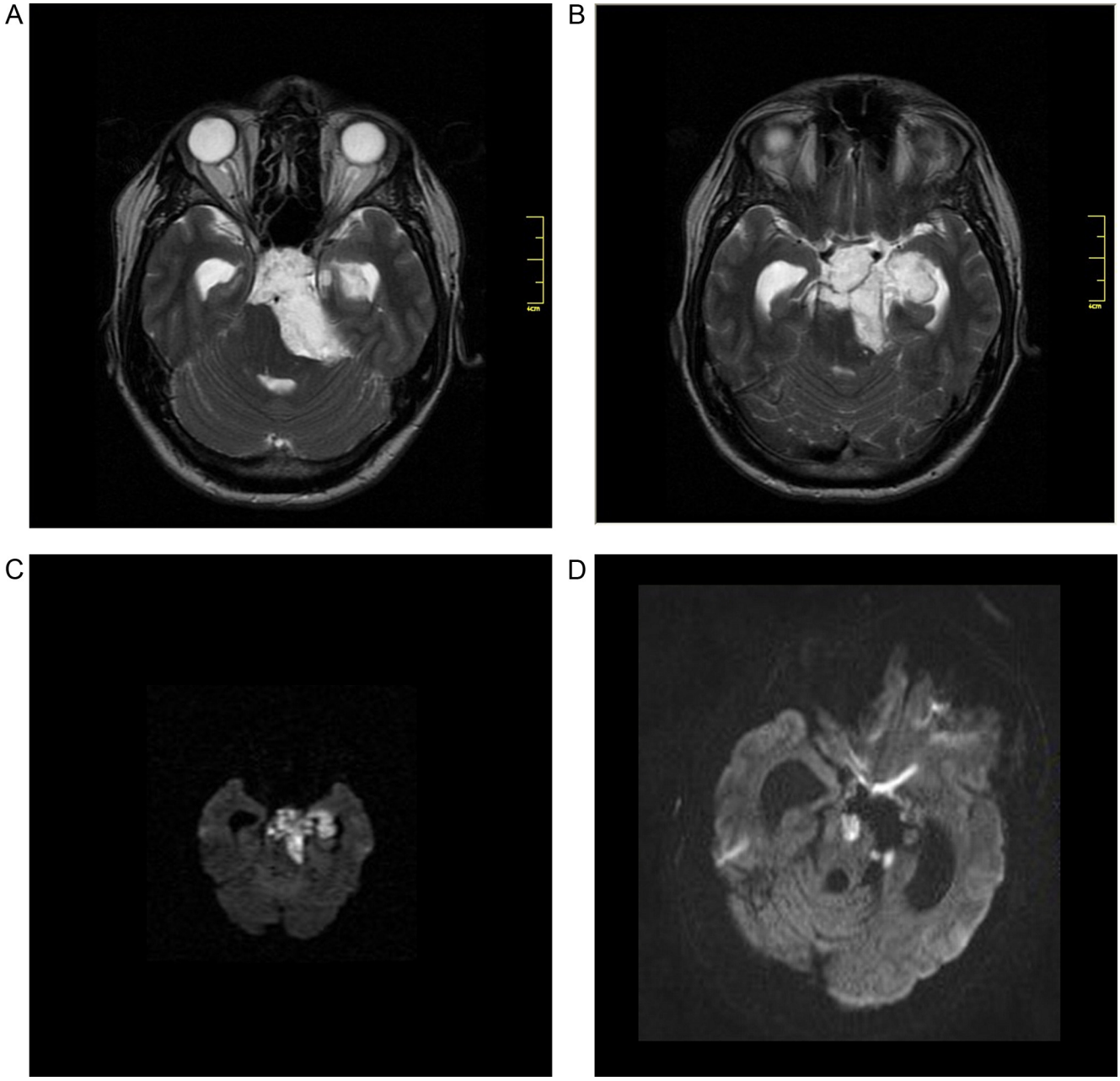

Fig. 2 – Preoperative MR examination in T2-weighted images (A,B) and DWI sequence (C) revealing epidermoid cyst located in the left cerebellopontine angle and extending supratentorially. Last follow-up MR obtained after incomplete tumor removal shows stable tumor remnants in DWI sequence (D).

during follow-up, and in another patient, a recurrence was noted after 32 months and he underwent two operations, the first one targeted at the contralateral tumor progression, and the second one to remove a recurrent tumor at the site of the primary surgery.

In all patients, high dose steroids were used for 2 weeks after the surgery to reduce the risk of aseptic meningitis, which developed in one patient. None of the patients died after the surgery. At discharge, preoperative neurological deficits were found to increase in 2 patients, and new deficits occurred postoperatively in 10 patients.

The extent of tumor expansion had no effect on the risk of an exacerbation preoperative deficits or occurrence new postoperative deficits (p = ns), and the risk of recurrence (p = ns). Total removal was most commonly possible with tumors limited to the cerebellopontine angle (Table 2).

3.3. *Evaluation of neurological deficits in the early and late period*

Before the surgery, neurological symptoms and signs were present in all patients. They worsened after operation in

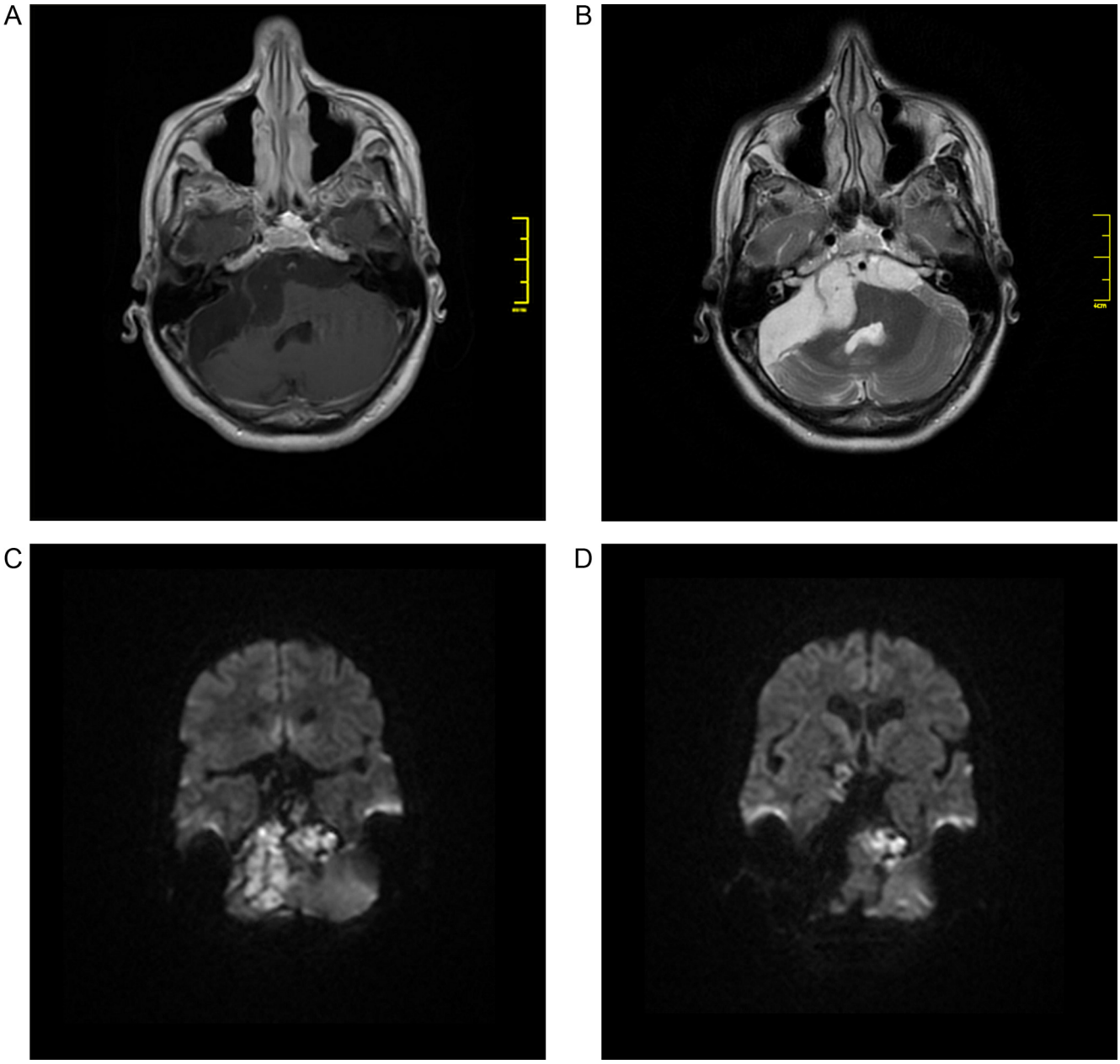

Fig. 3 – Preoperative MR examination in contrast enhanced T1-weighted (A) and T2-weighted (B) images as well as in DWI sequence (C) revealing epidermoid cyst located in the right cerebellopontine angle and extending along the skull base to the contralateral left cerebellopontine angle. After tumor removal in the first stage from the right side, patient did not consent to the second stage of surgical treatment and part of the tumor on the left side was stable during follow-up – MR image in DWI sequence (D).

2 patients (11.8%), including peripheral facial nerve paresis that progressed to a complete palsy in one patient, and hypoacusis that progressed to deafness in one patient. During long-term follow-up, an improvement compared to the preoperative status was mostly seen, with complete resolution of preoperative neurological symptoms and signs in 6 patients (35.3%), and their reduction in 5 patients (29.4%). In 5 patients (29.4%), neurological symptoms and signs remained similar to the preoperative status, and they worsened in one patient (5.9%). The incidence of present preoperatively neurological symptoms and signs at the moment of the discharge, and at long-term follow-up are shown in Table 3.

New neurological deficits occurred postoperatively in 10 (58.8%) patients. They were transient in the most of patients and in long-term follow-up resolved completely in 6 patients, improved significantly in 2 patients, and remained at an unchanged level in only 2 patients. Evolution of new neurological deficits is summarized in Table 4.

In long-term follow-up, 6 patients had no disease symptoms (modified Rankin score 0), 9 patients had mild symptoms

Table 1 – Initial symptoms of the disease.

Initial symptom	Number (%) of patients
Vertigo	6 (35.3%)
Trigeminal neuralgia	2 (11.8%)
Hearing impairment	2 (11.8%)
Seizure	2 (11.8%)
Headaches	1 (5.9%)
Dysphagia	1 (5.9%)
Hemiparesis	1 (5.9%)
Diplopia	1 (5.9%)
Hemianopsia	1 (5.9%)

Table 2 – The effect of the extent of tumor expansion on completeness of the excision.

Extent of tumor expansion	Complete removal	Incomplete removal
Limited to the cerebellopontine angle	4	3
Located in the cerebellopontine angle with extension supratentorially	0	7
Located in the cerebellopontine angle with extension to contralateral cerebellopontine angle	1	2

Chi-square Pearson test, $p = 0.06$

and were able to carry out all usual duties and activities (modified Rankin score 1), and only 2 patients had slight disability and were unable to carry out all previous activities, but were able to look after own affairs without assistance (modified Rankin score 2).

3.4. *Recurrences*

According to our criteria, a recurrence was found in 5 patients from 32 to 152 months after the surgery (with mean more than 9 years). Three patients were reoperated. One patient did not consent to reoperation, and one was disqualified due to presence of numerous serious comorbidities. Recurrences occurred in younger patients, i.e. with mean age 36.2 years vs. 41.5 years in those without a recurrence (p = ns) and always in the area of the primary tumor. New neurological deficits occurred in all three reoperated patients, but these had no effect on further patients functioning (modified Rankin score 1).

4. Discussion

Epidermoid cysts become symptomatic within a wide age range, i.e. between 20 and 60 years with a peak incidence about

Table 3 – The incidence of present preoperatively neurological symptoms and signs at the moment of the discharge, and in long-term follow-up.

Neurological symptoms and signs present preoperatively	Before the surgery	At the moment of the discharge	In long-term follow-up
Hypoacusis/deafness	10/0	9/1	5/1
CN VII paresis/paralysis	7/0	1/1	1/1
CN IV paresis	1	1	1
Facial hypoesthesia	3	1	0
Masseter weakness	1	0	0
CN IX–X paresis	5	2	1
CN XII paresis	2	1	0
Trigeminal neuralgia	2	0	0
Epilepsy	2	2	1
Hemiparesis	3	1	1
Dysmetria	3	1	0
Hemihypoesthesia	1	0	0
Hemianopsia	1	1	1
Vertigo	8	2	2
Headache	5	0	0

CN, cranial nerve.

Table 4 – The incidence of new neurological deficits immediately after the surgery, at the moment of the discharge, and in long-term follow-up.

New postoperative neurological deficits	Occurrence after the surgery	Present at the discharge	Present in long-term follow-up
Hypoacusis/deafness	1/1	1/1	1/1
CN VII paresis/paralysis	4/0	3/0	2/0
CN IV paresis	3	3	1
Facial hypoesthesia	1	1	1
CN IX–X paresis	4	2	1
CN III paresis	1	0	0
CN VI paresis	3	2	0
Hemiparesis	2	1	0
Dysphasia	1	0	0

CN, cranial nerve.

40 years [3–7,9,12]. Their incidence is similar in women and men [4–6]. Before the advent of CT and MRI imaging, they were difficult to identify until they become large and symptomatic. Their asymptomatic course for many years results from slow growth due to accumulation of normally desquamating epidermal cells, and the fact that the tumor fills normal subarachnoid spaces, with surrounding, but not displacing neurovascular structures [1,7]. Currently, the ability to identify these lesions is much improved, particularly with the DWI sequence, which allows detection of small tumors, often incidentally. Thus, questions arise regarding indications for surgical treatment and the optimal management of asymptomatic epidermoid cysts.

The most common presenting symptoms in patients with cerebellopontine angle epidermoids are trigeminal neuralgia and hearing impairment followed by dizziness, headaches, diplopia, and facial nerve paresis [3–6,12]. Trigeminal neuralgia and hemifacial spasm may result from nerve compression by an artery displaced by the epidermoid cyst or from nerve displacement toward the artery by the tumor. There were also often observed cases with trigeminal neuralgia, which resolved after the operation and no neurovascular conflict were identified during the surgery [3,6]. Kobata et al. [3] highlighted that in patients with epidermoid cysts, hemifacial spasm basically occurs only in cases of neurovascular conflict, while trigeminal neuralgia may often result also from displacement or kinking of the trigeminal nerve related to the presence of a tumor, and in cases unrelated to a tumor may be caused also by arachnoid adhesions or venous pathology. They believe that this difference is related to the length of the Redlich-Obersteiner zone, which is sensitive to direct compression or displacement and is nearly three times longer for the trigeminal nerve compared to the facial nerve (2.2 mm vs. 0.8 mm). As a result, neuralgia due to trigeminal nerve displacement is more likely than hemifacial spasm due to facial nerve displacement.

Surgical treatment is indicated in patients with symptomatic epidermoid cysts. Some authors also operate asymptomatic patients with tumors of considerable size with documented rapid growth. Due to the risk of recurrence, total tumor removal should be the goal of the surgery [5], but in other reports was found no difference in the risk of recurrence between completely and incompletely removed tumors [3,4]. This might have been related to problems with determining completeness of the excision, particularly when imaging studies, which allow objective evaluation of the extent of tumor removal, were not available in the past. It has been a quite commonly accepted view, that due to a benign nature and slow growth of these lesions, it is better to leave tumor capsule fragments on the neurovascular structures if their removal is difficult than to risk severe neurological deficits in case of inadvertent damage to these structures [1,3,4,6,7]. Taking into account a linear nature of epidermoid growth, a recurrence of a symptomatic tumor may be expected to occur after a period that is similar in duration to the period between birth and the moment when the primary tumor became symptomatic [1]. Thus, nearly complete tumor excision with only some small remnants left in a middle-age or elderly patient may mean a clinical cure, without the risk of symptomatic recurrence before natural death. On the other hand, the arguments in favor of complete removal are intraoperative problems encountered during the reoperation in a form of an extensive scar that adheres closely to blood vessels, nerves, and the brain itself, rendering complete or nearly complete removal of the recurrent tumor impossible without a risk of severe neurological deficits [1,5]. Rarely, epidermoids may undergo malignant transformation into squamous cell carcinoma, which is also an argument in favor of complete removal of these tumors [1,10].

Cerebellopontine angle epidermoids that do not penetrate supratentorially are operated by retrosigmoid suboccipital approach [3–5,8]. If the tumor spreads from the cerebellopontine angle, mostly supratentorially, a subtemporal transtentorial approach is used [4,7]. If a large tumor mass is located in the posterior fossa but also spreads supratentorially, combined supra- and infratentorial approach is used [4] or a two-staged surgery is performed. A two-stage surgical strategy is also used when tumor extend to the contralateral cerebellopontine angle, usually with some interval between the first and the second operation [7]. After opening of the dura mater and reaching the tumor, the overlying arachnoid and then the tumor capsule are opened, and the contents of the cyst is evacuated. Due to an avascular nature of the cyst, the keratinized debris can be removed without any bleeding. Another favorable aspect during the tumor removal is the fact that no brain collapse is observed after the contents of the cyst is evacuated, which makes the use of automatic spatulas unnecessary during the surgery. Tumor removal strategy consists in sequential opening of arachnoid cisterns, which were filled by growing tumor and tumor is removed successively from these spaces. Nerves and blood vessels are usually surrounded by the tumor, less frequently are distorted and displaced. Removal of the tumor around the cranial nerves is facilitated by identification of these nerves in the place of their exit at the skull base. Upon cranial nerve identification, surgical dissection proceeds along the nerves, allowing their separation from the tumor. In most patients, EMG is routinely used for intraoperative monitoring of the cranial nerves: V, VII, and IX–XII function, and brainstem auditory evoked potentials are used to monitor cranial nerve VIII function in patients with serviceable hearing [4,7]. Some authors also use an endoscope during surgery to inspect operative field corners for the presence of tumor remnants that are not seen under the microscope [7].

To avoid aseptic meningitis due to cholesterol spillage from interior of the cyst to the arachnoid cisterns during tumor removal, irrigation of the surgical field with hydrocortisone solution at the end of the procedure has been advocated by some authors [4,5], and long-term postoperative steroid administration is universally recommended [3–7,12]. The incidence of aseptic meningitis ranges from 0 to 18.2% [3–7,12] and was 5.8% in our material.

Following the surgery, worsening of preoperative deficits or occurrence of new cranial nerve deficits may be expected in a large group of patients [3–7]. However, these usually improve or resolve completely during long-term follow-up in most patients [3–7]. This transient worsening of symptoms is likely related to nerves manipulation or partial damage without their physical interruption during the surgery. In long-term follow-up, the neurological condition of a large majority of patients is

better than before the surgery, and no or only minor neurological deficits, such as hearing impairment, are seen in most patients [3,4,7].

Successive follow-up MRI, obligatorily using the DWI sequence, are indicated to evaluate for recurrence [2,4,6,7,9]. It is a matter of debate when to operate in case of a recurrence. We believe, as most authors do, that reoperation is indicated in case of worsening of a permanent neurological deficit or occurrence of a new deficit due to tumor regrowth, and not due to the mere fact of identification of tumor regrowth in imaging studies [4,5,7].

5. Conclusions

1) Cranial nerve deficits are the predominating symptoms in patients with cerebellopontine angle epidermoids.
2) The extent of the tumor expansion had no effect on the postoperative morbidity and the risk of recurrence.
3) The extent of tumor removal had no effect on the risk of recurrence, and thus it may be acceptable to leave fragments of the tumor capsule in places where adhere closely to blood vessels, nerves, or the brainstem, in order to avoid risk of serious neurological deficits related to an inadvertent damage of these structures.
4) During long-term follow-up, resolution or improvement of present preoperatively as well as new postoperative neurological deficits may be expected in most patients.

Conflict of interest

The authors declare no conflict of interest.

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Ethics

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; Uniform Requirements for manuscripts submitted to Biomedical journals.

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