INTRODUCTION

Epidermoids are rare benign congenital lesions of the central nervous system (CNS) accounting for approximately 0.2% to 1% of all intracranial tumors [1-3]. These lesions derive from aberrated ectodermal cells that develop into epithelium-like cells during the formation of the neural tube between the third and the fifth week of embryogenesis [4, 5]. Prevalently, epidermoids extend to or involve the cerebellopontine angle (CPA) and its vital neurovascular structures [6-8], thus commonly causing hearing loss, trigeminal neuralgia, vertigo, or facial nerve palsy [9]. As epidermoids are neither sensitive to chemotherapy nor to radiation [4], surgical resection constitutes the exclusive treatment modality for these lesions [4, 10]. These slow-growing, non-neoplastic tumors represent a challenge to neurosurgeons. Complete surgical tumor removal [11, 12] may reduce the risk of recurrence, thus leading to complete recovery of the affected patients. However, residual fragments of the tumor capsule often remain in situ because of their strong adherence to the brain stem or the encasement of cranial nerves and cerebral vessels [1, 2, 12, 13]. Thus, the best treatment modality is still being discussed in the
literature [2, 3, 9-25], i.e. whether initial aggressive surgery that is presumably associated with increased morbidity and mortality is preferable to multiple and subsequently subtotal resections that supposedly yield better short-term outcome.

To evaluate clinical presentation, surgical aspects, and neurological outcome, we selected patients with epidermoids of the posterior cranial fossa, who had been treated at our center over the past ten years.

PATIENTS AND METHODS

Between 2001 and 2012, ten consecutive patients with epidermoid tumors in the posterior cranial fossa underwent suboccipital craniotomy and consecutive microsurgical resection in our department. We retrospectively reviewed the patients’ clinical, neuroradiological, surgical, and histopathological records. No patient was excluded. All patients were treated according to our standardized postoperative treatment regime: 1. All patients were transferred to the intensive care unit for postoperative monitoring for at least 24 hours. 2. Corticosteroids were routinely administered preoperatively and postoperatively to avoid brain edema and chemical meningitis. 3. Post-surgical CT or MR imaging was obtained within 24 hours.

The nature and duration of symptoms, the surgical approach, the presence of adhesive neurovascular structures, and the duration of the surgical procedure were evaluated by means of patient charts and surgical records. Cerebral MRI and CT scans were assessed with regard to tumor localization, tumor size (maximum diameter), signal density in the T2 sequence, morphology (solid versus cystic), and the presence or absence of hydrocephalus. Preoperative hydrocephalus was diagnosed if external ventricular drainage placement was required. The extent of resection (EOR, total, near total, or subtotal) was determined by examining surgical records and early postoperative imaging, preferably diffusion-weighted imaging (DWI). Postoperatively, all patients received a CT (n=5) or MRI (n=5) scan as a control examination. During follow-up, all patients underwent an MR imaging examination to detect any residual or tumor recurrence. The EOR was considered total if the whole keratinous debris from the core of the tumor as well as the entire tumor capsule had been removed. The EOR was considered near total if the entire keratinous content had been resected but adhesive parts of the tumor capsule remained in situ. The EOR was considered subtotal if some part of the tumor could not be excised for any reason. We intraoperatively neuromonitored CN function of V (masseter), VII (orbicularis oculi and orbicularis oris), XI (trapezius), and XII (tongue), as well as somatosensory evoked potentials (SSEPs) or acoustically evoked potentials (AEPs), or both, in patients with preoperative serviceable hearing. Follow-up imaging was conducted to detect any tumor recurrence. Postoperative complications were inquired within 24 hours after surgery (early complications) and 24 hours up to 10 days postoperatively (late complications). Patient outcome was evaluated according to the modified Rankin scale (mRS) and the Glasgow Outcome Scale (GOS) immediately after surgery, at discharge, and if available at follow-up. Outcomes of mRS values of 0 to 1 or GOS values of 5 to 4 were considered good, mRS values 2 to 3 or GOS values of 3 fair, and mRS values 4 to 5 or GOS values 2 to 1 poor. The follow-up interval ranged from 1 to 43 months with a mean follow-up time of 17 months. No patient dropped out during follow-up.

We reviewed the current literature and discussed our findings in the context of previous clinical series on epidermoid tumors.

The study protocol was approved by the local ethics committee (14-101-0071).

RESULTS

Patient profile.

Our cohort included six men and four women with a mean age of 37.8 years (range 15 to 61 years) at the time of diagnosis. Seven patients had an epidermoid in the CPA, one in the prepontine area, and two patients in the cerebellar vermis area.

Clinical features.

The major presenting symptoms were vertigo or ataxia and CN deficits (e.g. trigeminal hypesthesia, diplopia, or hearing loss). The presenting clinical features are summarized in Table 1. The mean time to diagnosis was 121 weeks (range 0 to 624 weeks).

Neuroimaging.

On T2 MR images, epidermoids appeared as solid hyperdense lesions. When evaluating all preoperative DWI-MR images available, we found the typical restricted diffusion in epidermoid tumors that aids the differentiation between tumor and arachnoid cyst. The mean tumor size was 38.5 mm (range 18.8 to 66.1 mm). Preoperative hydrocephalus could not be detected. One patient showed
erosion of the petrous bone. None of the tumors spread supratentorially.

Surgery.

The ten operations were conducted by five different experienced neurosurgeons. Seven operations were done by means of the retrosigmoid suboccipital approach. Three operations were conducted via the medio-cerebellar route, and one operation included a laminectomy of the atlas. All patients were operated on in one single surgical procedure with a mean duration of 276 minutes (range 167 to 337 minutes). CN adherences were reported in eight patients, vascular adherences in six patients, brain stem adherences also in six patients, and cortical adherence in one patient. Brain stem compression due to tumor growth was found in one patient (Fig. 1). Complete resection was achieved in six patients (60%), near total resection in three patients (30%), and subtotal resection in one patient (10%). The histopathological findings confirmed the diagnosis of epidermoid tumor in all patients.

Postoperative course and long-term outcome. Within 24 hours postoperatively, nine patients did not show any new neurological deficit. One patient had transient dysphagia and transient facial nerve palsy, but the latter reversed within 24 hours after surgery. Within the first ten postoperative days, we found nuchal and cranio cervical cerebrospinal fluid (CSF) fistulas (n=2) that were associated with aseptic (Mollaret) meningitis in one patient. Both patients underwent wound revision and had no further CSF leak after the second intervention. Because of postoperative hydrocephalus, one patient required permanent ventriculoperitoneal shunting one month after surgery. No patient died during surgery.

At discharge, 80% of the patients showed no (n=4), unchanged (n=1), or improved symptoms (n=3; reversible diplopia, ataxia, and facial nerve palsy). One patient with unchanged facial nerve palsy improved after receiving a blepharoplasty postoperatively. The remaining patients (mRS 2-3) presented with persistent diplopia (n=1), newly developed hoarseness due to paralysis of the recurrent nerve, and a mild organic brain syndrome (n=1). According to GOS, outcome at discharge was good in all patients (n=10; GOS 5-4).

None of the patients with near total or subtotal resection underwent re-operation within the follow-up interval. One patient underwent regular MRI controls because of the recurrence of a small asymptomatic tumor that was stable within 43 months (‘watch and wait’). During follow-up, GOS was stable in all patients. According to mRS, one patient improved (mRS 3-0) during follow-up, and one patient slightly deteriorated (mRS 1-2).

Case illustration

The largest tumor diameter measuring 66.1 mm was noted in a 26-year old man (Fig. 1). This patient had diplopia and ataxia for 24 weeks before diagnosis of a medio-cerebellar epidermoid tumor compressing the brain stem and the fourth ventricle. The tumor adhered to the cerebellar cortex, the tentorium, and the rhomboid fossa. After surgery, the patient presented with transient facial nerve paresis and transient dysphagia and was discharged without any neurological deficits. Ten days after surgery, the patient developed a CSF fistula in the cranio cervical junction area, a condition that was clinically associated with Mollaret meningitis. The cause of delayed meningitis remained unclear. The patient fully recovered after surgical revision, lumbar drainage, and steroid therapy. At six-month follow-up, no tumor recurrence was detected, and the patient presented with a stable MRS value of 0 and a GOS value of 5.

DISCUSSION

Epidermoid tumors represent a rare benign tumor entity with a slow growth pattern over several years [3, 10, 12, 15, 19, 22-24, 26-30]. Histologically, epidermoids develop from displaced ectodermal cells in the third to the fifth week of embryonic life [4, 5]. The tumors are enclosed by a thin capsule of keratinized stratified squamous epithelium that develops into the cyst contents keratin and cholesterol after desquamation [31]. Because of the benign nature of the lesions, malignant transformation has only been described rarely [29, 31-36]. No malignancies were observed in our study population.

The lesions tend to spread along natural intracranial cleavage planes, preferentially in the CPA [6-8], and encase or extensively displace critical neurovascular structures. Thus, epidermoids usually become only clinically symptomatic after years of undetected development [31, 37-39]. According to Muzumdar et al. [40], these tumors are either diagnosed incidentally, i.e. in association with other intracranial lesions, or remain undiagnosed in most cases. We observed a mean duration from the onset of symptoms to the time of diagnosis of 121 weeks (2.3 years), ranging from 0 weeks (incidental finding) to 624 weeks compared with two to five years in other reports [2, 13, 14, 18, 22, 25]. In
contrast to other lesions of the posterior cranial fossa, epidermoids seem to be less aggressive in biological behavior. Recently, we have retrospectively analyzed a ten-year series of 24 patients with hemangioblastomas of the posterior cranial fossa (unpublished data). This analysis yielded a mean time to diagnosis of 14 weeks and even less (7 weeks) for the hereditary subgroup because of the more rapid onset of neurological symptoms. In the literature, the prolonged time to diagnosis for epidermoid tumors has been generally accepted. This delay may be partly due to the lesions’ histomorphological inert and non-vascularized nature and their protracted cystic growth pattern that is less aggressive than, for example, that of hemangioblastomas.

Our series comprised 6 men and 4 women with a mean age of 37.8 years (range 15 to 61 years) at the time of diagnosis. Consistent with our results, larger representative trials [1, 2, 13, 14, 19, 24, 41] have reported an almost equal incidence of epidermoid tumors in both sexes [10, 15, 19, 22-24, 26, 27] with the onset of symptoms between the second and fifth decade of life.

Approximately 40% to 50% of intracranial epidermoids are localized in the CPA, thus the most common intracranial site of this lesion [6-8]. Among our ten patients, 70% of the tumors (of four men and three women) were localized in the CPA. Accordingly, vertigo and ataxia were the most commonly reported presenting symptoms. CN dysfunction occurred in 4 patients with trigeminal hypesthesia and diplopia as the most frequently noted deficits, followed by dysfunction of the eighth and seventh nerve. Further symptoms are depicted in Table 1. One patient had no definite neurological deficit at the time of diagnosis. In a series including 24 consecutive patients with CPA epidermoids over 20 years, Schiefer and Link [25] reported headache (67%) and CN dysfunction (83%) – most commonly of the eighth nerve (54%) – as the major presenting symptoms. Earlier, in 2002, a meta-analysis of 263 cases of CPA epidermoids [9] described the following most commonly reported symptoms: hearing loss (37.6%), trigeminal neuralgia (29.7%), dizziness or vertigo (19.4%), facial palsy (19.4%), headache (17.9%), and diplopia (16.7%).

MR imaging is an indispensable radiological diagnostic tool for the detection of epidermoid tumors. MRI has superseded CT in accuracy, primarily because DWI allows a reliable differentiation between tumor tissue and CSF-filled cisterns and cysts [10, 22, 42-48]. This method is also helpful for differentiating epidermoid tumors from low-grade glioma and infarcts. DWI is particularly beneficial for postoperative control imaging to differentiate between residual tumor parts and CSF that shows great similarity in signal intensity and substitutes the resection cavity after surgery. In our MRI analyses, we exclusively identified solid lesions without any cystic components or supratentorial compartments. Goel and colleagues [49] presented a series of 96 anterior tentorial-based epidermoid tumors, and in 16 (17%) lesions more than 50% of the tumor bulk extended supratentorially. These authors described a mean tumor size of 44 mm, which is within our observed range from 18.8 to 66.1 mm (average maximum size, 38.5 mm).

We achieved total resection in six patients. In four patients, complete removal of the tumor or the tumor capsule was not possible because of their close localization to or the encasement of neurovascular structures or because of brain stem adherence. The most frequently involved structures were the cranial nerves V to VIII, the basilar artery, and the posterior inferior cerebellar artery. However, no tumor recurrence or progression of the remnant was detected within the follow-up period (mean 17 months). One limitation in the current literature including the present study is the limited duration of the follow-up period. Tumor recurrence has been reported 10 to 20 years after initial surgery [50], which underlines the importance of long-time follow-up imaging studies, particularly after incomplete removal of epidermoid tumors.

In the literature, the best treatment modality is still being discussed, i.e. whether radical tumor resection is superior to near or subtotal removal [3, 10, 12, 15, 19, 22-24, 26-30]. Yasargil and colleagues [12] advocated total resection (total EOR in 95% of patients) because of minimum patient morbidity and a recurrence rate of 9% after 5.2 years of follow-up. Other authors have abandoned aggressive surgical approaches. Berger and Wilson [14], for instance, did not attempt complete resection in any of their 13 patients but only removed the content and the non-adherent parts of the tumor capsule. These authors reported low morbidity and no recurrence over 4.5 years of follow-up. We favor the complete resection of epidermoid tumors provided that critical structures, such as cranial nerves, blood vessels, or the brain stem, are not affected. In our series, nine patients presented without any new neurological symptoms within 24 hours postoperatively, and the neurological performance was stable during follow-up. In one case, ventriculo-peritoneal shunting was required one month after the initial operation. Overall, no patient died perioperatively or postoperatively.
and morbidity was low.

Apart from tumor recurrence owing to partial tumor removal and subsequent residual capsule fragments, aseptic meningitis, also known as Mollaret meningitis [10, 51, 52], is a common therapeutic problem in epidermoid tumors. Postoperative Mollaret meningitis was observed in one patient in our study (see case illustration and Figure 1 a–d). Factors known to increase the risk of chemical or aseptic meningitis are the dissemination of the irritant keratinous debris from the interior of the tumor in the subarachnoid space as well as the rare and occasionally repeated occurrence of spontaneous cyst rupture [22, 53, 54]. Meng et al., for instance, reported that meningitis occurring after partial removal of intraventricular epidermoids improved after repeated lumbar punctures and treatment with steroids [55]. Radical tumor resection is assumed to contribute to avoiding or at least reducing the incidence of meningitis.

**CONCLUSION**

We correlated the results of our series with the various findings of previous clinical trials on epidermoid tumors. Increasing experience in the management of these lesions may further the understanding of this rare tumor entity. The canon of clinical trials, reviews, and meta-analyses allows the better preliminary assessment of patients’ intraoperative and perioperative morbidity risks and their therapeutic complication profiles. We would like to emphasize the importance of the preservation and integrity of vital neurovascular structures. As previously recommended by a number of authors, leaving remnants of the tumor capsule is preferable to radical resection because this method results in lower morbidity and mortality and thus increases expectation of a normal life.

| Table 1 |
| Preoperative clinical features of epidermoids in the posterior cranial fossa (n = 10 patients) |

<table>
<thead>
<tr>
<th>Symptom</th>
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<tbody>
<tr>
<td>Vertigo</td>
<td>6</td>
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<tr>
<td>Ataxia</td>
<td>6</td>
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<tr>
<td>Trigeminal hypesthesia</td>
<td>4</td>
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<tr>
<td>Diplopia</td>
<td>4</td>
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<tr>
<td>Hearing loss or ear noise</td>
<td>3</td>
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<tr>
<td>Headache</td>
<td>3</td>
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<tr>
<td>Nausea</td>
<td>2</td>
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<tr>
<td>Facial nerve palsy</td>
<td>1</td>
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<tr>
<td>Hoarseness due to vocal cord paralysis</td>
<td>1</td>
</tr>
<tr>
<td>Homihypesthesia</td>
<td>1</td>
</tr>
<tr>
<td>Recurring syncopes</td>
<td>1</td>
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</tbody>
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**Figure 1a**

Fig. 1. (a) T2-weighted image.
Figure 1b
Fig. 1. (b) diffusion-weighted MRI showing the large medio-cerebellar epidermoid tumor causing brain stem compression.

Figure 1c
Fig. 1. (c) Intraoperative view of the characteristically silvery, pearlized, shining, and soft nature of the epidermoid, exposed via a medio-cerebellar approach.
Figure 1d
Fig. 1. (d) The postoperative CT scan shows the partially persistent brain distortion as a result of the prolonged presence of the tumor. The space within the resection cavity, formerly occupied by the tumor, is taken up by CSF.

References

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