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Surgical treatment of intracranial epidermoid tumors: a retrospective analysis of 29 surgically treated patients

İntrakraniyal epidermoid tümörlerin cerrahi tedavisi: cerrahi olarak tedavi edilen 29 hastanın retrospektif analizi

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Abstract

Purpose: Intracranial epidermoid tumors are benign, slow-growing, and rare tumors. Although they are located in different regions of the brain and cranium, they predominate in the cerebellopontine angle and temporal region. In the present study, clinical presentations of epidermoid tumors, their location, the surgical treatment methods used, and their outcomes were examined.

Materials and methods: Medical records of 29 patients with intracranial epidermoid tumors diagnosed between 2012 and 2019 were retrospectively reviewed.

Results: The study cohort consisted of 16 female and 13 male patients. In 16 patients, the tumors were located in the cerebellopontine angle while in 13 patients, they were located in other regions. Two of the 16 patients with tumors originating from the cerebellopontine angle had both infra and supratentorial extensions. One of these patients underwent subtotal resection in two sessions via retrosigmoid and subtemporal approaches. The tumor was excised except for the capsule that was adherent to the eloquent vascular structures. The other patient underwent gross total resection in a single session via the subtemporal approach. The other 14 cases were only infratentorial. Gross total resection was performed in 25 patients while subtotal resection was performed in 4 patients. Four patients had postoperative complications, while one patient whose tumor was adherent to the brainstem died in the postoperative period. There was no recurrence in any of the patients.

Conclusion: The main treatment strategy for intracranial epidermoid tumors should be gross total tumor resection via surgery. However, subtotal resection may be performed by allowing a capsule adherent to the eloquent neurovascular structures that may cause morbidity and mortality. The risk of tumor recurrence after a total resection is performed is very low.

Key words: Epidermoid tumor, treatment, cerebellopontine angle, complication.

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Özet

Amaç: İntrakraniyal epidermoid tümörler iyi huylu, yavaş büyüyen ve nadir görülen tümörlerdir. Beynin ve kranyumun farklı bölgelerine görülebilmelerine rağmen, ağırlıklı olarak serebellopontin açı ve temporal bölgede yerleşirler. Bu çalışmada epidermoid tümörlerin klinik bulguları ve tümör yerleşimleri, cerrahi yöntemleri ve sonuçları incelendi.

Gereç ve yöntem: 2012-2019 yılları arasında tanı konulan intrakraniyal epidermoid tümörü bulunan 29 hastanın tıbbi kayıtları retrospektif olarak incelendi.

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Bulgular: Çalışma grubunda 16 kadın ve 13 erkek hasta vardı. Tümörler 16 hastada serebellopontin açıda ve 13 hastada diğer bölgelerde yerleşmişti. Serebellopontin açıdan köken alan tümörleri olan 16 hastanın ikisinde hem infra hem de supratentoryal uzanım mevcuttu. Bu hastalardan birine retrosigmoid ve subtemporal yaklaşımlarla iki seansta subtotal rezeksiyon uygulandı. Tümör, belirgin vasküler yapılara yapışan kapsülü dışında eksize edildi. Diğer hastaya ise subtemporal yaklaşımla tek seansla gros total rezeksiyon uygulandı. Diğer 14 olguda sadece infratentoryal yerleşim mevcuttu. 25 hastaya gros total rezeksiyon ve 4 hastaya subtotal rezeksiyon uygulandı. Dört hastada postoperatif komplikasyon gelişti. Tümörü beyin sapına yapışan bir hasta postoperatif dönemde kaybedildi. Hiçbir hastada nüks görülmedi.
Sonuç: İntrakraniyal epidermoid tümörlerin tedavisinin temel amacı cerrahi müdahale ile gros total tümör rezeksiyonu olmalıdır. Bununla birlikte, subtotal rezeksiyon morbidite ve mortaliteye neden olabilecek durumlarda hayati nörovasküler yapılara yapışık kapsüller bırakılarak yapılabilir. Total rezeksiyon yapılan tümörlerin nüks riski çok düşüktür.

Anahtar kelimeler: Epidermoid tümör, tedavi, serebellopontin açı, komplikasyon.

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Introduction

Epidermoid tumors are usually benign lesions that are usually intracranial, but rarely located in the cranium. They can be located intradurally (mostly extra-axial), extradurally, or in the diploic space of the calvarium. Intracranial epidermoid tumors constitute approximately 0.2% to 1.8% of all intracranial tumors [1, 2]. They are most commonly located in the cerebellopontine angle (CPA), temporal region, and parasellar cisterns [2-4]. They constitute about 40%-50% of CPA pathologies [3, 5, 6].

These tumors may have a wide range of clinical symptoms, including increased intracranial pressure and focal neurological deficit or seizure and these symptoms may be related to the localization of the tumors. Tumors located in the CPA may present with facial pain or paralysis, whereas tumors in the temporal region begin with a seizure complaint [7, 8]. Magnetic resonance imaging (MRI), fluid-attenuated inversion recovery (FLAIR) imaging, and diffusion-weighted imaging (DWI) are gold standard imaging techniques for the detection of these tumors [2, 8-10]. FLAIR and DWI sequences are important in distinguishing epidermoid tumors from other intracranial tumors or cysts, especially arachnoid cysts.

The aim of this study was to investigate the clinical presentations, tumor locations, surgical methods used, and surgical outcomes among the patients with diagnosed epidermoid tumors who underwent surgery in multicenter neurosurgery clinics in the last 7 years.

Materials and methods

The study was conducted according to the principles of the World Medical Association Declaration of Helsinki “Ethical Principles for Medical Research Involving Human Subjects” (amended in October 2013) and Institutional Review Board approval was obtained. This study included 29 patients with a histopathological diagnosis of epidermoid tumor who underwent surgery at 3 neurosurgery clinics between November 2012 and November 2019. Patients’ data including age, gender, preoperative and postoperative neurological conditions, radiological tumor location and dimensions, surgical methods used, recurrence, and postoperative complications were evaluated.

The surgery was planned according to the location of the lesion. As a routine application, supratentorial and infratentorial lesions were operated via craniotomies. Craniectomy was not done in any of the cases, except for intradiploic lesions. Tumor and bone tissue were resected together in the intradiploic lesions. Watertight dura closure was performed in all of the operations. Preoperatively, 1 gram of ampicillin-sulbactam was administered while 1 gram of ampicillin-sulbactam was administered 4 times daily for 3 days postoperatively. In all the cases, 16 mg of dexamethasone per day was started for postoperative aseptic meningitis prophylaxis. It was gradually reduced and discontinued in 10 days.

Statistical analysis

SPSS 25.0 (IBM Corporation, Armonk, New York, United States) program was used to analyze the variables. The Mann–Whitney U test was used with the Monte Carlo results to compare the categorical variables quantitatively. The quantitative variables were described as mean ± SD (standard deviation) and median (range, maximum-minimum) and categorical variables as n (%). The variables were examined at 95% confidence level and $p<0.05$ was considered significant.

Results

Patient demographics

The study cohort consisted of 16 female and 13 male patients. The mean age of the patients was 32.8±13 (14-67 interval). The tumors of 14 patients were located on the left side and the tumors of 14 other patients were located on the right side. One patient's tumor was spreading on both sides. Tumors were located in the cerebellopontine angle in 16 patients, intradiploic in 5 patients, in frontotemporal region in 4 patients, parasellar region in 2 patients, and frontal region in 2 patients (Table 1).

Patient symptoms

The most common symptom was headache (82.7%). Other symptoms identified were dizziness (51.7%), cranial nerve dysfunction (20.6%), bone thickening (17.4%), hemiparesis (10.3%), seizure (10.3%), confusion (6.9%), and visual loss (3.4%). Most frequently, seventh cranial nerve (4 patients) and eighth cranial nerve (3 patients) dysfunctions were detected in patients with CPA tumors (Table 1).

Table 1. Demographic data of the patients

Characteristics		Treatment Group n=29 (%)
Age (Mean)		32.8±13(14-67)
Gender	Female	16 (55)
	Male	13 (45)
Symptoms		
Headache		24 (82.7)
Dizziness		15 (51.7)
Cranial nerve dysfunction		6 (20.6)
Bone thickening		5 (17.4)
Hemiparesis		3 (10.3)
Seizure		3 (10.3)
Confusion		2 (6.9)
Visual loss		1 (3.4)
Tumor location		
Cerebellopontine angle		16 (55)
Intradiploic		5 (17.4)
Frontotemporal		4 (13.8)
Frontal		2 (6.9)
Parasellar		2 (6.9)
Tumor size (cm^3)		53.8±42.9 (7.2-214.5)
Extent of resection		
Total		25 (86)
Subtotal		4 (14)
Complications		
Aseptic menengitis		1 (3.4)
Vagal nerve dysfunction		1 (3.4)
Left hemiparesis		1 (3.4)
Exitus		1 (3.4)

Neuroimaging

Contrast-enhanced MR imaging of all of the patients was performed preoperatively. There were no cases with atypical imaging findings. In all the cases, imaging was performed including DWI and FLAIR sequences for the diagnosis of epidermoid tumor, in addition to unenhanced and enhanced T1 and T2 sequences. One patient underwent preoperative MR angiography on detection of a parasellar epidermoid tumor and left middle cerebral artery (MCA) saccular dilatation coexistence (Figure 1). All the tumors were hypointense in T1 sequences and hyperintense in T2 sequences. None of the tumors had intense contrast enhancement. In DWI and FLAIR sequences, tumor boundaries were determined and preoperative preparations were made according to these imagings.

Surgery

Craniotomies were applied for the resection of supratentorial tumors in order to dominate the lesion localization and its borders. Total resections could be performed in all of the supratentorial lesions. Total tumor resection and muscle strengthening to the saccular dilatation was performed in the same session in the patient with left-sided parasellar epidermoid tumor and

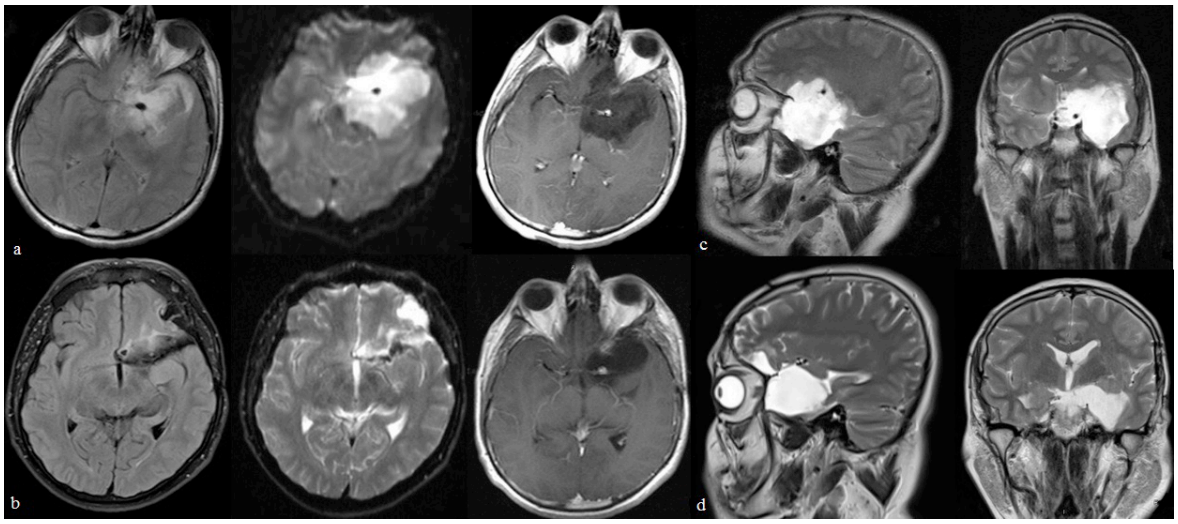

Figure 1. (a) Preoperative axial FLAIR, DWI and T1-weighted images of first patient demonstrating left parasellar localized epidermoid tumor and left MCA dilatation. (b) Postoperative axial FLAIR, DWI and T1-weighted images revealing gross total resection of the tumor. (c) Preoperative sagittal and coronal T2-weighted images of first patient demonstrating left parasellar localized epidermoid tumor. (d) Postoperative sagittal and coronal T2-weighted images revealing gross total resection of the tumor

left MCA saccular dilatation (Figure 1). Muscle wrapping was applied around the dome, as the aneurysmatic dome was not compatible with clipping. Postoperative course of the patient was uneventful.

Two of the 16 patients with tumors originating from the CPA had both infra and supratentorial extension. One of these patients underwent resection in two sessions via retrosigmoid and subtemporal approaches. The tumor was excised except for the capsule adherent to the eloquent vascular structures (Figure 2). The other patient underwent a total resection in a single session via the subtemporal approach. The other 14 cases were only infratentorial. Three of them had midline extension and 3 of them had foramen magnum extension (Figure 3). One patient's tumor had a bilateral CPA localization and fourth ventricular extension. In all of these patients, craniotomies were performed with a single session via the retrosigmoid approach. Twelve patients underwent total resection (Figure 4). Four patients underwent subtotal resection because of the neurovascular involvement of the tumor capsule and capsule excision was not insisted (Table 2). The mean follow-up period of the patients was 5 years (1-7 years).

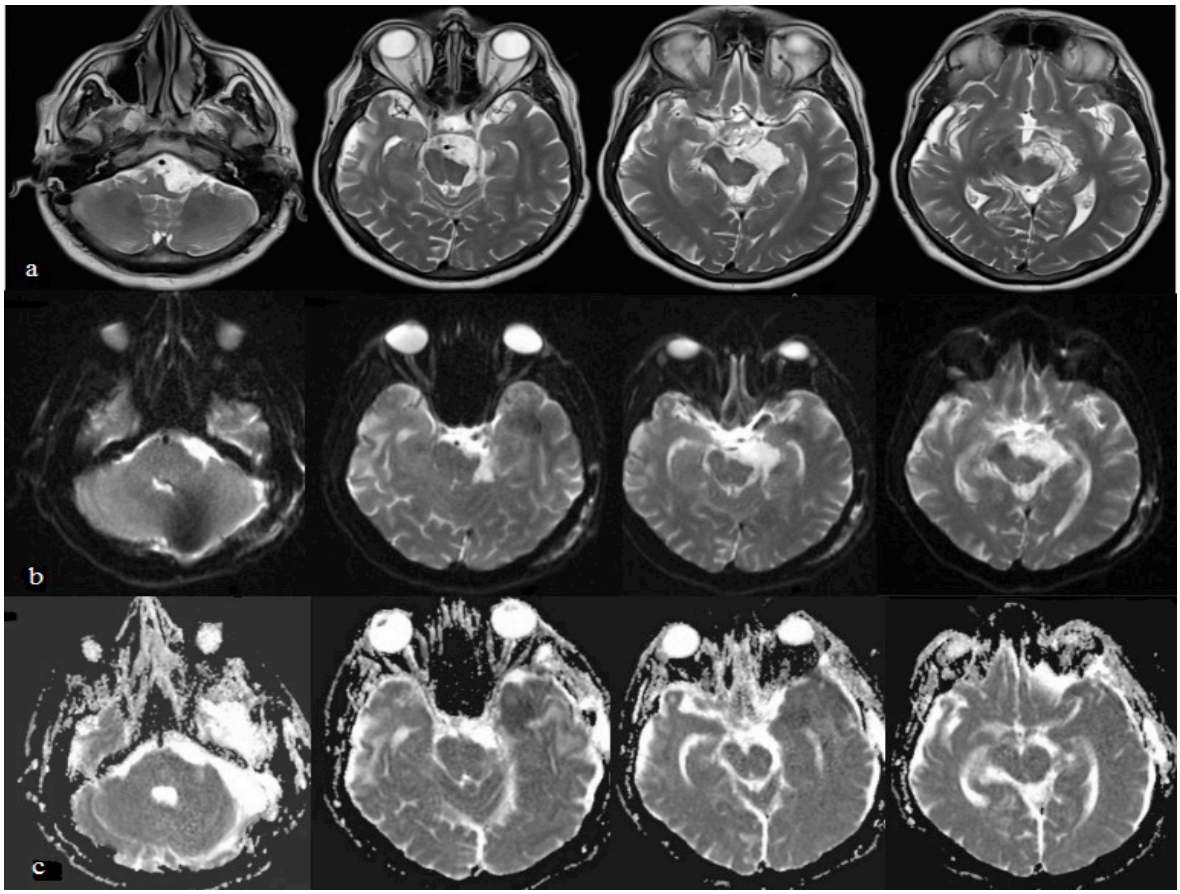

Figure 2. (a) Preoperative T2-weighted images of fifth patient demonstrating a left CPA localized epidermoid tumor with supratentorial extension. (b) Postoperative axial DW images revealing subtotal resection of infratentorial part of the tumor after the first session via the retrosigmoid approach. (c) Postoperative axial DW images revealing gross total resection of supratentorial part of the tumor after the second session via the subtemporal approach

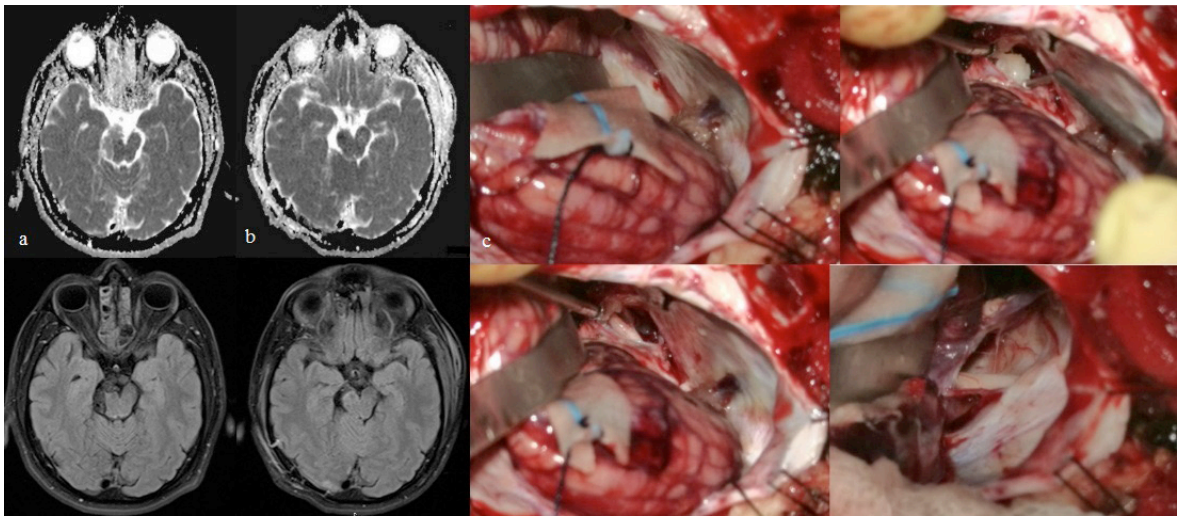

Figure 3.(a)Preoperative axial ADC and FLAIR images of eighth patient demonstrating right CPA localized epidermoid tumor with midline extension. (b) Postoperative axial ADC and FLAIR MR images revealing gross total resection of the tumor. (c) Peroperative images of the same patient revealing gross total resection of the tumor

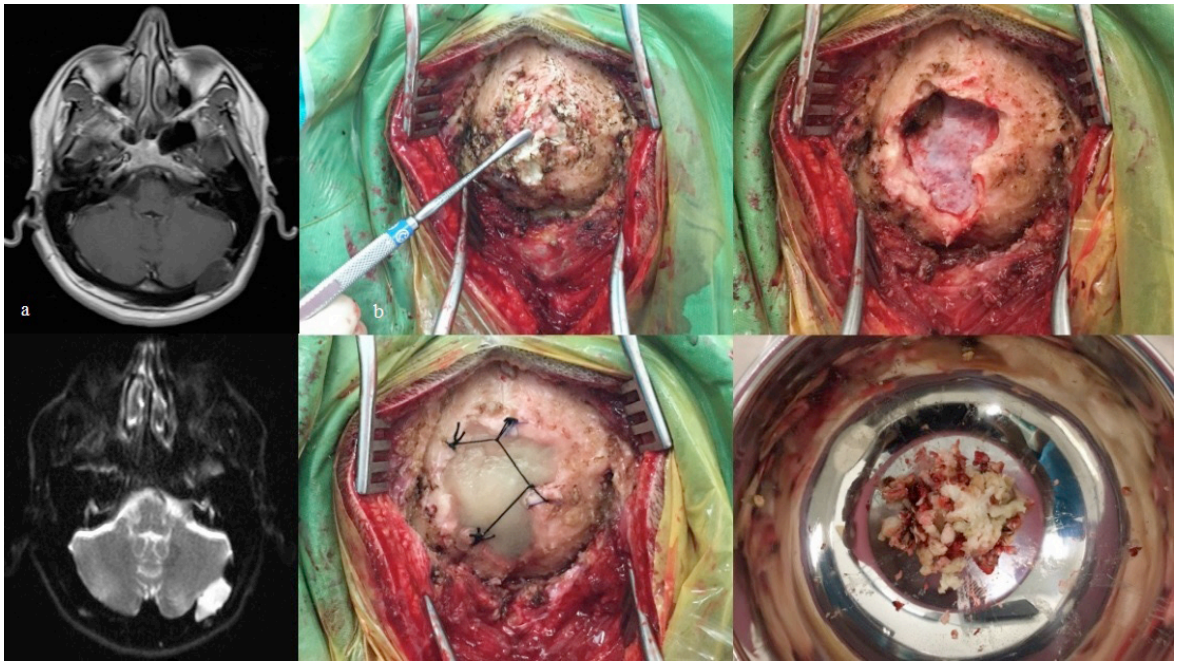

Figure 4. (a) Preoperative axial contrast enhanced T1-weighted and DWI images of twenty-ninth patient demonstrating a left occipital intradiploic epidermoid tumor. (b) Peroperative images of the same patient revealing gross total resection of the tumor and reconstruction of the craniectomy defect via cranioplasty

Table 2. Lesion extension and surgical characteristics of the patients with cerebellopontine angle localized tumors

Patient	Lesion extension	Surgery	Resection
4	CPA alone	Retrosigmoid approach	Total
5	CPA + supratentorial extension	Retrosigmoid + subtemporal approaches	Subtotal (in 2 session)
6	CPA alone	Retrosigmoid approach	Total
8	CPA + midline extension	Retrosigmoid approach	Total
9	CPA + foramen magnum extension	Retrosigmoid approach	Total
11	CPA + supratentorial extension	Subtemporal approach	Total
14	CPA + foramen magnum extension	Retrosigmoid approach	Subtotal
17	CPA + midline extension	Retrosigmoid approach	Subtotal
19	CPA alone	Retrosigmoid approach	Total
21	CPA + foramen magnum extension	Retrosigmoid approach	Subtotal
22	CPA alone	Retrosigmoid approach	Total
23	CPA + midline extension	Retrosigmoid approach	Total
24	CPA alone	Retrosigmoid approach	Total
25	Bilateral CPA + 4. ventricle extension	Suboccipital approach	Total
26	CPA alone	Retrosigmoid approach	Total
28	CPA alone	Retrosigmoid approach	Total

CPA: Cerebellopontin angle

Complications

Four patients had complications in our clinical series. Aseptic meningitis was detected in the patient who underwent 2 sessions of surgery. After application of the steroid treatment, the patient was discharged without a permanent sequela. Transient vagal nerve involvement was detected in the patient with the CPA tumor having a foramen magnum extension. After 6 months of medical and physical therapy, the paralysis was fully recovered. In another case with CPA tumor, a transient hemiparesis due to a transient ischemic attack was developed. She recovered without any sequela with physical therapy (Table 1).

In a patient with a fourth ventricular localization tumor, in whom dissection of the capsule was attempted from the underlying fourth ventricle floor, lower cranial nerve function and the brainstem were affected in the postoperative period. Bulbar paralysis resulted in inadequate and superficial respiration, causing pulmonary atresia and pneumonia which complicated the post-operative period and led to patient dead. The patients experienced no recurrences during the follow-up period.

Discussion

Epidermoid tumors were first named by Love and Kernohan in 1936. They are rare congenital lesions of ectodermal origin, constituting approximately 0.2%-1.8% of all intracranial tumors [7, 11, 12]. It is believed that they are composed of ectodermal squamous epithelial cell remnants, which is an anomaly occurring during the closure of the neural tube between the third and fifth weeks of fetal life [2, 9, 13, 14]. These tumors are surrounded by a fibrous capsule and keratinized stratified squamous epithelial cells and are composed of cholesterol crystals, keratin, protein, and cerebrospinal fluid [14-16]. Calcifications are detected in 10% of intracranial epidermoid tumors [9, 17].

The lesions are frequently extra-axial and have a pathological irregular shaped known as “pearl tumors” because of their cauliflower-like appearance. The lesions are often surrounded by a definite capsule; however, no definite capsule structure can be detected in some cases [18]. Their most important features are slow progression, progressive formation towards cavities, and invagination into adjacent brain tissue and neurovascular structures. Therefore, it is generally the advance forms of the lesions that become symptomatic [4, 19]. Although these tumors are benign lesions, malignant transformation or bleeding lesions have been identified in rare cases [14, 20, 21].

Epidermoid tumors can be located either in the intradural or extradural compartments of the cranium in each region. They are frequently located in the intradural and paramedian regions. The most common location is reported as CPA (40%-50%), which accounts for approximately 5%-10% of all CPA lesions [3, 4, 22, 23]. Subsequently, other common locations include the fourth ventricle (17%), parasellar cisterns (10%-15%), cerebellar hemispheres, and brainstem [2, 16, 24]. Approximately half of all intracranial epidermoid tumors have a tentorial contiguity and these lesions may show supra and infratentorial extensions [25]. Sixteen patients (55%) had CPA localization in our series of 29 patients and 2 of them had infra and supratentorial extensions (Table 2).

Epidermoid tumors are usually asymptomatic until the third decade, but most of the patients are usually diagnosed in the fourth decade [7, 23]. Symptoms may vary widely depending on the tumor localization. Intradiploic lesions usually occur as a local thickening [8, 26]. The most common symptom of intradural tumors is headache. Decreased visual acuity, narrowing of the visual field, and hypothalamic affections are frequently observed in parasellar lesions. Temporal lobe localized tumors usually present with seizures [2]. Another less common symptom of epidermoid tumors is aseptic meningitis, which results from the rupture of the lesions. In the literature, there are cases of tumors that ruptured in the third and fourth ventricles, leading to death [7, 16, 24, 27].

Symptoms of epidermoid tumors located in the CPA include cranial nerve involvements. Hearing loss, trigeminal neuralgia, facial paralysis, hemifacial spasm, dizziness, gait ataxia, dysphagia, and diplopia are the most common symptoms [2, 4, 23, 28]. Hasegawa et al. reported a study that included 22 patients with CPA epidermoid tumors. They found that 12 (54.5%) of them had trigeminal neuralgia, 6 (27.2%) had facial paralysis and hemifacial spasm, 4 (18.2%) had diplopia due to abducens

nerve involvement, 3 (13.7%) had hearing loss, and 2 (9.1%) had dysphagia and soft palate paralysis due to the involvement of the lower cranial nerves [3].

Intracranial epidermoid tumors are defined as homogeneous hypodense lesions with no surrounding edema in computed tomography (CT) scans and 10% of these tumors may contain calcifications. The differential diagnosis of epidermoid tumors includes arachnoid cysts, Rathke's cleft cysts, craniopharyngioma, and other cystic tumors. The differential diagnosis with arachnoid cysts is the most problematic issue. The finding that the content of the epidermoid cysts has more fat density than that of cerebrospinal fluid is useful for making the differential diagnosis [2, 9, 14, 29]. Unlike arachnoid cysts, epidermoid tumors mostly show growth pattern towards the subarachnoid space. In rare cases, high-density masses in CT images are seen as "white epidermoid", making the diagnosis difficult [11, 16, 24]. The reason for the white epidermoid is the white appearance of tumors in the T1-weighted series. This appearance is caused by the high protein or lipid content of the tumor [11, 16, 24].

MRI is the main diagnostic method for epidermoid tumors as well as for other brain tumors. They may be identified on MR images at different densities, ranging from hypointense to hyperintense according to the amount of cystic content and are usually identified as heterogeneous and multiloculated lesions. Typically, the lesions are hypointense on T1-weighted images and hyperintense on T2-weighted images [10, 14, 16]. They usually do not show contrast enhancement; however, peripheral rim contrast enhancement is observed in 25%-35% of the patients [2, 8].

It is difficult to distinguish epidermoid tumors from arachnoid cysts using the standard and spin echo MRI sequences. However, DWI and FLAIR sequences are useful for making this distinction. Because epidermoid tumors are hyperintense on both sequences [9, 14, 28, 30]. It should be kept in mind that artefacts may be caused by cerebrospinal fluid flow in FLAIR sequences during the imaging of lesions located in the prepontine, basal cistern, foramen monro, and fourth ventricle [7, 31-33]. Hakyemez et al. in a study including 15 patients with epidermoid tumors found that FLAIR sequences were superior to classical MRI in the presentation of epidermoid cysts and that DW images were superior to other MRI sequences in determining the boundaries of the epidermoid cysts [31].

The goal of treatment for epidermoid tumors is gross total resection of the lesions [2-4, 22, 23, 28]. However, this is not possible for all tumors. Although the contents of epidermoid tumors can be easily aspirated and excised, the hypovascular capsules surrounding the tumors could adhere to vital organs, making total resection risky; therefore, subtotal resection is done in such cases to avoid neural and vascular injury. In our series, gross total resection when the capsule adhered to the brain stem caused respiratory problems and death. In these types of cases, allowing the adherent capsules to the eloquent structures yields better results. However, there is a risk of recurrence in patients who underwent subtotal resection [6, 34]. Yaşargil et al. reported a total resection rate of 95% and recurrence rate of 9% in their clinical series [34]. According to the hypothesis created by Hasegawa et al., it is thought that cranial nerve paralysis, which progresses rapidly in younger patients, eventually occurs due to strangulation of the cranial nerves caused by the tumor capsules [3]. Although tumor capsules cannot be totally removed in these types of cases, it is thought that relaxation of the bands causing the strangulation and decompression in the early period of the symptoms is important for obtaining good prognosis [3].

Clinicians should be aware that chemical meningitis and hydrocephalus that develop in the postoperative period increases morbidity and mortality. The keratinous cystic components of these tumors are responsible for the inflammatory reactions that cause the meningitis [35]. Steroid therapy has good outcomes in patients with chemical meningitis [7, 35]. Ventriculoperitoneal shunt operation may be needed in approximately 20%-30% of the patients with epidermoid tumors who develop hydrocephalus [2, 5]. Neuroimaging controls of the lesions are performed within specific intervals. According to the literature so far, there is no place for chemotherapy or gamma knife treatment in the treatment of epidermoid tumors [8].

In conclusion; intracranial epidermoid tumors are slow-growing tumors, having varying clinical

symptoms depending on their location and are generally silent for many years. The main goal of the treatment should be gross total tumor resection by surgical intervention. However, subtotal resection may be performed by allowing the capsule when it is attached to neurovascular structures that may cause morbidity and mortality. Combined surgical interventions may be applied in lesions with infra and supratentorial extensions. However, it is possible to remove both components of the tumors via combined surgery in the appropriate cases, extending from the posterior fossa to the temporal region. Surgical experience may reduce morbidity and mortality. The risk of recurrence is significantly lower when gross total resection is performed.

Conflict of interest: No conflict of interest was declared by the authors.

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Contributions of the authors to the article

K.O. and A.G. were involved with the conception and design of the manuscript. M.Y. and H.S. developed the theory and edited the material method section. E.G., E.A. and A.D. were involved with acquisition, analysis and interpretation of data. K.O. wrote the discussion section of the article. O.N.S. and V.K. reviewed and revised the discussion section of the article. All authors involved in revising and final approval of the manuscript.