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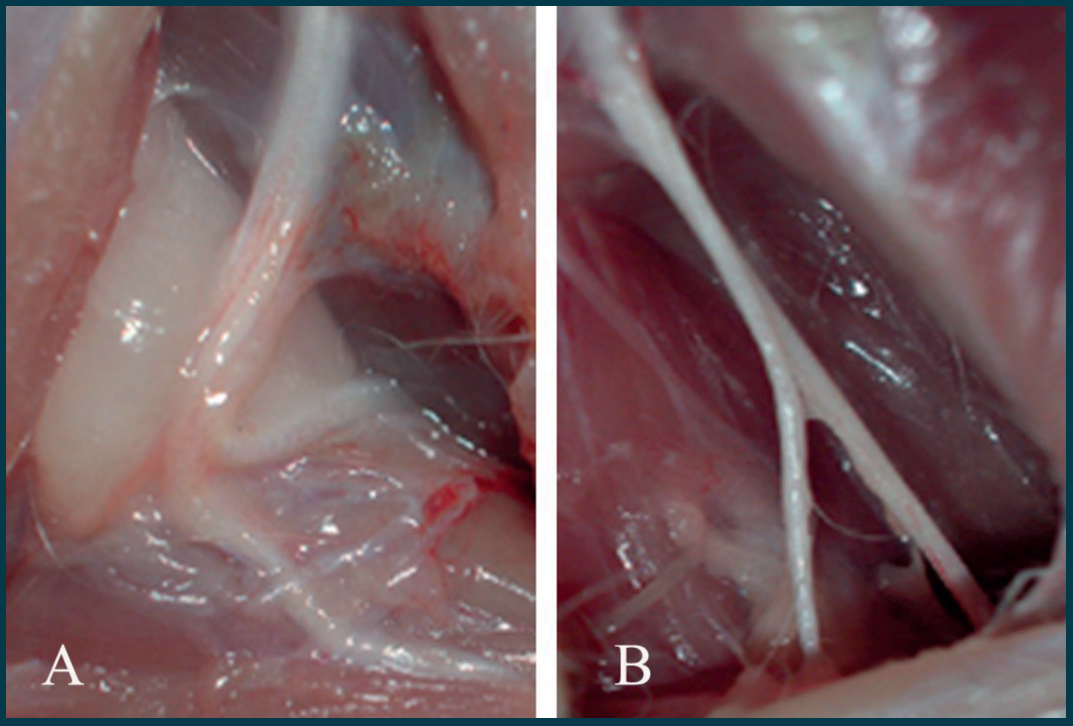

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Research Article / *Araştırma Makalesi*

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Effect of Valproic Acid on Vasospasm at Experimental Subarachnoidal Hemorrhage Model

Deneysel Subaraknoid Kanama Modelinde Valproik Asidin Serebral Vazospazm Üzerine Etkisi

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ABSTRACT

Background and Purpose: The main purpose of our study was to observe the changes occuring on arterial walls due to experimental SAH model and to investigate the effects of valproic acid on the basilar artery and brain tissues to prevent these changes and vasospasm.
Material and Method: We used 24 New Zeland rabbits. Animals were randomly divided into three groups as control (C), subarachnoidal hemorrhage (SAH) and valproic acid (VPA) groups. Cisterna magna puncture was done to all animals. SAH occured by giving non heparinised autologous blood except control group. 100 mg/kg of Valproic acid was given intra peritoneally to treatment group. All animals were sacrified after 48 hours. All experimental and surgical procedures were approved by İnönü University Animal Research Comittee.
Results: Our expectation was the arterial lumen area of SAH group will be smaller than control group. After statistical calculations we found that our expectation was similiar with our findings that the smallest artery lumen was seen in SAH group and the largest artery lumen was seen in control group. These differences were statistically significant.
Conclusion: Our findings showed that Valproic acid can prevent vasospasm by preventing arterial wall changes induced by SAH. It may be clinically beneficial at patients suffering from vasospasm due to SAH.

Keywords: Brain damage, Neuroprotective effect, Subarachnoid hemorrhage, Valproic acid, Vasospasm

ÖZ

Amaç: Çalışmamızın amacı deneysel subaraknoid kanamada arteryel damar duvarlarındaki değişiklikleri gözlemlemek ve bu değişiklikleri ve vazospazmı engellemek için valproik asidin baziller arter ve beyin dokusu üzerindeki etkilerini incelemektir.

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Materyal ve Metod: Çalışmamızda 24 adet Yeni Zelanda tavşanı kullanıldı. Denekler randomize olarak kontrol (K), subaraknoid kanama (SAK) ve valproik asid (VPA) olarak üç guruba bölündü.Tüm deneklere sisterna magna ponksiyonu yapıldı. Kontrol gurubu haricindekilere heparinize olmayan otolog kan verilerek subaraknoid kanama oluşturuldu. Tedavi gurubuna intra peritoneal 100 mg/kg valproik asid verildi. Tüm denekler 48 sanra sakrifiye edildiler. Tüm deneysel ve cerrahi prosedürler İnönü Üniversitesi Deney Hayvanları Araştırma Komitesi tarafından onaylandı.

Bulgular: Beklentimiz SAK grubunun arteriyel lümen alanının kontrol grubundan küçük olacağı yönündeydi. İstatistiksel hesaplamaların sonunda bulduğumuz sonuçların beklentimiz ile uyumlu olarak en küçük arter lümeninin SAK gurubunda ve en büyük arter lümeninin kontrol grubunda olduğunu gördük. Aradaki farklar istatistiksel olarak anlamlıydı.

Sonuç: Elde ettiğimiz sonuçlar valproik asidin SAK tarafından indüklenen arteryel duvar değişikliklerini önleyerek vazospazmı engelleyebileceğini göstermiştir. Valproik asid subaraknoid kanamaya bağlı gelişen vazospazmla mücadele eden hastalarda klinik olarak faydalı olabilecek bir ajandır.

Anahtar Kelimeler: Beyin hasarı, Nöroprotektif etki, Subaraknoid kanama, Valproik asid, Vazospazm

INTRODUCTION

Subarachnoidal hemorrhage (SAH) is one of the most important type of intracranial hemorrhage models with high mortality and morbidity rates. Also there are many factors causing SAH, rupture of intra cranial aneurysm is the most common reason. Vasospasm and cerebral ischemia due to this process occurring after SAH is one of the most important reasons of mortality and morbidity of SAH.

Results of many researches have shown that some excitator and inhibitor chemicals presenting after SAH play significant roles at cellular damage or neuronal protection [1-4]. Also recent studies have shown that there are many similarities between cerebral damaging and autoprotective mechanisms occurring after cerebral ischemia and epilepsy [5]. According to these demonstrations many researches have been done by using antiepileptic agents with the idea that the agents used to minimize the cerebral damage after epileptic seizure can also be used to minimize the ischemic damage.

Valproic acid (VPA) is used as an anti epileptic agent and it acts by several mechanisms. It acts as a sodium channel blocker and decreases the number of T type calcium channels on primary afferent neurons. And it is also observed that Gamma-amino-butyric-acid (GABA) level is increased in whole brain due to VPA. VPA also decreases glutamate secrection. Recent researchs have shown that VPA also increases anti-apoptotic-bcl family receptor numbers and by this way decreases the apoptotic cellular deaths [6].

There is an uncontrolled release of glutamate and aspartate after SAH. In seconds after neurons are sustained to glutamate. N-methyl-D-aspartate antagonist (NMDA) and Alfa-methyl-propionic acid (AMPA) receptors are activated. As a result; this causes entrance of sodium, calcium, and water through cells at damaged area. Increasing amount of intra cellular calcium causes the increase of oxidative stress. And VPA can prevent the changes on cerebral vessels due to ischemia by preventing this pathways.

Vasospasm generally starts after 3rd day of SAH and its severity increases between 4th and 12th days. It effects only intra dural cerebral arteries and the main effected vessels are the large brain stem arteries. Angiographic vasospasm can be demostrated with digital substraction angiography and it is more common although clinical vasospasm is less common, it causes cerebral ischemia and neurological deficit.

Many researchs have explained the clinical appereance of vasospasm with decrease of cerebral blood flow, disorder of cerebral micro circulation and micro embolies [7-9], and about in %50 of the patients the effects due to this process

is permanent. Unlike other types of ischemia vasospasm appears much later and is predictable. These facts a treatment period for this pathology.

Experimental SAH models of animals or biopsies of patients who have gone under angiographic vasospasm have shown some pathological changes at walls of effected vessels. Electron microscobic studies have shown many changes like vacuolisation of endothelial cells, disorder of interendothelial tight junctions, endothelial spillage and luminal micro thrombosis. Tunica intima has caused contraction of underlying media layers like internal elastic lamina [10,11]. Recent studies have shown edema, infiltration of polymorphic cells, formation of granulation tissue, fibroplasia due to migration and prolifaration of smooth cell muscles and intimal thickening due to collegenization.

The common qualification of vessels both at experimantal and human vasospastic process is thickened media layer, inflamatory and hypertrofic reactional changes at arteriel walls after SAH.Some myonecrosis at tunica media accompany to vasospasm. Cerebral arteries do not contain external elastic lamina but adventisia is generally thickened after SAH due to formation of granular tissue because of fibrin and erythrocytes [12].

Because cerebral blood flow decreases in spastic vessels, the most important factor to avoid from cerebral vasospasm is protection from hypotension to sustain cerebral perfusion. Systemic blood pressure must be kept in mild hypertensive (130-160 mm Hg). Surgical removal of the blood clot may be another method and also it is shown that some medical agents are protective in the process of vasospasm. These agents are high dose methyl prednisolone, vasodilator calcitonin releated peptid, hydroxil radical scavengers, papaverine, ET-1 inhibitors and calcium channel blockers. One of the action methods of valproic acid is blocking sodium channels and decreasing the number of T type calcium channels on primary afferent neurons. And also it is demonstrated that at high concantrations GABA levels are increased in whole brain and apoptotic cellular death is decreased by regulation of anti apoptotic bcl family [13].

MATERIAL and METHOD

We used 24 New Zeland rabbits each weigh between 2,4 and 3,3 kg. Animals were grouped into three as control (C), subarachnoidal hemorrhage (SAH) and valproic acid (VPA) groups.

GROUP I (Control: 6 rabbits): Cisterna magna was punctured without forming SAH in this group. They were sacrificed at the end of 48 hours.

GRUP II (SAH: 9 rabbits): Autologous blood is given after sisterma magna puncture to this group. All of the animals were sacrificed after 48 hours. %0.9 saline solution was given intra peritoenally to animals in this group.

GROUP III (SAH+VPA: 9 rabbits): Autologous blood is given after sisterna magna puncture. After formation of SAH 100 mg/kg intra peritoneal valproic acid is given for every 12 hours to these animals for 48 hours. (Depakin 400mg/4ml-Sanofi-Synthelobo)

Animals went under anesthesia before surgical procedure by giving 35 mg/kg Ketamin -hydrochloride (Ketalar %5 solution Parke Davis/ Eczacıbaşı, İstanbul), and xylazine (Rompun %2 solution, Bayer)

All animals were positioned at lateral position. The heads of animals were placed at hyperflexion

and sisterna magna puncture was performed via 23 gauge scalp vein set from atlanto occipital region. 2-3 cc cerebro spinal fluid was drained from animals. After CSF drainage, 2.5-3 cc non-heparinized autologous blood taken from ear artery was given into cisterna magna to all animals in SAH and valproik acid group to perform SAH at posterior circulation.

For occurence of clot formation around basillar artery, animals were positioned head down for 10 minutes. %0.9 saline solution was given to all animals at SAH group for every 12 hours for 48 hours.To all animals in VPA group 100 mg/kg valproic acid was given every 12 hours for 48 hours.All animals underwent ansthesia after 48 hours and thoracotomy was performed for each. By a catheter entering from left atrium to aorta . 1000 cc of %0.9 saline solution is given at 150 cm H2O pressure. Given saline solution is drained by exploring right atrium. We continued perfusion till solution gets clear. After this animals were sacrified by decapitation, brain and brainstem were extracted together.

Histo pathological researchs were studied at Erciyes University Veterinary Faculty Pathology Laboratory. The cerebrum of animals were put in %10 formaldehyde fixing solution for 5 days. Later tissues were passed through alcohol, methyl benzoate and benzol respectively and blocked with paraffin. 5µm sections obtained by microtome were stained with hematoxylin-eosin. Brain sections were observed with microscope (Olympos B X 51) and the sections of basillar artery were determined. Later with Leica DMD 108 model digital imaging systems the lumen diameters of basiller arteries of each group were measured from two opposing different points. The mean value of two measurements were defined as the single diameter of each basillar artery. Each vessel was was accepted as a circle by using ∏r2. Formula. Data was shown as mean values +/- SEM. Statistical analysis between groups were calculated by TUKEY multiple comparison method after One-Way-ANOVA and P<0,05 was accepted as statistically significant.

RESULTS

Macroscopically clot formation was observed around basillar arteries of SAH and SAH+VPA group but no clot formation was seen in control group (Figure 1, 2, 3).

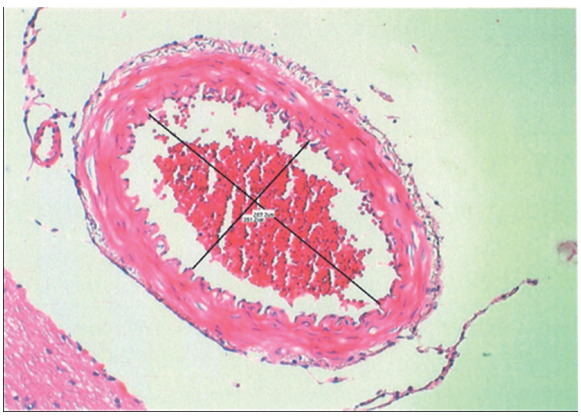

Figure 1. View of basillary artery of a control group rabbit.

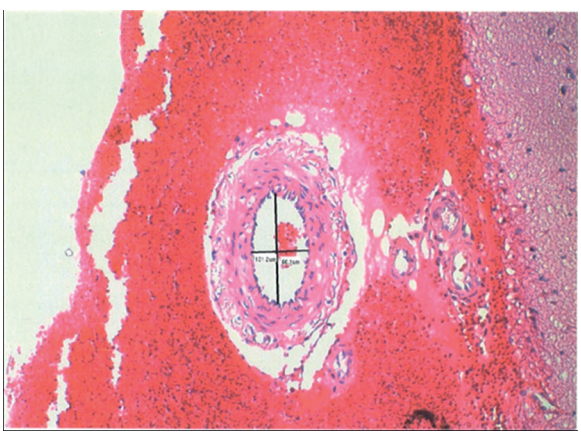

Figure 2. View of basillary artery of a SAH group rabbit.

Lumen surface areas of all animals in 3 groups were calculated and mean values were determined (Table 1). The mean value of Group C was 63171+638, Group SAH was 38350+3352, Group SAH+VPA was 43475+6060.

Table 1. Distribution of mean values of arterial lumen areas between groups.

	Control (n:6)	SAH (n:9)	SAH + Valproic acid (n:9)
	$\bar{X} \pm S\chi$	$\bar{X} \pm S\chi$	$\bar{X} \pm S\chi$
Arterial lumen area (μm^2)	63171±6386[a]	38350±3352[b]	43475±6060[b]

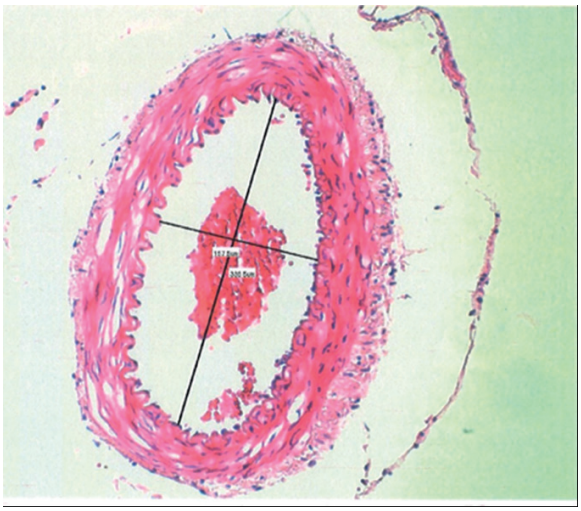

Figure 3. View of basillary artery of a treatment group rabbit.

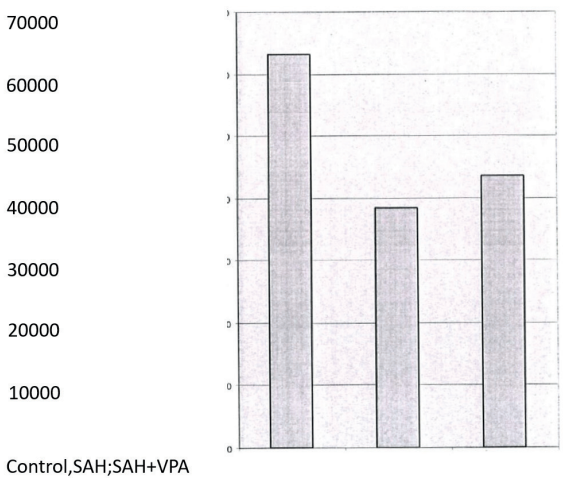

Figure 4. The graphical distribution of mean values of vessel lümen areas.

Differences between groups were statistically significant and it is shown appereantly on Figure 4 Statistical values of differences between grups are shown at Table 2.

Table 2. Statistical values of differences between groups.

Comparison of C-SAH	P-O.003
Comparison of C-SAH+VPA	P-O.008
Comparison of SAH-SAH+VPA	PzO.03

And we also studied immunohistochemical Terminal Deoxynücleotdyl Transferase dUTP Nick and labeling (TUNEL) for detection of nucleus fragmentation of DNA during apoptotic cell death in situ, by using apoptosis detection kit.

DISCUSSION

Symptomatic vasospasm occurs at about %20-40 of patients who has faced with SAH. Vasospasm generating after SAH is still a complicated and multifactorial process. It has a high mortality and morbidity rate due to the fact that it is the most difficult problem to over come; because we still could not understand its pathogenesis clearly. İschemic pathologies cause about %50 of early deaths of the patients who has survived from first SAH and aneurysm treatment. And the proper treatment for this process is still indeterminate [14-18].

H-H-H treatment (hypertension, hypervolemia, hemodilution) has been used as basic treatment method for SAH patients. Keeping away from hemoconcantration by hypervolemia is reasonable bu it is also intuitave. And also thypervolemia and hypertension may have side effects like pulmonary edema, cardiac and renal disfunction and increase of cerebral edema

Due to these factors; studies to understand and explain the pathogenesis of vasospasm which still keeps uncertanity and complicity are still going on being performed. Many treatment strategies are built and experienced acoording to the results of these researches. Understanding the pathogenesis of this process is indispensable.

Cerebral vasospasm is arterial narrowing due to blood clots in subarachnoidal space [19]. the most significant indicator for vasospasm is narrowinf basilar artery lümen and shortening of internal elsatic lamina. Also thickening of basilar arterial wall is accepted as another criteria of vasospasm.

As we mentioned before many treatment strategies targeting the factors which are playing role in pathogenesis of vasospasm have been tested and still going on to be tested. One of theses strategies is using antiepileptic agents. There are many similarities between the development of cerebral damage or auto protective mechanisms against these and epileptic seizures or protective effects of antiepileptic agents against these seizures. Due to this similarity it is thought that antiepileptic agents can minimize the damage after ischemia and many studies habe been done according to this idea by using several agents.

Antiepileptic agents are used against this process because of their multıble different acting ways but common property of them is they target the beginning or generation of seizures. While doing this they can also block toxic mechanisms which can cause neuronal damage releated with ischemia. For examole fenitoin, carbamazepine, topiromate like sodium channel blockers can prevent secrection of exitotoxic amin acids. Carbamazepine has also anti-inflammatory effects and this also improves neuronal protection.

Agents which are active on sodium channels like felbamate, gabapentin and levetiracetam can prevent calcium influv into ischemic cells and can reduce ischemic damage. They can do this by reducing glutamate secrection. Agents which can be activated by glutamate receptors like NMDA or AMPA can reduce exitotoxicity. These are some examples for neuro protective effects and their acting mechanisms for antiepileptic agents.

Valproic acid is one of these agents. It may act with several mechanisms. VPA may act by blocking sodium channels and it is also demonstrated that it can reduce calcium channels of T type on primary afferent neurons. At high concantrations of VPA GABA of wholw brain can decrease. It is also demonstrated that VPA can decrease apoptotic cellular death due to nincreasing of anti-apoptotic bcl receptor numbers. As aresult VPA can increase neuroprotective effect of GABA in brain while it decreases secrection of glutamate. According to all these factors and effects of VPA it is highly neuoroprotective agent.

CONCLUSION

The main purpose of our study was to observe the changes occuring on arterial walls due to experimental SAH model. Our expectation was the arterial lumen area of SAH group will be smaller than control group. After statistical calculations we found that our expectation was similiar with our findings that the smallest artery lumen was seen in SAH group and the largest artery lumen was seen in control group.

In our study we measured lumen area of basillar artery in SAH grup which is performed by sisterna magna puncture.

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Discriminative MRI Findings of Pituitary Adenomas from Craniopharyngiomas

Hipofiz Adenomlarının Kraniyofarinjiomlardan Ayırıcı MRG Bulguları

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ABSTRACT

Purpose: The aim of this study is to determine and define differential magnetic resonance imaging (MRI) findings of pituitary adenomas and craniopharyngiomas.
Materials and methods: This retrospective analysis was performed on MR imaging findings of 45 pituitary adenomas and 41 craniopharyngiomas with solid and cystic mixed appearance. MRI findings including shape ovoid, snowman, lobulation, chiasma compression, cavernous sinus invasion, 3rd ventricle compression, calcification, predominant type – cystic vs solid, contrast enhancement patterns – homogenous, reticular and extension were assessed.
Results: Among MRI findings superiorly lobulated shape, third ventricle compression and reticular enhancement of solid parts were common in craniopharyngiomas while snowman shape, predominantly solid content, homogenous enhancement of solid parts were compatible with adenomas significantly at $p < 0.05$ for all.
Conclusion: Tumor shape and contrast enhancement patterns of solid parts seem discriminative MRI features for pituitary adenoma and craniopharyngiomas.

Keywords: Pituitary adenoma, craniopharyngioma, magnetic resonance imaging

ÖZ

Amaç: Bu çalışmanın amacı hipofiz adenomları ve kraniyofarenjiyomların ayırıcı manyetik rezonans görüntüleme (MRG) bulgularını belirlemek ve tanımlamaktır.
Gereç ve yöntem: Bu retrospektif analiz, solid ve kistik mikst görünümde 45 hipofiz adenomu ve 41 kraniyofarenjiyomun MR görüntüleme bulguları üzerinde yapıldı. Ovoid şekil, kardan adam şekli, lobülasyon,

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kiazma kompresyonu, kavernöz sinüs invazyonu, 3. ventrikül kompresyonu, kalsifikasyon, baskın tip – kistik vs katı, kontrast tutma paternleri – homojen, retiküler ve ekstansiyon gibi MRG bulguları değerlendirildi.
Bulgular: MRG bulguları arasında lobüle şekil, üçüncü ventrikül kompresyonu ve solid kısımların retiküler kontrastlanması kraniyofarenjiomlarda yaygın iken, kardan adam şekli, ağırlıklı olarak solid içerik, solid kısımların homojen kontrastlanması adenomlada anlamlı bulgu olarak $p<0.05$'te uyumlu bulundu.
Sonuç: Tümör şekli ve solid kısımların kontrastlanma paternleri, hipofiz adenomu ve kraniyofarenjiomlar için anlamlı ayırt edici MRG özellikleri olarak görülmüştür.

Anahtar Kelimeler: Hipofiz adenomu, kraniyofarenjiyom, manyetik rezonans görüntüleme

INTRODUCTION

Pituitary adenomas are benign epithelial lesions and account for about 10–15% of all intracranial tumors representing the most common intrasellar pathology and the most common lesions involving both intrasellar and suprasellar regions [(1)]. An uncomplicated pituitary adenoma is isointense to grey matter on T1 and T2 weighted magnetic resonance imaging (MRI), and shows homogeneous enhancement pattern after contrast administration [(2-4)]. When a pituitary adenoma is complicated with necrosis, hemorrhage and cystic degeneration, it shows various signal intensity and enhancement pattern that can be similar with craniopharyngioma [(2-4)].

Craniopharyngiomas are neoplasms arising from squamous epithelial cell rests of Rathke's pouch. Typical appearance of a craniopharyngioma is a mixed cystic and solid mass in suprasellar region. Cystic component usually shows high signal intensity on T1-weighted images. Intrasellar involvement by a large craniopharyngioma is found in about 20-25% [(5)].

When a lesion involves both intrasellar and suprasellar regions, the differential diagnosis is important because surgical planning depends on it. While pituitary adenomas are usually approached by the transsphenoidal route, craniopharyngiomas require craniotomy and radical surgery [(6-8)].

In this study, we aimed to investigate the differential MRI findings of mixed cystic-solid pituitary adenomas and craniopharyngiomas involving both intrasellar and suprasellar regions.

METHODS

Study population

This retrospective study was approved by Kocaeli University institutional review board. We retrospectively reviewed pituitary MR imaging and electronic medical records in our center between 2010 and 2018.

The inclusion criteria were as follows: (a) both sellar end suprasellar involvement, (b) mixed cystic-solid character, (c) histopathologically proven adenoma or chraniopharingioma and the exclusion criteria were: (a) the mass involved only sellar or suprasellar region, (b) pure solid or pure cystic character, (c) any mass except from adenoma or chraniopharingioma.

86 patients with pituitary adenoma (n=45) and craniopharyngioma (n=41) were included in the study. Patients' ages ranged between 28 and 66 years (mean 44 years) for adenomas, and between 2 and 63 years (mean 30 years) for craniopharyngiomas. Forty-seven patients were men (22 adenoma, 25 craniopharyngioma) and 39 patients were women (23 adenoma, 16 craniopharyngioma). Demographic data of patients are shown in Table 1.

Table 1. Demographic data of patients.

		Pituitary adenoma (n=45)	Craniopharyngioma (n=41)	p value
Sex	Female	23	16	0.616
	Male	22	25	0.616
Age	Mean (SD)	44 (9.7)	30(21)	0.001

MRI protocols

MR images were obtained using 1.5 Tesla MRI (Gyroscan Intera, Philips Medical Systems, Eindhoven, The Netherlands) and 3 Tesla MRI (Achieva Interna: Philips Medical Systems, Eindhoven, The Netherlands) scanners in our center, using a 16-channel head coil.

Sagittal fat-saturated precontrast T1W images were acquired on both MRIs with TE 15 ms, TR 570 ms; coronal T2W images were acquired with TE 120 ms, TR 3000 ms; precontrast coronal and sagital T1W images were acquired with TE 10 ms, TR 500 ms. All sequences were performed with a slice thickness of 3 mm, a gap of 0.3 mm, and a FOV of 120 mm. Dynamic coronal T1W images were obtained on both MRIs with TE 10 ms, TR 500 ms with a slice thickness of 2 mm, a gap of 0.2 mm, and a FOV of 120 mm three minutes following the injection of contrast agent.

MRI assesment

All MRI images were reviewed on a picture archiving and communication system (PACS) workstation. Two radiologists evaluated MRI findings by consensus.

Tumour shapes were classified as ovoid, snowmanlike, or superiorly lobulated. A snowman shape was defined as a figure of eight-like shape, and superiorly lobulated shape as having two or more lobes in the suprasellar compartment.

Superior extensions were graded as below the optic chiasm, compressing the optic chiasm, and compressing the third ventricle. Compression of the third ventricle was considered to occur if the third ventricle floor was indented. A lateral extent was classified as one within or beyond the lateral margin of the cavernous intracranial carotid artery (ICA).

Tumour characteristics were classified as predominantly solid or predominantly cystic. Signal intensities of the solid portion of tumours on T2-weighted MRI images were classified as hyperintense (higher than the signal intensity of grey matter) or not. Signal intensities of the cystic portion of tumours on T1-weighted MRI images were also classified as hyperintense (higher than the signal intensity of whiter matter), or not. Enhancement patterns of solid portions were classified as homogeneous or reticular (mesh-like enhancements with intervening non-enhancing tiny defects).

Statistical analysis

All statistical analyses were performed using the IBM SPSS 20.0 (SPSS Inc., Chicago, IL, USA). Numerical variables were expressed as mean +/- standard deviation and categorical variables were expressed as frequency (percentage). The normality of the data distribution was evaluated by the KolmogorovSmirnov test. Numerical variables were evaluated using Student's t tests since the normal distribution was achieved. The relationship between categorical variables was evaluated by χ^2-test. $p<0.05$ was considered statistically significant.

RESULTS

The MRI features of pituitary adenoma, and craniopharyngioma are summarized in the Table 2. The most common shape of pituitary adenomas was snowman (Fig. 1 and 2) appearance (55.6%, 25 of 45 patients), while the most common shape of craniopharyngiomas was superior lobulation (Fig. 3 and 4) (78%, 32 of 41 patients). There was statistically significant difference between groups ($p<0.001$).

Table 2. The MRI features of pituitary adenoma, and craniopharyngioma are summarized.

	MRI features	Pituitary adenoma (n=45)	Craniopharyngioma (n=41)	p value
Shape	Ovoid	11 (24.4%)	5 (12.2%)	0.337
	Snowman-like shape	25 (55.6%)	4 (9.8%)	<0.001
	Superior lobulation	9 (20%)	32 (78%)	<0.001
Component characteristics	Predominantly solid	18 (40%)	11 (26.8%)	0.024
	Predominantly cystic	27 (60%)	30 (73.2%)	0.287
Signal intensity	T2 hyperintense solid component	9 (20%)	9 (22%)	0.949
	T1 hyperintense cystic portion	17 (38%)	25 (61%)	0.102
Extension	Compressing optic chiasm	36 (80%)	34 (82.9%)	1.000
	Compressing third ventricle	14 (31.1%)	29 (70.7%)	0,003
	Cavernous sinus invasion	10 (22.2%)	1 (2.4%)	0,011
Enhancement pattern of solid portion	Homogeneous	42 (93.3%)	5 (12.2%)	<0.001
	Reticular	3 (6.7%)	36 (87.8%)	<0.001

There was no statistically significant difference in the signal intensity of the solid portion on T2 weighted images between pituitary adenoma and craniopharyngioma (p=0.949). Also, in terms of the signal intensity of the cystic portion on T1-weighted images, although the high signal intensity of the cystic portion was more frequently observed in craniopharyngioma (Fig. 4 and 6) (61%, 25 of 41 patients) than in pituitary adenoma (Fig. 2 and 5), there was no statistically significant difference (p=0.102).

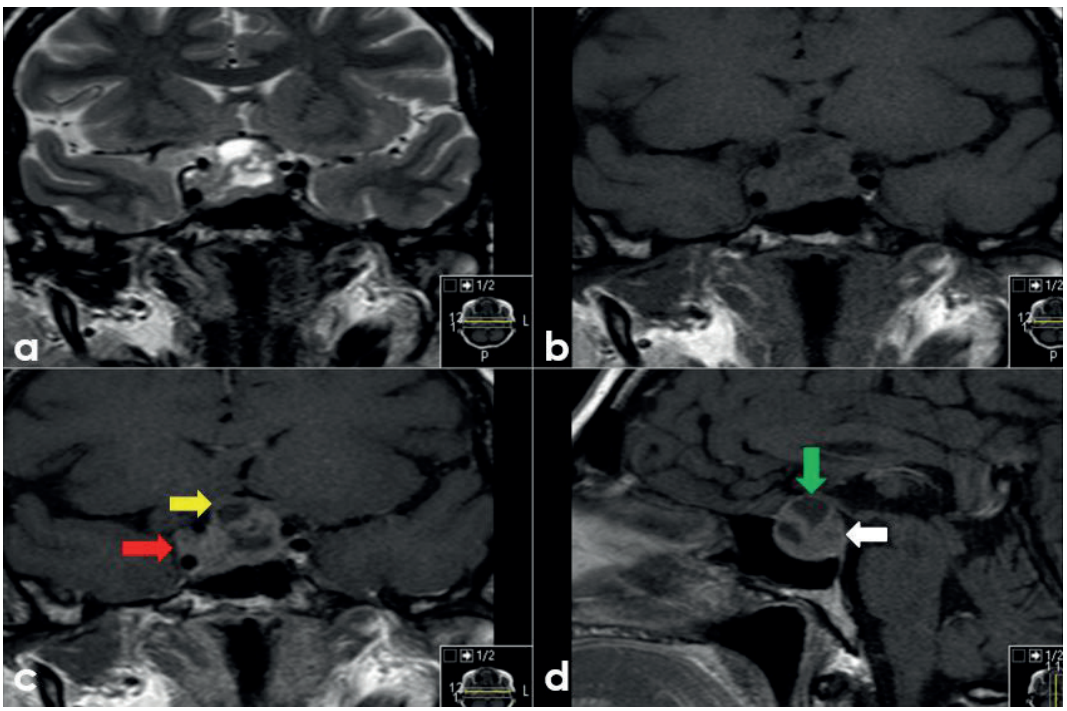

Figure 1. Pituitary adenoma in a 45-year-old woman with a snowman-like shape, homogeneously enhancing solid portion (white arrow in d) and T1 hypointense cystic portion (green arrow in d). The superior portion compresses the optic chiasm (yellow arrow in c). Also it invades the right cavernous sinus (red arrow in c).

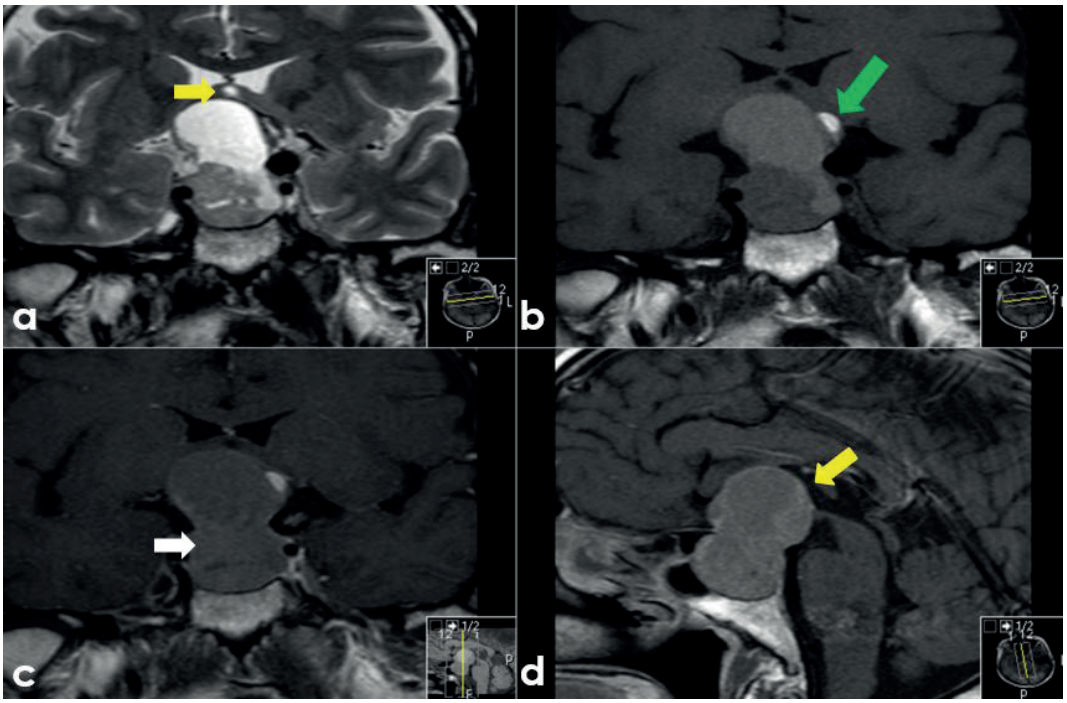

Figure 2. Pituitary adenoma in a 53-year-old male patient with a snowman-like shape, T1 hyperintense cystic portion (green arrow in b) and homogeneously enhancing solid portion (white arrow in c). The superior portion compresses the third ventricle floor (yellow arrows in a and d).

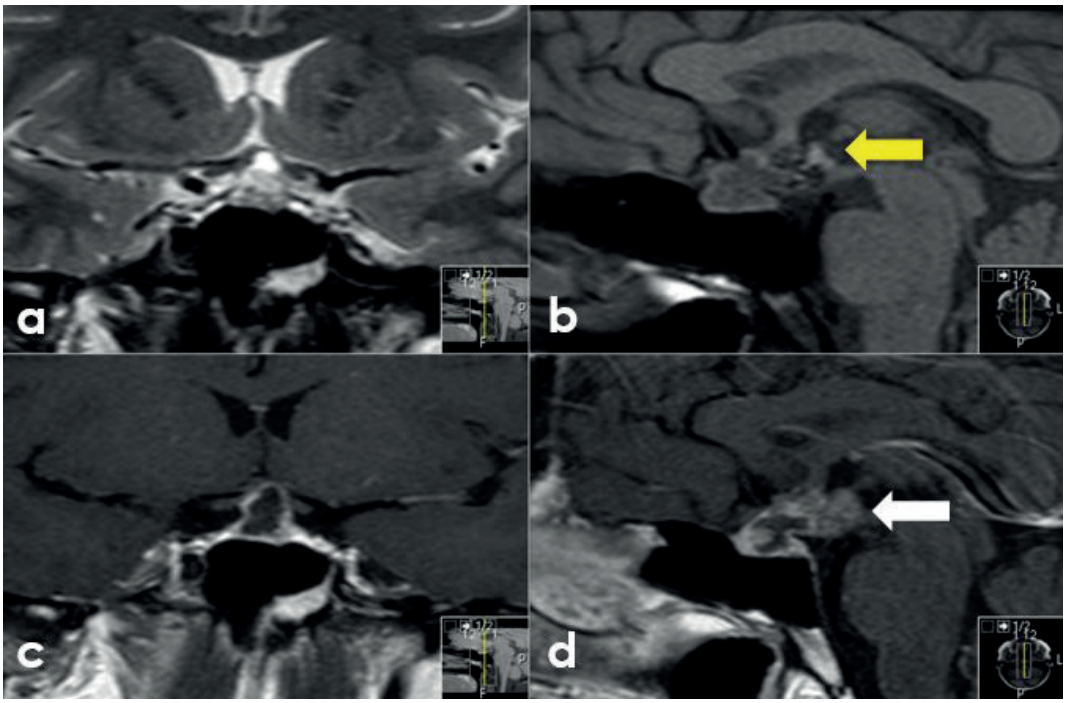

Figure 3. Craniopharingioma in a 32-year-old male patient with a superior lobulated shape, and heterogeneously enhancing solid portion (white arrow in d). The superior portion compresses the third ventricle floor (yellow arrow in b).

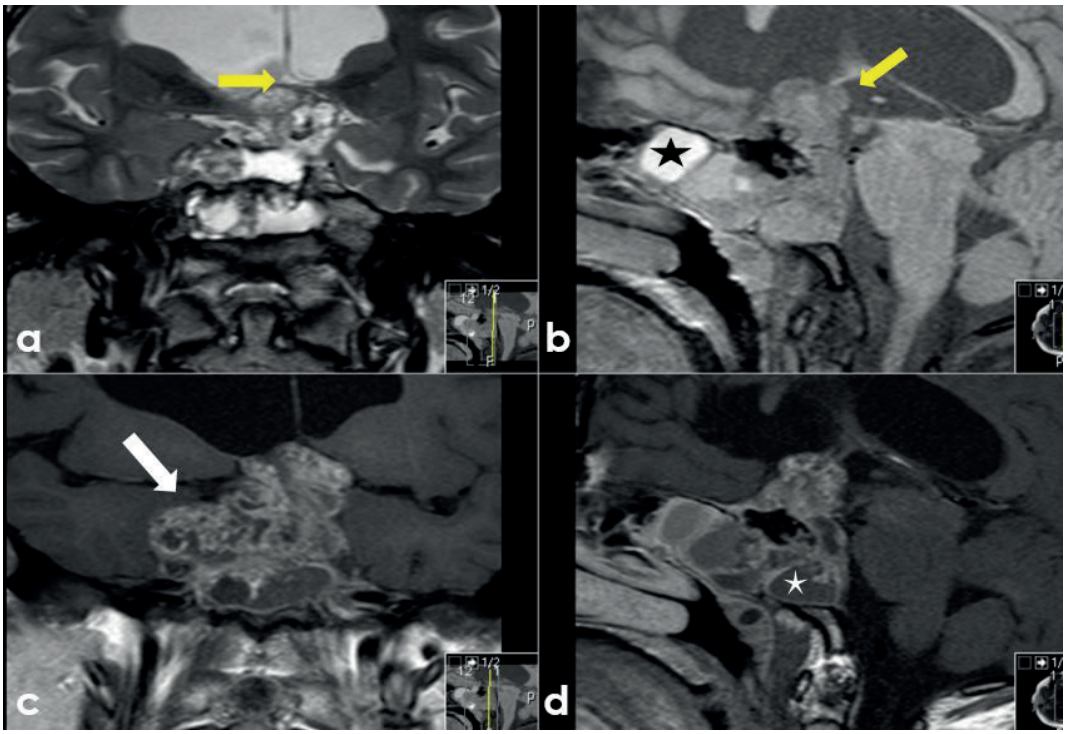

Figure 4. Craniopharingioma in a 20-year-old male patient with a superior lobulated shape, T1 hyperintense (black star in b) and hypointense (white star in d) cystic portions and heterogeneously enhancing solid portion (white arrow in c). The superior portion compresses the third ventricle floor (yellow arrows in a and b).

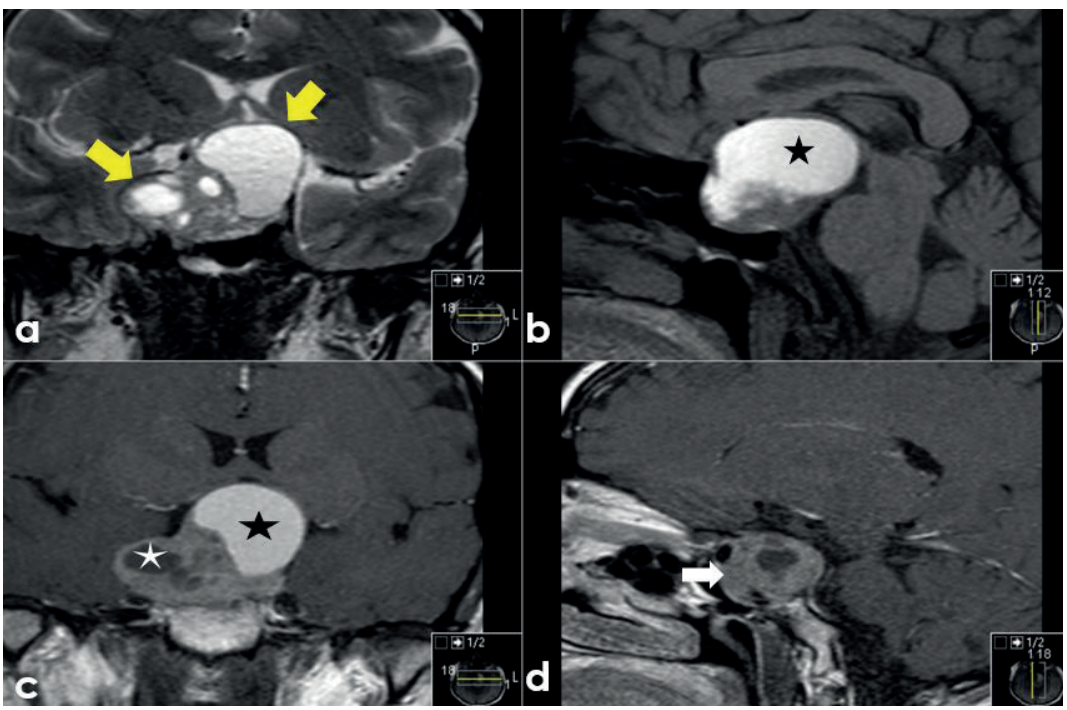

Figure 5. Pituitary adenoma in a 34-year-old female patient with a superior lobulated shape (yellow arrows in a), T1 hyperintense (black stars in b and c) and hypointense (white star in c) cystic portions and homogeneously enhancing solid portion (white arrow in d).

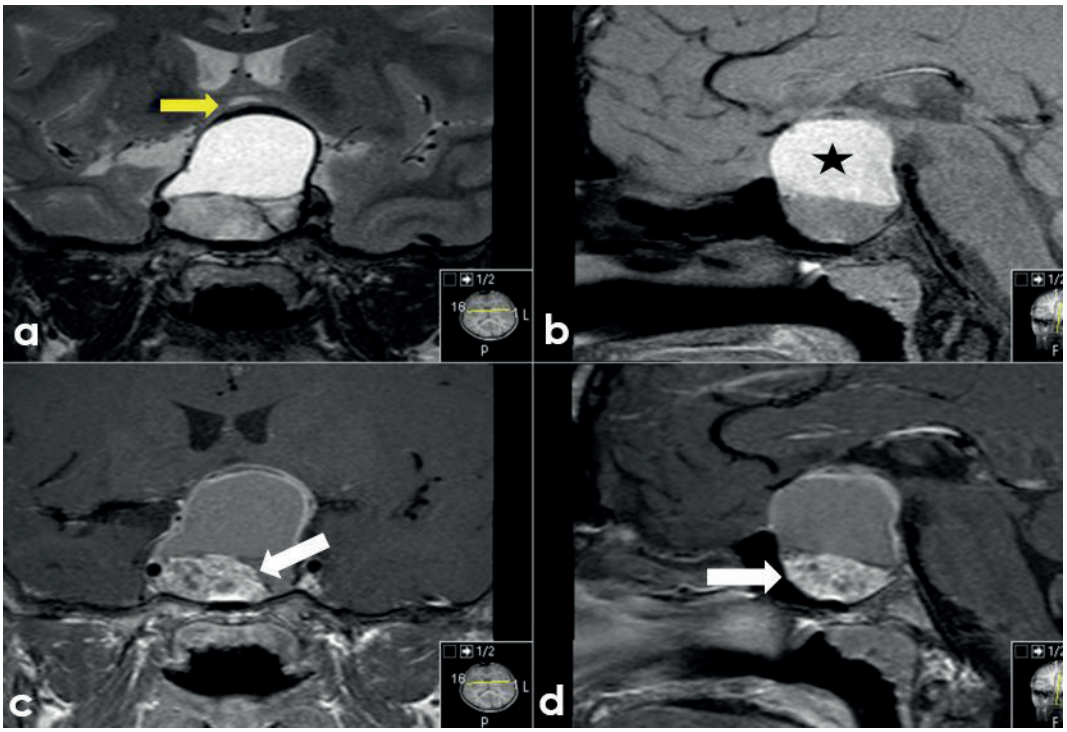

Figure 6. Craniopharingioma in a 14-year-old female patient with a snowman-like shape, T1 hyperintense cystic portion (black star in b) and heterogeneously enhancing solid portion (white arrows in c and d). The superior portion compresses the third ventricle floor (yellow arrow in a).

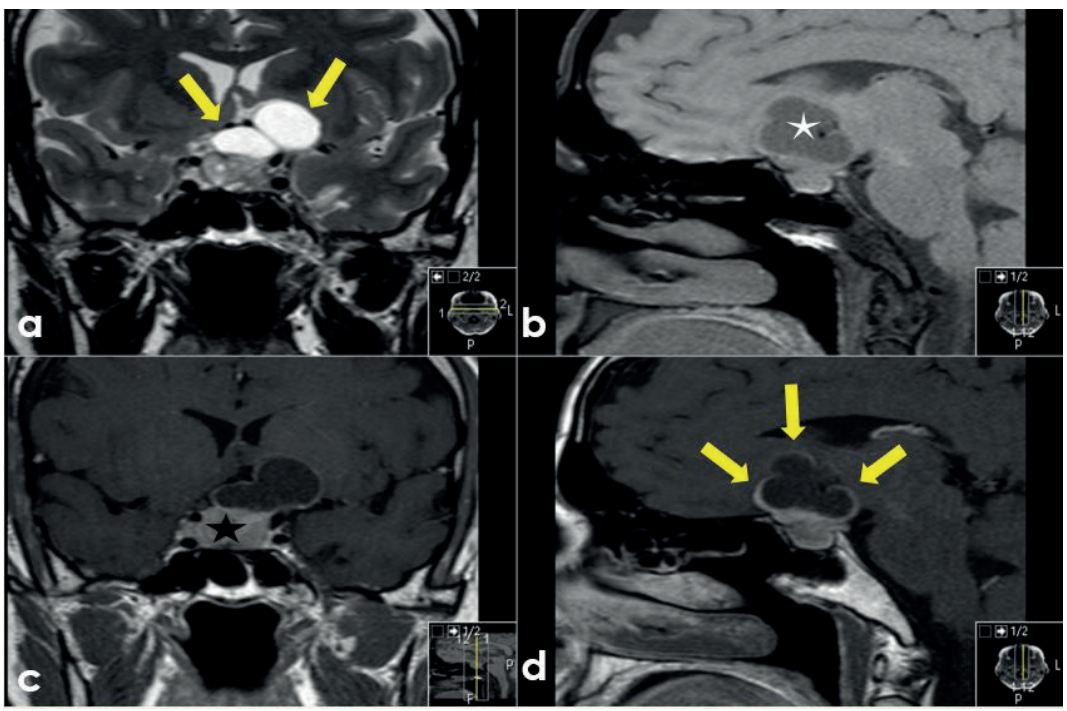

Figure 7. Pituitary adenoma in a 49-year-old female patient with a superior lobulated shape (yellow arrows in a and d), T1 hypointense (white star in b) cystic portion and homogeneously enhancing solid portion (black star in c).

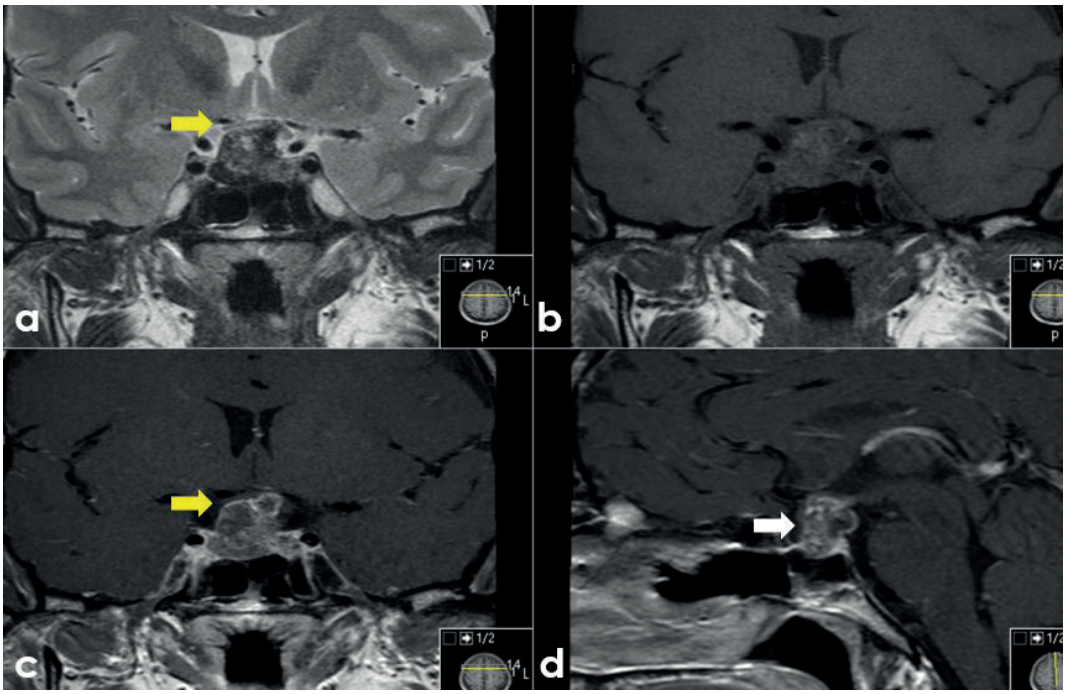

Figure 8. Craniopharingioma in a 35-year-old male patient with a snowman-like shape and heterogeneously enhancing solid portion (white arrow in d). The superior portion compresses the optic chiasm (yellow arrows in a and c).

With respect to extention, compression of the third ventricle was more commonly observed in craniopharyngiomas (Fig. 3, 4 and 6) (70.7%, 29 of 41 patients) than in pituitary adenomas (Fig. 2, 5 and 7) (p=0.003). By contrast, cavernous sinus invasion was more commonly observed in adenomas (Fig. 1, 5 and 7) (22.2%, 10 of 45 patients) than in craniopharyngiomas (Fig. 6) (p=0.011).

In terms of the enhancement patterns of solid portions, most of the pituitary adenomas (94.3%) showed homogenous pattern (Fig. 1, 2, 5 and 7) (93.3%, 42 of 45 patients), while craniopharyngiomas showed reticular pattern (Fig. 3, 4, 6 and 8) (87.8%, 36 of 41 patients). There was statistically significant difference between groups (p<0.001).

The sensitivities and specificities of statistically significant MRI findings are summarized in Table 3. The enhancement pattern of solid component was found to be the most sensitive and specific MRI finding in distinguishing mixed solid-cystic pituitary adenomas from craniopharyngiomas involving both sellar and suprasellar regions.

Table 3. The sensitivities and specificities of statistically significant MRI findings.

Tumor	MRI findings	Sensitvity (%)	Spesifity (%)
Pituitary adenoma	Snowman-like shape	86	65
	Predominantly solid	62	53
	Cavernous sinus invasion	91	53
	Homogeneous enhancement	89	92
Craniopharyngioma	Superior lobulation	78	80
	Compressing third ventricle	67	72

DISCUSSION

Patients with pituitary adenoma or craniopharyngioma, involving both sellar and suprasellar regions, usually present with similar symptoms such as headache, visual disturbance, or hypopituitarism. Clinically, the differential diagnosis is not easy [2,9-11]. On the other hand, the characteristic MRI findings of these tumours are well known, and their differential diagnosis is not problematic if they show typical imaging findings.

Pituitary adenomas with suprasellar extension typically have a "figure of eight" or "snowman" appearance with homogeneous enhancement [4]. Craniopharyngiomas divide into two histological types, squamous-papillary and adamantinous, have been described in the literature, although in some cases they cannot be divided into distinct histological types [11,12]. On MRI the typical features of squamous-papillary craniopharyngioma include a predominantly solid spherical tumour in the suprasellar region in adults [11]. The solid part shows heterogeneous but intense enhancement with small necrotic areas [11]. The cystic part contains a watery liquid that is hypointense on T1-weighted images and hyperintense on T2-weighted images [11]. On the other hand, adamantinous craniopharyngioma is a cystic or predominantly cystic, lobulate tumour, which is often observed in the intrasellar or suprasellar regions in children or adults [11]. On T1 weighted images, they have single or multiple hyperintense cysts with thin peripheral enhancing rims [11]. On T2-weighted images these cysts are either hyperintense or hypointense. Despite these well-known imaging findings, it is challenging to arrive at differential diagnosis in some cases [13].

Most pituitary adenomas arise from the pituitary gland and extend through the diaphragm sella up to the optic chiasm, and laterally to the cavernous sinus; most craniopharyngiomas arise from the suprasellar region extending up to the third ventricle with lobulation and down to the intrasellar region [13]. Concordant with this extension pattern, in our study, the cavernous sinus invasion was seen more commonly in adenomas, while the third ventricle compression was more common in craniopharyngiomas.

The cystic portions of the two tumours are believed to be composed of various entities: necrosis, haemorrhage, and cystic degeneration in pituitary adenoma [2,4]; and a high protein concentration, cholesterol, or methaemoglobin in craniopharyngioma [13]. In a previous study, Choi et al. [13] concluded that the signal intensity of the cystic fluid did not help in distinguishing adenomas from chraniopharingiomas. The results of the present study are concordant with this conclusion. T1-hyperintensecystic portion was more frequently observed in craniopharyngiomas but there was no statistically significant difference.

Homogeneous and reticular enhancement patterns were found to be key elements in the differential diagnosis of solid containing pituitary adenomas and craniopharyngiomas, respectively. Histopathological reviews of published studies suggest that the observed reticular enhancement pattern of solid containing craniopharyngiomas is caused by small regions of necrosis, keratin debris, or calcification [11,12]. Although Choi et al.[13] reported a reticular enhancement pattern in all solid containing craniopharingiomas in their study, homogeneous enhancement pattern was observed in five craniopharyngiomas in our study. One of them was adamantinous and the others were not specified. Squamous-papillary craniopharyngiomas presenting as homogeneously enhancing solid masses were reported by Sartoretti-Schefer et al.[11] previously. In our study there were two squamous-papillary

craniopharyngiomas which showed reticular enhancement.

In conclusion, MRI features, including tumour shape, extent, characteristics and enhancement patterns of solid portions are useful in the differentiation of mixed cystic-solid pituitary adenoma and craniopharyngioma involving both sellar and suprasellar regions. The enhancement pattern of the solid component is the key finding.

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Research Article / *Araştırma Makalesi*

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Effects of Topical Cyclosporin A Application on Preventing Epineural Scar Formation in Rats: Experimental Study

Sıçanlarda Topikal Siklosporin A Uygulamasının Epinöral Skar Oluşumunu Önlemedeki Etkileri

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ABSTRACT

The aim of this study is to evaluate macroscopic, histopathologic and immunohistochemical effects of topical cyclosporin administration on prevention of epineural scar formation in rats.
This experimental study was performed in two groups, each consisting of ten rats. Sciatic nerve was opened bilaterally. Tibial and peroneal components were set apart with blunt dissection. Abrasion injury was achieved by repetitive rubbing over biceps femoris muscle. In the control group saline sucked cotton peds were administered over opened sciatic nerve region bilaterally, whereas cyclosporin sucked peds were administered in the second group for five minutes duration. Eight weeks after surgery both groups were sacrificed and nerve complexes were evaluated microscopically, histopathologically and immunohistochemically.
No side effects were observed after 5 minutes single dose topical cyclosporine administration in our study. Cutaneous, muscular and deep fascial repairment were almost completed according to Petersen's numerical grading system ($p<0.05$). Nerve adherence was significantly decreased ($p<0.001$) in the ones treated with cyclosporin than the control group. FGF expression was demonstrated and individual evaluations of the control and the study groups immunhistochemically. The ratio of fibroblast/fibrosit number showed that both groups results were parallel. Single dose topical cyclosporin administration is shown to be successfull in preventing epineural scar formation after peripheric nerve neurolysis.

Keywords: Epineural scarring, Cyclosporin A, Pheripherial Nerve Surgery

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ÖZ

Bu çalışmanın amacı, sıçanlarda epinöral skar oluşumunun önlenmesinde topikal siklosporin uygulamasının makroskopik, histopatolojik ve immünohistokimyasal etkilerini değerlendirmektir.

Bu deneysel çalışma, her biri on rattan oluşan iki grupta gerçekleştirildi. Siyatik sinir iki taraflı açıldı. Tibial ve peroneal komponentler künt diseksiyonla ayrıldı. Biceps femoris kası üzerine tekrarlayan sürtmelerle abrazyon hasarı oluşturuldu. Kontrol grubuna açılan siyatik sinir bölgesine bilateral salin emdirilmiş pamuklu ped, ikinci gruba 5 dakika süreli siklosporin emdirilmiş ped uygulandı. Ameliyattan sekiz hafta sonra her iki grup da sakrifiye edildi ve sinir kompleksleri mikroskobik, histopatolojik ve immünohistokimyasal olarak değerlendirildi.

Çalışmamızda 5 dakikalık tek doz topikal siklosporin uygulamasından sonra herhangi bir yan etki gözlenmedi. Petersen'in sayısal derecelendirme sistemine göre deri, kas ve derin fasiyal onarım neredeyse tamamlandı ($p<0.05$). Siklosporin ile tedavi edilenlerde sinir adezyonu kontrol grubuna göre anlamlı olarak azaldı ($p<0.001$). FGF ekspresyonu gösterildi ve kontrol ve çalışma gruplarının bireysel değerlendirmeleri immünhistokimyasal olarak yapıldı. Fibroblast/fibrosit sayısının oranı her iki grubun sonuçlarının paralel olduğunu gösterdi. Tek doz topikal siklosporin uygulamasının, periferik sinir nörolizinden sonra epinöral skar oluşumunu önlemede başarılı olduğu gösterilmiştir.

Anahtar Kelimeler: Epinöral skar, Siklosporin A, Periferik Sinir Cerrahisi

INTRODUCTION

Although new surgical techniques have been developed, epineural scar formation following peripheral nerve surgery is still one of the major problems on the postoperative period of clinical outcome. Especially for the recurring surgical requirement, epineural scar formation plays an important role on the surgical success.

Epineural scarring is one of the important factors affecting postoperative clinical results and success of surgical procedure. Epineural scarring restricts the nerve mobility by tethering the peripherial nerves during the limb movement. Severe and prolonged tethering of the nerves may cause ischemia and further nerve injury. In the clinical course tethering of the nerves results not only pain but also sensorial and motor deficits due to compression of the nerves [1-4].

Preventing from or reduction in epineural scarring increases the peripherial nevre surgery sucsess, decreases the complications and facilitates the secondary operations [5,27].

Cyclosporin A, a wellknown nonpolar cyclic oligopeptid immunsupressif agent widely used in organ transplantation and in the field of ophthalmology for preventing postoperative fibrosis.

Studies reveal that cyclosporin A prevents fibroblastic proliferation and decrease the fibroblast collagen synthesis [19-21,23]. Intraoperative topical cyclosporin administration which may prevent epineural fibrosis was examined by gross anatomically, histopathologically and immunohistochemically

MATERIALS AND METHODS

Twenty adult male Wistar rats weighing 250–300 g were housed in a temperature- and humidity-controlled room (22±3°C and 67±7%, respectively) in which a 12- to 24-h light–dark cycle was maintained. The animals were fed standard rat chow and tap water ad libitum. Ethical approval was granted by the University Ethics Committee.

Surgical Procedure

General anesthesia was established by ether inhalation. Sciatic nerve was opened bilaterally set apart from the neighboring structures by sterile technique. Tibial and peroneal components were separated via blunt dissection toward the sciatic foramen. Abrasion injury was achieved by repetitive rubbing of the nylon tooth-brush over biceps femoris muscle. Meanwhile the nerves were kept retracted carefully. Saline sucked peds were administered around sciatic nerves bilaterally of the control group and 0.3ml of 50mg/ml cyclosporin-A sucked peds were

administered around sciatic nerves bilaterally of the control group for five minutes duration. Afterwards fascia was closed with 3/0 vicryl and skin was closed with stapler.

Evaluations

Evaluations were performed macroscopically, histopathologically and immunohistochemically respectively.

Postoperative observations

After the operation, rats were examined weekly for healing characteristics of the wound site and for sciatic nerve functions, including abnormal foot posture, toe spreading, foot dorsoflexion, and plantar flexion.

Gross anatomical evaluations

Blind surgical dissection was performed to the neurolysis sites of half the rats in the Cyclosporine treated group and the untreated control group under deep ether anesthesia after 8 weeks surgery. Perineural adhesions during anatomical dissection were evaluated concerning the numerical grading scheme described by Petersen et al.[4], (Table 1).

Histolopathologic and Immunohistologic study

The remaining half of the rats in the cyclosporine treated group and the untreated control group were used for histological evaluation after 8 weeks surgery. All animals were sacrificed by deep ether anesthesia and perfused-fixed with 0.9% saline followed by 2% paraformaldehyde. The entire sciatic nerve and surrounding scar tissue were removed en bloc and immersed in 10% neutral buffered formalin overnight. Tissues were embedded in paraffin and cross-sectioned at 5 µm. Sections were stained with hematoxylin and eosin. Connective tissue was evaluated using Masson trichrome stain. The thicknesses of scar and nerve tissue were measured under light microscopy (Olympus BX51, Tokyo, Japan) using an ocular micrometer (Olympus), and the scar tissue formation index was obtained by dividing the value of the thickness of the scar tissue by the value of the thickness of the nerve tissue [6,27].

Under 40× magnification, the fibroblasts/fibrocytes were counted for four different quadrants around the epineurium for each nerve, and the mean number of fibroblasts/fibrocytes was calculated. Each specimen was graded according to the following scale, which has been reported by some authors [7,27]. Grade 1 less than 100 fibroblasts, Grade 2 100–150 fibroblasts, Grade 3 more than 150 fibroblasts.

The sections were waited in etui at 56°C for a night, prepared with xylol, absolute and normal alcohol, boiled in sitrate buffer for 30minutes and undergone hydrogen-peroxide for immunohistochemical study. Antibody (fibroblast growth factor) (Santa Cruz Biotechnology 147 sc-79) primary antibody and chromogen were performed. Adverse staining with Mayer hematoxilene was made. Fibrosis of perineurium was evaulated under 40x and 100x light microscope. Staining degrees of epineural area with FGF-2 were evaluated via semi-quantitative method by two investigators, who were blind to the groups.

A modified scale smiliar to the litreture was used for statistical evaluation [28]. Staining for FGF-2 (increasing of the brown dansity of the epineural area) was rated as normal (+), increased (++) and extremely increased (+++).

Statistical Analysis

Statistical analysis was performed with software SPSS 10 program under windows XP. Independent t-test is used for the significance among the groups and dependent t-test is used for

comparing right and left leg sciatic nerve for each rat. $p<0.05$ is accepted as significant.

RESULTS

Clinical Results

There was no statistical significance between characterization of wound area healing and the neurological function of the leg among the rats treated with cyclosporine and the non-treated ones ($p>0.05$).

Anatomical Results

Cutaneous sutures were removed at the end of the 8th week and the original incision areas were reopened and evaluated carefully. Enflammautory reaction findings were not observed. The epineural adhesions surrounding the nerves were significantly less than the control group (Fig 1 A, B). Cutaneous, muscular and deep fascia closure according to Petersen's numerical grading scale was almost completed ($p>0.05$). Nerve adhesions in the cyclosporine treated group was significantly decreased compared to the control group ($p<0.001$). Gross anatomical evaluation results are summarized in Table 1.

Histopathological Results

Dense epineural connective tissue, like a thick band surrounding the nerves in the saline administered control group and the tissue surrounding the nerves in the control group were demonstrated and compared with 40X magnifing with the light microscope (Fig 2 A, B).

Statistical significance was not determined among the right and left siatic nerves in both group by qualitative analysis of the connective tissue surrounding the nerves (scar tissue index), however there was a statistically significance between the cyclosporine treated group and the control group ($p<0.01$) (Table 2,3).

The ratio of fibroblast per fibrosit number were found to be significantly increased in the control group than the cyclosporine treated group ($p<0.001$) (Table 4).

Immunohistochemical Results

In immunohistochemical studies, after staining for FGF-2, FGF expression was demonstrated at 40X and 100X magnifing with light microscope. As mentioned in the literature[28] and due to our

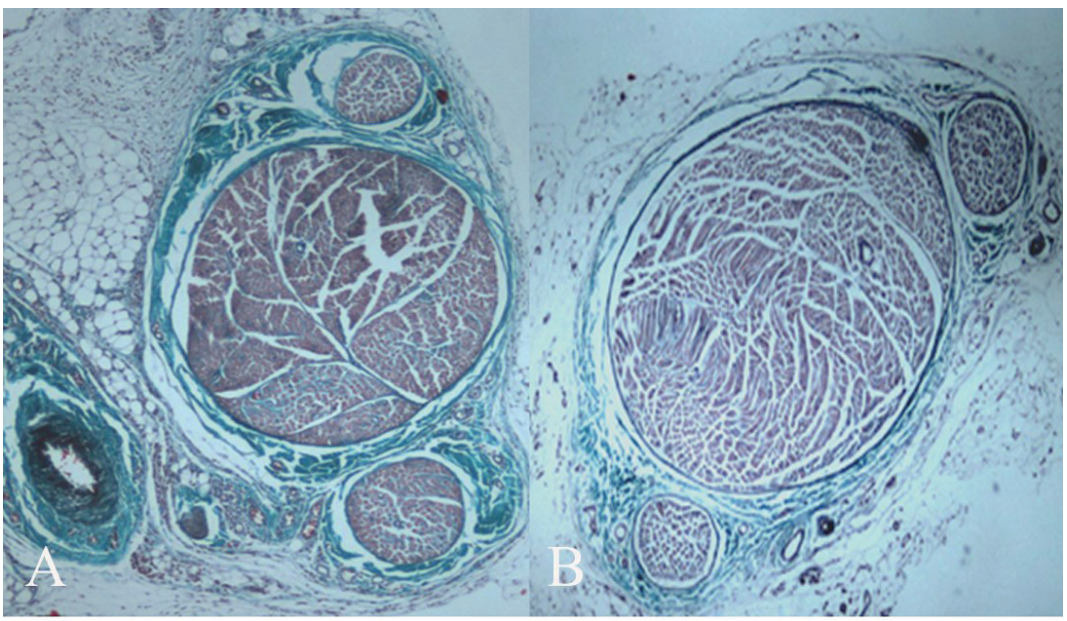

Figure 1. The epineural adhesions surrounding the nerves. A: Control group, B: Study group.

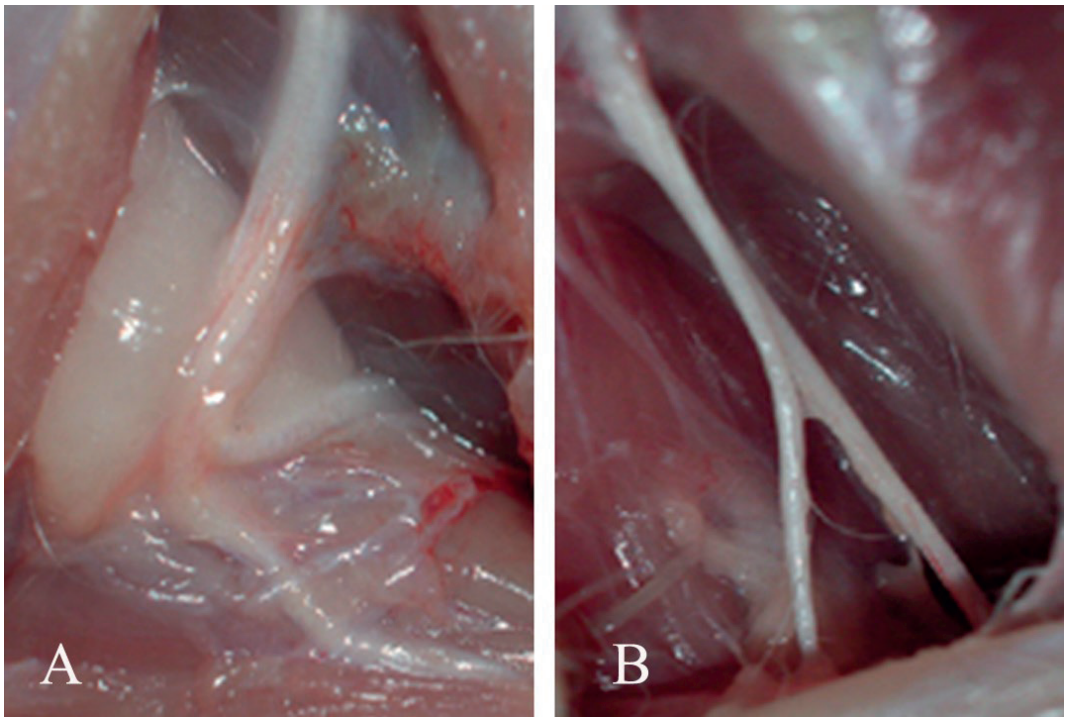

Figure 2. Images under 40X magnifying light microscope of epineural tissues in the (A) control and (B) study group respectively.

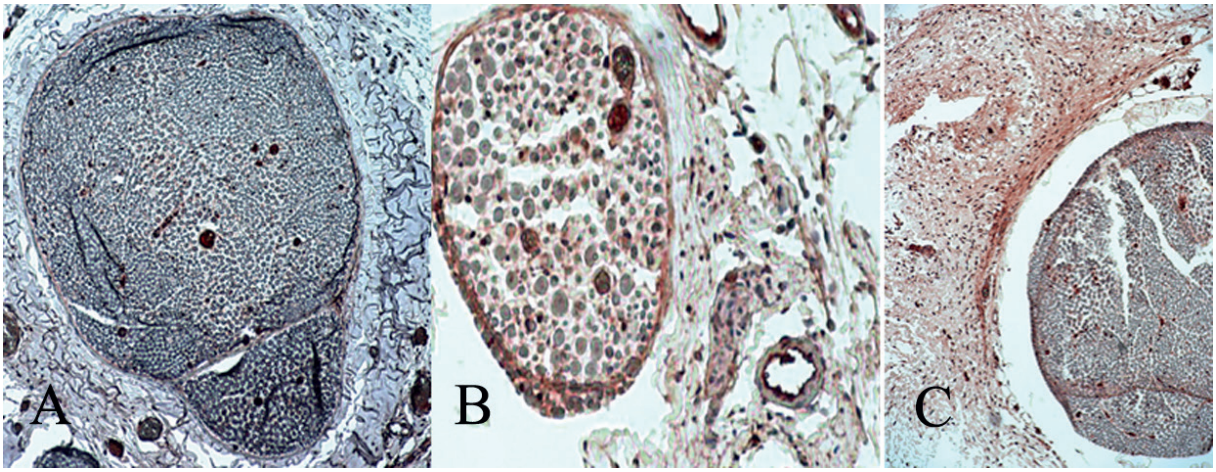

Figure 3. FGF Staining. The brown color of the epineural area increases as the (+) increase. A: 1(+) FGF expression, B: 2(++) FGF expression, C: (+++) FGF expression.

modified scale, as (+) increase, increasing of the brown dansity of the epineural area was observed (Fig 3 A, B, C). Both investigators' blind evaluation results were evaluated statistically. Independent t test results revealed significance among the study group and the control group ($p<0.001$) (Table 5).

Individual evaluations of the control and the study groups immunhistochemically, the ratio of fibroblast /fibrosit number showed that both groups results were parallel (Table 6).

Table 1. Peterson grading and gross anatomical evaluation results. Independent t-test results of comparing with control group (p<0.001).

Nerve No	Skin Closure		Muscular fascia		Nerve tissue		Separateness	
	control	CsA	control	CsA	control	CsA	control	CsA
1	1	1	1	2	2	1	2	1
2	1	1	1	1	2	2	2	1
3	1	1	2	1	2	1	3	1
4	1	1	2	1	2	1	2	1
5	1	1	1	2	3	2	2	2
6	1	1	1	1	3	1	3	1
7	1	1	1	1	3	2	2	1
8	1	1	1	1	2	1	3	1
9	1	1	1	1	3	1	2	1
10	1	1	1	2	2	2	3	1
Mean±SD	1,00±0,00	1,00±0,00	1,20±0,42	1,30±0,48	2,40±0,52	1,40±0,52*	2,40±0,52	1,10±0,32*

Table 2. Comparison scar tissue index of each rat's right and left sciatic nerve and dependent t test results. Dependent t test results revealed that there was no statistical significance between right and left legs of control group (p=0,608) or the study group (p=0,800).

Nerve no R-L	Group 1		Group 2	
	R	L	R	L
1-6	0,139	0,164	0,081	0,053
2-7	0,189	0,116	0,046	0,055
3-8	0,112	0,150	0,047	0,052
4-9	0,142	0,131	0,043	0,047
5-10	0,157	0,122	0,028	0,049
Mean±SD	0,1478±0,03	0,13660±0,02	0,0490±0,02	0,0512±0,003

Table 3. Comparison of scar tissue formation among control group and the study group and the results of independent t-test. Independent t-test results of comparing with control group (p<0.001).

Nerve no	Control	CsA
1	0,139	0,081
2	0,189	0,046
3	0,112	0,047
4	0,142	0,043
5	0,157	0,028
6	0,164	0,053
7	0,116	0,055
8	0,150	0,052
9	0,131	0,047
10	0,122	0,049
Mean±SD	0,14220±0,02	0,05010±0,01*

Table 4. Comparing Fibroblast/fibrosit number. Independent t-test results of comparing with control group (p<0.001).

Nerve No	Control	CsA
1	3	1
2	3	2
3	3	1
4	1	2
5	2	1
6	2	1
7	3	2
8	3	2
9	2	1
10	3	1
Mean±SD	2,50±0,7	1,40±0,5*

Table 5. Staining for Fibroblast growth factor. Independent t-test results of comparing with control group (p<0.001).

Nerve No	Control	CsA
1	3	2
2	2	1
3	3	2
4	2	2
5	2	1
6	2	1
7	3	2
8	3	1
9	2	2
10	3	1
Mean±SD	2,50±0,5	1,50±0,5*

In recent years many agents including human amniotic fluid, fibrine glue, cis-hydroxyprolin, antitransforming growth factor-ß antibody, aprotinin, ADCON_T/N, mitomycine and low dose radition therapy were tried on the prevention of epineural scar formation [14-18,27]. Moreover large clinical series that reports the usefullness of these materials are not present.

Cyclosporin A, a chemotherapoetic agent that is used especially in ophtalmatology, is shown to be effective for prevention of postoperative fibrosis.

Table 6. Comparison fibroblast/fibrosit number of histopathologic evaluation and immunohistochemical results among both control and study groups.

Nerve No	Fibroblast number		Degree of staining for Fibroblast growth factor	
	Control	CsA	Control	CsA
1	3	1	3	2
2	3	2	2	1
3	3	1	3	2
4	1	2	2	2
5	2	1	2	1
6	2	1	2	1
7	3	2	3	2
8	3	2	3	1
9	2	1	2	2
10	3	1	3	1
Mean ±SD	2,50±0,7	1,40±0,5	2,50±0,5	1,50±0,5

DISCUSSION

Prevention or decresing of epineural scar formation increases the success of peripheric nerve surgery, fasciliates the following surgical procedure and decreases the complication rates [8,9].

Many surgical techniques were developed to decrease or prevent the amount and frequency of epineural scar formation, secondary neurolysis, microsurgical techniques, endoscopic techniques, nerve transposition, dermofascial fat grafts, vein packing and muscular flaps [10-14]. However performing of very special techniques can not prevent postoperative adhesion formation.

On acute rejection of transplated organs, intragraft fibroblasts increases hyaluronan production. Cyclosporine, decreases this production about 50% [16].

Literature on cyclosporine proposes that it affects as decreasing the enflammatory cells by incresing the number of mucine producing Goblet cells [22,24-26]. A study has shown that cyclosporine directly affects the natural duration of fibroblasts and increases apoptozis on fibrotic tissues clinically [19]. Furthermore some studies have shown the relation between cyclosporine A effect on pericardial enflammation on complete and stable remission [20]. It's shown that in contrast to chemotreapotic agents like azotioprine and

cyclophosphamides, cyclosporin does not destroy the immun effectors, but inhibites the activation and proliferation of T cells especially T helpers. Cyclosporine's molecular mechanism is shown to be associated with IL-2 synthezis [20,24].

Invivo and invitro studies revealed that cyclosporin A prevents fibroblastic proliferation and decreases fibroblast collagen synthesis [19-22].

Our results demonstrate that single dose topical cyclosporine administration was significantly effective on prevention of epineural scar formation. Skin closure were completed on both groups. In the study group, there was no faillure of siatic nerve and surrounding tissues were significantly decreased in the study group, also nerve could be easily put apart from surrounding muscular gap. Significant scar formation was observed in the control group. Nerve adhesion scores were found to be significantly low in the cyclosporine treated group compared with the control group.

Results of quantitative histological and immunological evalutaion of the scar tissue supported the gross evaluation results. Scar tissues thickness were significatly higher in the control group compared with the cyclosporine treated group. Fibroblast/fibrocite number ratio was found to be significantly lower in the study group. After painting with FGF, FGF expression was significantly incressed in the study group compared with the control group.

Local and systemic administration of cyclosporine may result with dose related complication. However low dose and short administration time decreases these complications. We did not observe any side effect after single dose topical administration for 5 minutes.

CONCLUSION

In peripheric nerve surgery epineural scar formation plays an important role on the postoperative clinical results and evaluation of surgical success. Single dose topical cyclosporine administration is shown to be successfull in preventing epineural scar formation after peripheric nerve neuronalysis. Local advers effect was not seen. However further studies should be performed on the neccessary concentration and exposure time of the long term security.

Ethical Approval: This study was approved by the Kocaeli University Ethics Committee (No: 97 / 04.05.2005).
Conflict of interest: There is no conflict of interest in our study.
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İyi Huylu Kalvaryal Lezyonlar: Klinik Deneyim

Clinical Experience with Benign Calvarial Lesions

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ÖZ

Amaç: Kalvariyum dayanaklı bir yapı olarak beynimizi korumada primer öneme sahiptir. Kalvariyumda kötü huylu ya da iyi huylu tümoral oluşumlar ile birlikte çeşitli metabolik tümör benzeri değişikler görülebilmektedir. Bu makalede bir sağlık merkezinde iyi huylu kalvariyal lezyonlar nedeni ile ameliyat edilen olgular irdelenmektedir.
Materyal Metod: Çalışma retrospektif karakterde olup hastaların yaş cinsiyet gibi demografik verileri yanında başvuru şikayeti, kitlenin yerleşim yeri, geçirilmiş ameliyat öyküsü, radyolojik görüntüleri, lezyon çapı, patolojik tanı, ameliyat şekli, dural etkilenim, nüks edip etmediği, komplikasyon gelişimi ve takip süresi not edilmiştir.
Sonuçlar: Çalışmaya toplamda 13 hasta dahil olmuştur. Bu hastaların 12 tanesi erişkin yaşta hasta iken sadece bir tanesinin çocuk hasta olduğu tespit edildi. 9 hastanın erkek cinsiyette olduğu belirlendi. En sık başvuru şikayeti kafada ağrılı şişlik idi. En sık iki tanı fibröz diplazi ve osteom olarak belirlendi. Bir hastada intraserebral komplikasyon gelişimi oldu. Hiçbir hastada nüks görülmedi.

Anahtar Kelimeler: Kalvariyum, fibröz displazi, osteom, eozinofilik granülom, intraosseoz menengiom

ABSTRACT

Aim: The calvarium is of primary importance in protecting our brain as a strong structure. Various metabolic tumor-like changes can be seen in the calvarium, together with malignant or benign tumoral formations. In this article, patients who were operated for benign calvarial lesions in a health center are discussed.
Material Method: The study was retrospective and in addition to demographic data such as age and sex of the patients, the complaint of application, location of the mass, previous surgery history, radiological images, lesion diameter, pathological diagnosis, type of surgery, dural involvement, recurrence, complication development, and follow-up period were noted.

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Results: A total of 13 patients were included in the study. While 12 of these patients were in adulthood, only one of them was found to be a pediatric patient. It was determined that 9 patients were male. The most common complaint was a painful swelling on the head. The two most common diagnoses were fibrous dysplasia and osteoma. Intracerebral complication developed in one patient. No recurrence was observed in any patient.

Keywords: Calvarium, fibrous dysplasia, osteoma, eosinophilic granuloma, intraosseous meningioma

GİRİŞ

Kalvarium dayanaklı bir yapı olarak başta travmalar olmak üzere beynimizi korumada primer öneme sahiptir. Bununla birlikte zaman zaman kafatasında çeşitli lezyonlar gelişebilmektedir. Bu lezyonlar primer olarak kemik yapıdan kaynaklanabildiği gibi sekonder olarak cilt, cilt altı ve serebral kökenli lezyonların kemiğe invazyonuna bağlı olarak da gelişebilmektedir. Kafatasındaki lezyonlar primer tümörler, metastatik tümörler veya metabolik hastalıkların tümör benzeri değişiklikler olabilir [(1)]. İyi huylu kalvariyal lezyonlar sklerotik veya litik karaketerde olabilmektedir. Bu lezyonlar arasında fibröz displazi, osteom, meningiom, paget hastalığı, eozinofilik granülom, epidermoid-dermoid, osteoblastom, hemanjiom ve anevrizmal kemik kisti sayılabilir. Ayrıca kronik anemiler, renal osteodistrofiler ve osteopeni gibi sistemik hastalıkların da kafatasında kemik değişikliklerine yol açtığı bilinmektedir [(1,2)].

Bu çalışmada 2013-2021 yılları iyi huylu kalvariyal lezyon nedeniyle ameliyat edilmiş hastalar retrospektif olarak değerlendirilmiştir.

MATERYAL METOD

Bu çalışmada 2013-2021 yılları arasında Gaziantep Medikal Park hastanesinde iyi huylu kalvariyal lezyonu nedeniyle ameliyat edilen 13 olgu çalışmaya alındı. Retrospektif olarak olguların yaş, cinsiyet gibi demografik verileri yanında başvuru şikâyeti, lezyon yeri, daha önce aynı veya benzer bir kalvariyal lezyon için cerrahi geçirip geçirmediği, ameliyatta ne yapıldığı, komplikasyonlar, dura ve parankimal invazyon varlığı, patolojisi, takip süresi not edildi. Bunlara ilaveten lezyon boyutu, lezyonun beyin tomografisi, T1 ve T2 ağırlıklı manyetik rezonans görüntülemede lezyonun görünüm özelliği, kontrast tutup tutmadığı ve ekstradural yayılımın olup olmadığı da not edildi. Herhangi bir verisinde eksiklik olan hasta ya da hastalar çalışmaya dahil edilmedi.

BULGULAR

Çalışmamıza 9'si kadın (%69.2) 4'ü erkek (%30,8) toplam 13 olgu dâhil edildi. Bunların 1'i çocuk, 12'si erişkindi. Olgularımızın yaş aralığı 3–74 yaş, yaş ortalamaları ise 33,61'dır. Lezyon yerleşimi 6 olguda frontal, (%46,1) 6 olguda temporal (%46,1)ve bir olguda ise temporal (%7,8) kemik üzerindeydi. En sık geliş şikâyeti kafada ağrılı şişlik (%61,1) idi. Başka merkezden gelen 2 olgu nüks (%15,3) kabul edilerek aynı yerden aynı tanı nedeni ile ameliyat öyküsü mevcuttu. 13 olguda kraniektomi ile lezyonun total olarak çıkarıldığı ve 10 olguda (%76,9) metakrilat ile 1 olguda (%7,6)ise lezyon titanyum plak ile kraniyoplasti yapıldığı tespit edildi. Radyolojik dura invazyonu ve frontal sinüs invazyonu olan 2 olguya duraplasti, diğer 1 olguya ise frontal sinüs tamiri yapıldı.

Lezyonların histopatolojik incelemelerine bakıldığında tanılar, 4 olguda (%30,7) fibröz displazi ve 4 olguda (%30,7) osteom, 2 olguda (%15,3) eozinofilik granülom, 1 olguda(%7,6) kolesteatom, (%7,6) 1 olguda intraosseoz meningiom ve 1 olguda (%7,6)ise kronik subgaleal hematomdu.

Sadece bir olguda (%7,6) komplikasyon olarak intraparankimal hematom gelişimi ve bunun da medikal tedavi ile takip edildiği tespit edildi. Ortalama 73 aylık takip ve kontrollerde rekürrens ve mortalite olmadığı belirlendi (Tablo 1). Lezyonların radyolojik tetkik sonuçları olgu bazında Tablo 2'de gösterilmiştir.

TARTIŞMA

Kalvariyal bening lezyonlar sıklıkla asemptomatiktir. Semptomatik olanlar da en fazla sınırlandırılmış ağrı şişlik gibi kitle etkisi sonucu radyolojik tetkiklerle tanı konulur. Beynin BT veya MRI sırasında rastlantısal olarak da görülebilir [1,3-8]. Kalvaryumun radyolojik değerlendirmesinde ilk adımın, lezyonların litik veya sklerotik olarak değerlendirilebileceği düz radyografi olduğu bildirilmekle birlikte, bilgisayarlı tomografinin gelişimi ile düz radyografinin kalvariyal lezyonların tansında klinik önemi kalmamıştır diyebiliriz çünkü tomografi (BT) ile iç ve dış tabuladaki destrüksiyon, litik yada sklerotik yapı, lezyon içerisindeki kalsifikasyon, sklerotik kenar ve lezyonun dansitesi değerlendirilebilmektedir. Manyetik rezonans görüntüleme (MRG) erken evredeki lezyonların gösterilmesinde, eşlik eden yumuşak doku komponentinin ve parankimal invazyonun değerlendirilmesinde tomografiden daha üstündür [1]. Çalışmamıza baktığımızda olguların hiçbirinde tanı rastlantısal radyolojik görüntülemeye dayanmamaktadır. 1 olgu haricinde tüm olgularda ele gelen şişlik mevcuttu. 6 aylık çocuk hariç diğerlerinde ağrı şikayeti mevcuttu. 3 olguda bulantı kusma baş dönmesi şikayetleri eşlik etmekteydi.

Çeşitli çalışmalarda en sık pariyetal ve frontal kemik tutulumu bildirilmiştir (%67-71) bildirmiştir [3,9]. Bizim çalışmamızda da literatüre benzer şekilde en sık yerleşim yerinin %92 oranı ile parietal ve frontal kemikler olduğu tespit edildi. Çalışmamızda bu kadar yüksek oran tespit edilmesini bahsi geçen çalışmalara göre kısmi hasta sayısı azlığına bağlamak mümkündür. Histopatolojik değerlendirmeye göz atıldığında Tucker ve ark.'nın çalışmasında en sık tanı osteom (%58, 18 olgu) olarak tespit edilmiştir. Bizim çalışmamızda en sık iki tanıdan biri osteom (%31, 4olgu) ve diğeri ise yine dört olgu ile fibröz displazi olmuştur. Histopatolojik olarak da çalışmamız literatür ile uyum göstermektedir.

Fibröz displazi, tüm iyi huylu kemik tümörlerin% 7'sini teşkil eder [8,9]. Fibröz displazi, normal kemik yerine olgunlaşmamış osteoblastların anormal farklılaşmasından kaynaklanmaktadır. Yaygın olarak genç erişkinde ve ergenlerde görülür [4,6,8,10]. Fibröz displazi, tercihen frontal ve temporal kemikleri etkiler ve sütürleri geçebilir [4]. Bizim çalışmamızda saptanan dört fibröz displazi olgusunun ikisinin frontal ikisinin ise parietal kemikte yerleşim gösterdiği tespit edilmiştir. Tanı sıklıkla tesadüfidir. Fakat kitle etkisi ile foramenleri daraltıp kraniyal sinir basısı ile semptom verebilmektedir [4,6,8,10]. Bizim çalışmamızda ise tüm olguların semptomaitk olduğu ve en sık yakınmanın ele gelen ağrılı şişlik olduğu tespit edildi.

Fibröz displazi tomografide lezyonun büyük bir kısmında karakteristik "buzlu cam matriks" ile intradiploik, genişleyen bir lezyon göstermektedir [1,4-6,8]. Dış tabula, iç tabulaya göre daha belirgin bir şekilde etkilenir [1,4,6,8]. Mix litik, sklerotik, homojen sklerotik olarak üç tip tarif edilmiştir, Homojen sklerotik (buzlu cam yoğunluğu) paterni genellikle görülür [1,8]. Çalışmamızda da benzer tomografi görüntüleri tespit edilmiştir.

Fibröz displazi, fibröz dokunun mineralize matriks oranına bağlı olarak MRG'de değişken sinyal ve kontrast artışı gösterebilir [1,4,8]. Lezyon, homojen olarak sklerotik formun en sık görüldüğü düşünüldüğünde, tipik olarak T1 ve T2 ağırlıklı görüntülerde düşük sinyaldir [1,8]. Yüksek mineralli

Tablo 1. Klinik Bulgular

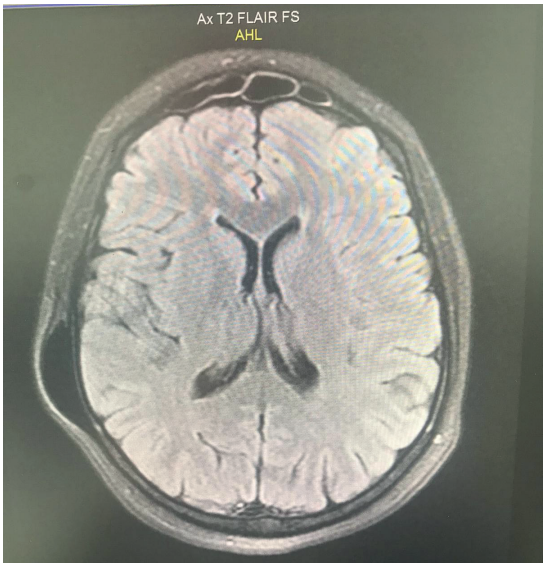
NO	YAŞ	CİNSİYET	KLİNİK	LOKALİSAZYON	ÖNCEKİ OPERASYON	PATOLOJİ	KRANİOPLASTİ	DURAL PARANKİM TUTULUM	KOMPLİKASYON	NÜKS	TAKİP SÜRESİ/Ay
1	18	K	AĞRI ŞİŞLİK	FRONTAL	-	EOSNOFİLİK GRANÜLOM	METAKRİLAT	-	-	-	101
2	27	E	AĞRI	TEMPORAL	-	KOLESTEATOMA	-	-		-	100
3	23	K	ŞİŞLİK	FRONTAL	-	OSTEOM	METAKRİLAT	-	-	-	97
4	35	K	ŞİŞLİK	FRONTAL	2 yıl önce aynı tanı yer	OSTEOM	METAKRİLAT	-	-	-	96
5	31	E	AĞRI ŞİŞLİK	FRONTAL	-	FİBRÖZ DİSPLAZİ	METAKRİLAT	-	-	-	90
6	38	K	ŞİŞLİK	FRONTAL	-	OSTEOM	METAKRİLAT	FRONTAL SİNÜSGALEAL		-	82
7	21	E	AĞRI ŞİŞLİK KİBAS	PARİATAL	5 yıl önce aynı tanı aynı yer	FİBRÖZ DİSPLAZİ	METAKRİLAT	-	-	-	68
8	56	K	AĞRI ŞİŞLİK KİBAS	FRONTAL	-	FİBRÖZ DİSPLAZİ	METAKRİLAT	DURAPLASTİ GALEAL	-	-	62
9	46	K	AĞRI ŞİŞLİK KİBAS	PARİATAL	-	FİBRÖZ DİSPLAZİ	METAKRİLAT	-	PARNKİMAL HEMATOM	-	50
10	20	K	AĞRI ŞİŞLİK	PARİATAL	-	EOSNOFİLİK GRANÜLOM	METAKRİLAT	-	-	-	46
11	3	E	ŞİŞLİK	OKSİPİTAL	-	KRONİK SUBGALEAL HEMATOM	-	-	-	-	71
12	45	K	ŞİŞLİK	PARİATAL	-	OSTEOM	TİTANYUM MATCH	-	-	-	47
13	74	K	AĞRI ŞİŞLİK	PARİATAL	-	İNTEROSSEOZ MENİNGİOM	METAKRİLAT	DURAPLASTİ GALEAL	-	-	39

Tablo 2. Görüntüleme Bulguları

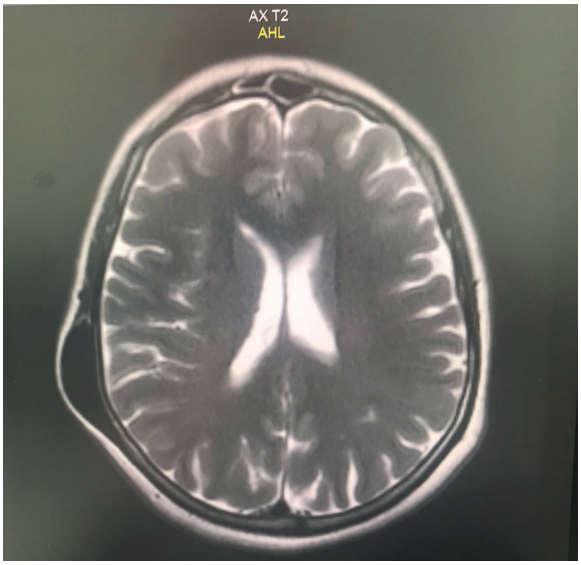
NO	LEZYON BOYUTU MM	BT	MRI T1	MRI T2	KONTRASLANMA	EKSTRADURAL YAYILIM
1	15*20*20	Düzensiz litik görünüm	-	-	-	-
2	24,5*20*14,5	Mastoidte havalanma azlığı,yumuşak doku densitesi	Hiperintense	Hipointense	Minimal periferal kontraslanma	Ekstradural yayılım
3	30*20*15	Sclerotik	Hipointense	Hipointense	Kontras tutulumu yok	Ekstradural yayılım
4	35*30*30	Juksta kortikal, Sclerotik	Hipointense	Hipointense	-	-
5	16*40*33	Sclerotik ,Buzlu cam manzara,intternal tabula inceltilmiş	Hipointense	Hipointense	Homojen kontraslanma	-
6	18*10*32	Minimal sclerotik,Buzlu cam manzarası	Hipointense	Hipointense	Homojen minimal kontraslanma	Ekstradural yayılım
7	80*60*23,3	Minimal sklerotik	Hipointense	Hipointense	Heterojen kontraslanma	-
8	100*110*120	Dağınık yama tarzında düzensiz kontürlü hieperdems lezyon	Hipointense	Hipointense	Heterojen kontraslanma	Ekstradural yayılım Dural invazyon
9	120*80*90	Sklerotik, Buzlu cam manzara	izointense	Hiperintens	Heterojen kontraslanma	-
10	40*40*40*	Eğimli kenarlar ile litik lezyon.	İzointens	Hiperintens	Homojen kontraslanma	Ekstradural yayılım
11	57*33*25	Çevresi kalsifik,İçinde yer yer kalsifik veya hemorojik ürünlere ait hipodensite	-	-	-	-
12	42*17*28	Juksta kortikal,Sclerotik	Hipointense	Hipointense	-	-
13	62*21*15	Düzensiz kontur ve şekilli, fırçamsı, kemik dansitesinde ancak yer yer litik alanlar içeren oldukça heterojen	Hipointense	Yaygın hipointense yer yer hiperintense	Dural kontraslanma	Dural invazyon

stromaya sahip lezyonlar, T1 ve T2 ağırlıklı görüntülerde daha düşük sinyal yoğunluğu gösterme eğilimindeyken, yüksek lifli doku içeren lezyonlar, T1 ağırlıklı görüntülerde orta sinyal yoğunluğuna ve T2 ağırlıklı görüntülerde yüksek sinyal gösterme eğilimindedir. Yüksek kontrast tutma eğilimindedir [1,4,8,10]. Çalışmamızda da 3 olguda T1 ve T2 ağırlıklı görüntülerde düşük sinyal, 1 olguda ise T1 ağırlıklı görüntülerde orta sinyal yoğunluğu T2 ağırlıklı görüntülerde de yüksek sinyal manyetik rezonans görüntüleme bulguları tespit edilmiştir. Tüm olgularımızda kontrast tutulumunun olduğu tespit edilmiştir. 1 olgu başka merkezde opere olmuş nüks olarak kabul edildi. Fibröz displazinin tek küratif tedavisi radikal rezeksiyondur. Estetik amaçlı yapılan kemiğin traşlanması son zamanlarda tercih edilmesine rağmen yüksek nüks oranları bildirilmiştir [11-13]. Çalışmamızda tüm olgularda lezyonu total çıkarma amaçlı kraniektomi yapılmıştır. Takiplerimizde nüks rastlanmamıştır.

Osteoma en sık yaşamın dördüncü ile beşinci on yılları arasında ve erkeklerde daha sık görülen ve de iyi huylu kalvariyal tümörler arasında en fazla tanı alan lezyondur [3]. İyi farklılaşmış kompakt ve spongioz kemikten oluşan bir juxta-kortikal tümördür [1,3,5,6] . En sık şikâyet sebebi ağrı, hassasiyet ve yavaş büyüyen kitledir [14,15]. BT'de osteoma, juxta-kortikal, iyi tanımlanmış, sklerotik, homojen bir lezyondur [1,4,6,7,8]. MR görüntülerinde T1 ağırlıklı görüntülerde homojen düşük sinyal, kompakt ve süngerimsi trabeküler kemik miktarına bağlı olarak hipointens, T2 ağırlıklı görüntülemede ise değişken görünüme sahiptir (Şekil 1, 2). Literatürde uzun aralıklar takip sonrası nüks gelişimini bildiren yayınlar mevcuttur [15]. Bizim çalışmamızda da bir olgumuzun 2. yılda nüks geliştirmiş olduğu tespit edildi. Tüm olgularımız frontal kemik yerleşimliydi. Radyolojik bulgularımızda T1 ağırlıklı görüntülerde hipointens, T2 ağırlıklı görüntülemede hipointense olarak tespit edildi.



Şekil 1. Osteom MR T1 hipointens görüntü

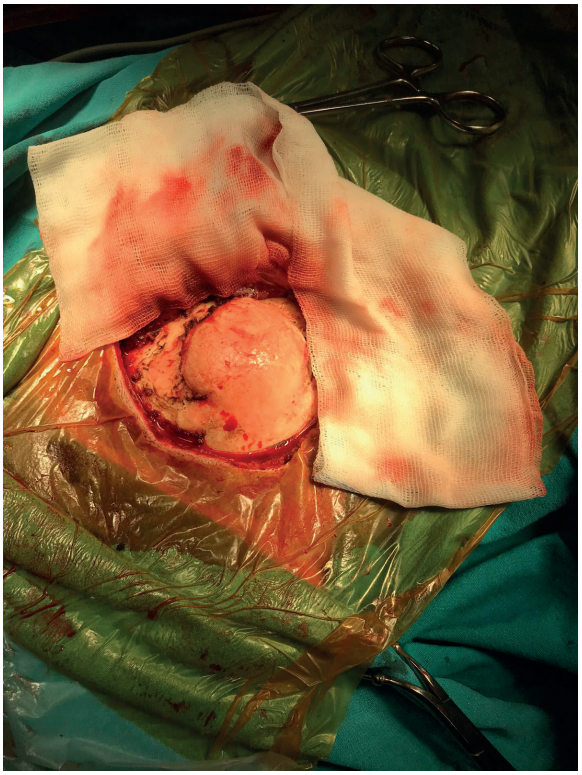


Şekil 2. Osteom MR T2 hipintens görüntü

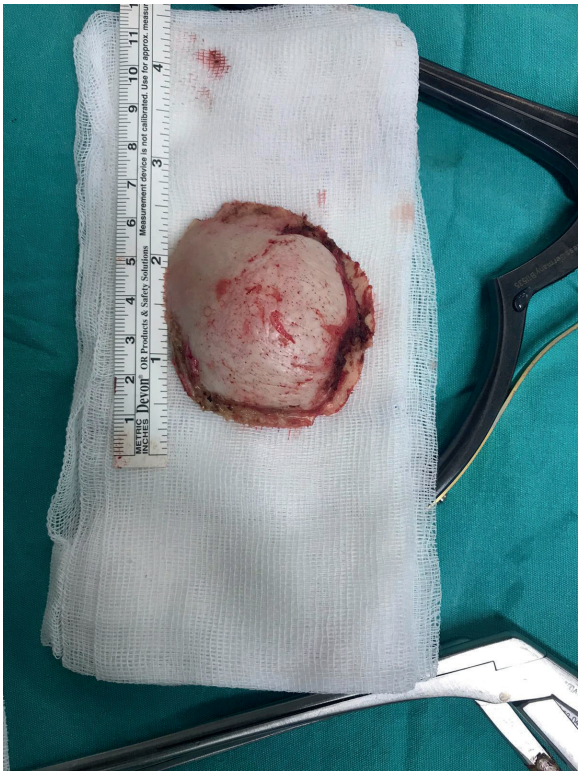
Olgularımızın hepsi total olarak çıkartıldı (Şekil 3, 4, 5). 1 olgumuzun başka merkezden bize gelerek nüks kabul edildi. Hastanın frontal sinüs üzerinde ve sinüse invazyon göstermesi sonucu ilk operasyonda lezyonun total olarak çıkartılamadığını düşündürdü. Kendi takiplerimizde nüks gelişimi görülmemiştir.

Eozinofilik granülom en sık görülen langerhans hücreli histiyositoz formu olup sıklıkla kalvariyumu tutabilmektedir [1,4,8]. Lezyonlar parietal ve frontal bölgelerde daha sık görülür [1,4,8]. Eozinofilik granülom (EG) özellikle erkekler olmak üzere çocukları, ergenleri ve genç yetişkinleri daha sık etkilemektedir. Lezyon BT'de iç ve dış tabulaların eşit olmayan tutulumuna bağlı olarak eğimli kenarları olan osteolitik bir lezyon olarak görülebilmektedir [1,4,6,8,16]. Lezyonun merkezi, rezidüel sağlam kemik olan bir "düğme sekansı" (button sekestrum) içerebilir [1,4,6,8]. Ayrıca yumuşak doku invazyonu ile ekstradural veya ekstrakranial uzantıya sahip olabilirler [1,4,7,8]. Spontan veya tedavi ile iyileşen lezyonlar sklerotik hale gelmektedir [1,4,8]. MR'da bu lezyonların sinyal yoğunluğu spesifik değildir. T1 ağırlıklı görüntülerde düşük ila orta sinyale ve T2 ağırlıklı görüntülerde yüksek sinyale sahiptir, ancak iyileşme aşamasında T2 sinyal görüntülemede düşük meydana gelir [1,8]. Eozinofilik granülom kuvvetli kontrast tutar ve sıklıkla reaktif dural veya galeal kontrastlanma olur [1,4,7,8]. Bu lezyonlar tipik olarak cerrahi küretaj veya eksizyon ile tedavi edilir [17-19]. Serimizdeki 2 olgu genç erişkin olup, frontal ve pariatal kemik tutulumu vardı. BT iç ve dış tabulaların eşit olmayan tutulumuna bağlı eğimli kenarları olan düzensiz osteolitik lezyon mevcuttu. MR görüntülemesinde T1 ağırlıklı görüntülerde düşük sinyale ve T2 ağırlıklı görüntülerde yüksek sinyale sahip homojen kontraslanan lezyon mevcuttu. Her iki olguya kraniektomi yapıldı. Takibinde nüks ve yeni bir kitle görülmedi.

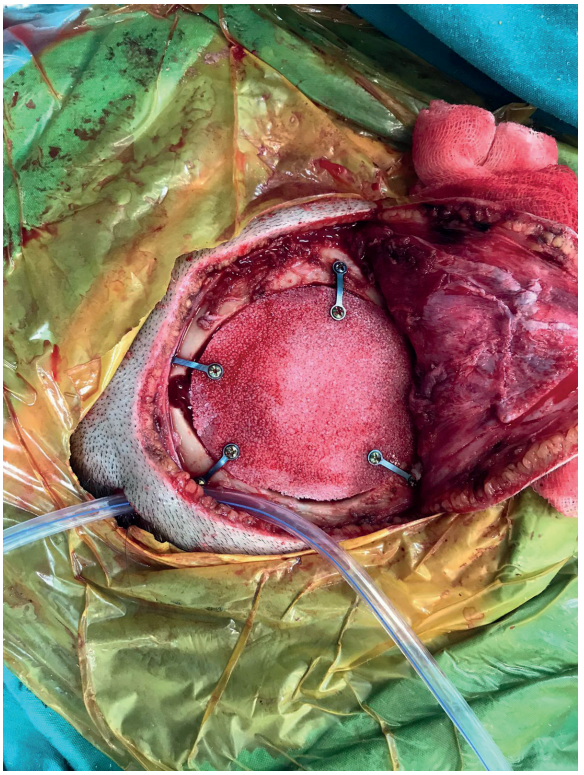
Kolesteatoma konjenital ve edinsel olabilir. Orta kulak boşluğunda gelişen hiperproliferatif bir hastalık olup temporal kemikte oluşturduğu defekten yayılıma bağlı olarak menenjit ve beyin apsesi gelişebilmektedir [20,21]. Yaşamın 3. ve 4 dekatlarında ve erkeklerde daha sık görülmektedir. Kolesteatoma asemptomatik olabileceği gibi ateş, baş ağrısı, bulantı, kusma, epilepsi, yüz ve kolda parezi, görme kaybı, afazi, vertigo gibi ilerleyici



Şekil 3. Osteom



Şekil 4. Osteom total çıkartılıp Metil metakrilat kranioplasti eklendi.



Şekil 5. Osteom

nörolojik bozukluklarında eşlik edebileceği geniş bir semptom yelpazesine sahiptir [20]. Erken dönemde yumuşak doku tutulumundan dolayı MR görüntüleme BT ye göre daha üstündür. Geç dönemde ise oluşan enkapsülasyondan dolayı eşit oranda duyarlılığa sahiptir denebilir [20-25]. Kulalı ve ark. kültürlerde üreme oranlarını %50 olarak göstermiş ve en sık *Stafilokokus, Proteus ve E.coli* ürediğini rapor etmişlerdir [33]. Sennaroglu ve arkadaşaları ise %39 üreme olmamış, *%41 Proteus, %8 Streptococcus ve % 6 Staphylococcus* ürediğini bildirmiştir [20,25]. Bizim olgumuz baş ağrısı şikâyeti olan, temporal kemik tutulumu yapan, durayı invaze etmeyen, kültürde *staf aures* üreyen, epidural tutulumlu apse görüntüsü mevcuttu. Ameliyat sonrası takiplerinde ek sorun ve nüks görülmedi.

Subgaleal hematom insidansı müdahaleli ve zor doğumlarda 10.000'de 59'a kadar çıkabilmektedir [26,27]. Olgumuzda doğumdan 2 hafta sonra oluşan travma sonrası, parietal

bölgede subgaleal hematom gelişimi görülmüş ve 6 aylık takip sonrası rezorbe olmayınca cerrahi yapılmıştır. BT yer yer kalsifikasyonu olan dış tabulaya ulaşan ekstrakranial kitle görüntüsü varlığı tespit edilmiştir. Subgaleal hematom tanısı histopatolojik olarak da doğrulanmıştır.

İntraosseoz meningiomalar, tüm meningiomaların %2'sinden daha azını oluşturur [8,28,29]. Frontopariatal ve orbita en çok tutulan yerleşim yeridir [8]. intraosseöz meningiomlar kadınlarda ve erkeklerde aynı sıklıkta görülür. Yaşamın ikinci on yılında en yüksek tutulma sıklığına sahiptir [28]. BT'de intraosseöz meningiom tipik olarak kemiğin hiperostozisi ve düzensiz ve sınırları olan sklerotik bir lezyon olarak görülür [8]. MRG'de tümör T1 ağırlıklı görüntülerde düşük sinyal ve T2 ağırlıklı görüntülerde değişken sinyal yoğunluğuna sahiptir [8]. İntrasosöz meningiomlar nadiren osteolitik olabilir ve bu vakalar daha sık malign olma potansiyeline sahiptir [8,28]. Semptomatik primer intraossöz meningiomda, geniş cerrahi rezeksiyon ile total tümör çıkarılmalı ve ardından kranyal rekonstrüktif tedavi yapılmasıdır [8,28]. Bizim olgumuz pariyetal bölge tutulumu olan yaşlı bir kadın hastaydı. Beyin BT'de lezyon düzensiz kontür ve şekilli, fırçamsı, kemik dansitesinde, yer yer litik alanlar içeren hetorojen yapıdaydı. Beyin MRG'de T1 ağırlıklı kesitlerde hipointansite, T2 ağırlıklı görüntülerde yaygın hipointansite ve yer yer hiperintens hetorojen tutulum mevcuttu. Kontrastlı çekimlerde sadece dural tutulum olduğu tespit edildi. Ekstra dural yayılım yoktu. Hastaya geniş cerrahi rezeksiyon ile total tümör çıkarılması, fasia lata grefti ile duraplasti ve metakrilat ile kraniyoplasti yapıldı. Takiplerinde rezidüe ya da nüks gelişimi görülmedi.

Kalvariumun iyi huylu lezyonlarında basit kraniyektomi genellikle yeterli olup kraniyoplasti aynı seansta veya daha sonra yapılabilir [10,15]. Kraniyoplasti amacıyla metil metakrilat, poröz polietilen, titanyum yama gibi esnek fakat dayanıklı materyaller kullanılabilir [14,15]. Metil metakrilat, kraniyoplasti'de yaygın şekilde kullanılmasına rağmen, ekzotermik reaksiyon sırasında serbest kalan toksik monomerin neden olduğu lokal doku hasarı ve sistemik reaksiyon meydana getirebilmektedir. İlaveten paranazal sinüslere bitişik yerlerde kullanılması enfeksiyon riskini artırabilmektedir [15]. Gözenekli polietilen implant kullanımı, acil kraniyoplasti için hızlı ve etkili bir yöntemdir. Bu impantın minimum yabancı cisim reaksiyonu gösterdiği ve insanlarda yıllarca istikrarlı olduğu kanıtlanmış oldukça inert bir malzemedir [15,30]. Titanyum yama acil kranioplastide hızlı etkili olmakla beraber şekil verilmesinin zorluğu ve sonraki dönemlerde bası bulgusuyla beraber oluşan cilt nekrozu görülebilmektedir. Bizim 10 olgumuzda metil metakrilat,1 olgu da ise titanyum yama kullanıldığı tespit edilmiştir. Kraniyoplasti materyali ve titanyum yama nedeniyle herhangi bir doku reaksiyonu veya enfeksiyon gözlemlenmediği tespit edilmiştir.

Sonuç olarak iyi huylu kalvariyal lezyonlarda olabildiğince total cerrahi çıkarım yapılmalı ve cerrahi işlem esnasında nöral yapıların titizlikle korunması hastanın prognozuna katkıda bulunan temel faktörlerdendir. Kalvarium lezyonlarında cerrahi çıkarım sınırlarının iyi tanımlanması elzemdir.

Etik Kurul: Tek merkez ve retrospektif çalışma olduğu için etik kurul alınmamıştır.
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Ethical Approval: Ethics committee was not taken because it is a single center and retrospective study.
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