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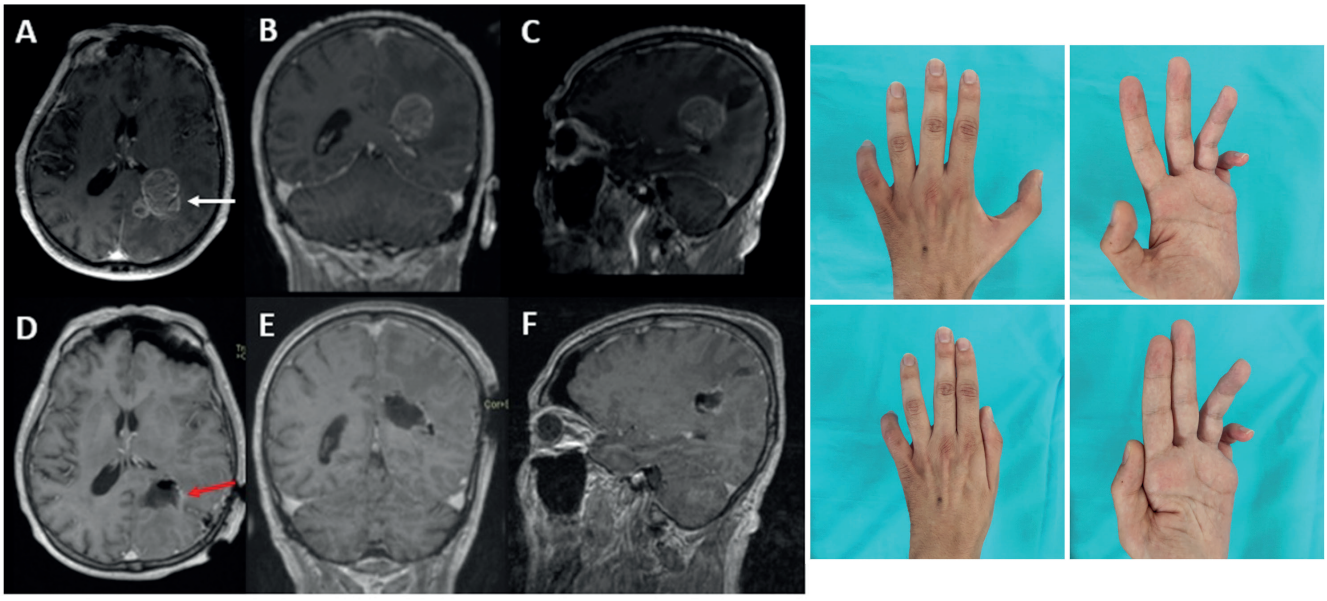

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Surgical Management and Postoperative Outcome in patients with Brain Metastases: Our Surgical Experience

Beyin Metastazı Olan Hastalarda Cerrahi Tedavi ve Postoperatif Sonuç: Cerrahi Deneyimimiz

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ABSTRACT

Aims: Metastatic brain tumors are the most commonly seen intracranial lesion in adults and an important cause of morbidity and mortality in patients with cancer. This study aimed to evaluate the postoperative mortality, morbidity, and survival rates of patients who underwent surgery in our clinic for metastatic brain tumors
Method: Clinical data of 131 patients, including age, sex, symptoms, localization, primer site, surgical methods, resection, complications and recurrence were collected.
Results: Fifty patients (38.1%) were female, and 81 (61.8%) patients were male. The average age of the patients was 54,9. The most common reason for hospital admission was headache (68.7%). Lesions were detected in the cerebral hemisphere in 108 (82.4%) patients and the posterior fossa in 23 (17.5%) patients, and 16 (12.2%) patients had multiple lesions. All patients (n=131) underwent surgery with neuronavigation. Total resection was performed in 25 (19%) patients, gross total resection in 83 (63.3%), subtotal resection in 18 (13.7%), and biopsy in 5 (3.8%). The most commonly seen tumor originated from the lungs (n=63, 48%), according to the histopathological examination. The mean overall survival was 5.3 (range, 1–36) months during the follow-up period. Twelve (9.1%) patients had recurrence and underwent surgery again.
Conclusion: Multidisciplinary treatment methods are used in the treatment of metastatic brain tumors. Effective surgical intervention to eliminate peritumoral edema and increased intracranial pressure improves postoperative survival rates. In addition, post-surgical whole-brain radiotherapy reduces recurrence and improves survival.

Keywords: Brain, metastasis, surgery, prognosis

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ÖZ

Amaç: Metastatik beyin tümörleri erişkinlerde en sık görülen intrakraniyal lezyondur ve kanserli hastalarda önemli bir morbidite ve mortalite nedenidir. Bu çalışmada, kliniğimizde metastatik beyin tümörü nedeniyle ameliyat edilen hastaların postoperatif mortalite, morbidite ve sağkalım oranlarının değerlendirilmesi amaçlandı.
Yöntem: 131 hastanın yaş, cinsiyet, semptomlar, lokalizasyon, primer bölge, cerrahi yöntemler, rezeksiyon, komplikasyonlar ve nüks gibi klinik verileri toplandı.
Bulgular: Hastaların 50'si (%38.1) kadın, 81'i (%61.8) ise erkekti. Hastaların yaş ortalaması 54,9 idi. En sık hastaneye başvuru nedeni baş ağrısıydı (%68.7). 108 (%82.4) hastada serebral hemisferde, 23 (%17.5) hastada posterior fossada ve 16 (%12.2) hastada multisentrik bölgede lezyon saptandı. Tüm hastalara (n=131) nöronavigasyon ile cerrahi uygulandı. Hastaların 25'ine (%19) total rezeksiyon, 83'üne (%63,3) gros total rezeksiyon, 18'ine (%13,7) subtotal rezeksiyon ve 5'ine (%3,8) biyopsi yapıldı. Histopatolojik incelemeye göre en sık görülen tümör akciğer kaynaklı (n=63, %48) idi. Ortalama genel sağkalım, takip süresi boyunca 5.3 (aralık, 1-36) aydı. On iki (%9.1) hastada nüks görüldü ve tekrar ameliyat edildi.
Sonuç: Metastatik beyin tümörlerinin tedavisinde multidisipliner tedavi yöntemleri kullanılmaktadır. Peritümöral ödem ve artan kafa içi basıncını ortadan kaldırmak için etkili cerrahi müdahale, postoperatif sağkalım oranlarını arttırır. Ek olarak, cerrahi sonrası tüm beyin radyoterapisi, nüksü azaltır ve sağkalımı artırır.

Anahtar Kelimeler: Beyin, metastaz, cerrahi, prognoz

INTRODUCTION

Brain metastases are the most common intracranial tumors in adults [11,19,29]. Brain metastasis is the most important cause of morbidity and mortality in patients with cancer [29].

The incidence of brain metastases ranges from 8.3 to 14.3 per 100,000 [29]. These tumors are estimated to occur 10 times more frequently than primary malignant brain tumors [20,29]. However, these incidence rates vary according to the primary tumor, tumor stage, and even the subtype of cancer, among other factors. The most commonly detected brain metastasis originates from the lung upon diagnosis [10]. The incidence of brain metastasis is 15%–40% in adults and 6%–10% in children among all patients with cancer [4]. Brain involvement is a poor prognostic criterion because of its late occurrence in the course of metastatic cancer [2]. In recent years, the number of confirmed brain metastases has increased because of the increased survival of patients with cancer and the widespread use of imaging modalities [3,24]. Brain metastases are mostly seen in the fifth and seventh decades of life and are more common in men [1].

The most common source of brain metastasis is the lung (40%–50%), followed by the breast (15%–25%), malignant melanoma (5%–20%), kidney (5%–10%), and colon (4%–6%) [11,14,20,28,29,34]. Sarcomas metastasizing to the central nervous system are very rare [17]. The primary cancer site could not be identified in 5%–10% of the patients with brain metastases [29,35].

Approximately 80% of the metastases occur in the cerebral hemisphere, with less involvement of the cerebellum and brainstem (10%–15% and 2%–3%, respectively) [30]. Unlike the cerebrum, primary parenchymal metastases to the spinal cord are rare [30].

Symptoms caused by brain metastases may be the only sign of a certain cancer type such as lung cancer, breast cancer, or melanoma [8]. Most brain metastases are diagnosed when they become symptomatic. Patients with brain metastases often present with neurological symptoms such as headache, cognitive impairment, seizure, and focal deficit, all of which accelerate the decline in the quality of life and survival [29]. Brain metastasis usually presents with symptoms localized to that particular area of the brain [22,33]. Seizures

may be seen in 10%–20% of patients with brain metastasis [22]. Seizures are more common in supratentorial and cortical lesions than in infratentorial masses [22].

Frequently used diagnostic tests aim to detect an underlying lesion. Computed tomography (CT) and magnetic resonance imaging (MRI) remain the most widely used imaging techniques. Positron emission tomography (PET) and single-photon emission computed tomography are used to evaluate the primary tumor site and to identify other possible metastases [1,25]. Two MRI sequences, namely, diffusion-weighted MRI and diffusion-tensor imaging, can reveal the microstructure of the brain and its deterioration caused by tumor growth and edema [15]. Histopathological examination is an important diagnostic tool that detects the morphology of metastatic malignancy and possible tumor origin [9].

Patients with brain metastases generally have a poor prognosis and survival of approximately 4 weeks without treatment [37]. Depending on the primary tumor, the mean survival ranges from 2 to 27 months [37].

Radiation therapy, surgery, and chemotherapy are used in the treatment. Radiation therapy includes whole-brain radiotherapy (WBRT), stereotactic radiosurgery, or a combination of these modalities. WBRT has been accepted as the standard treatment of brain metastases [15].

This study aimed to retrospectively evaluate the clinicopathological features and postoperative survival rates of patients who underwent surgery for brain metastases in our clinic.

MATERIALS and METHODS

Patient population

This study was approved by the ethics committee (2020/304). In this study, we retrospectively analyzed 131 patients who were admitted with an intracranial mass and histopathologically confirmed metastasis between September 2016 and November 2020. Of these patients, 50 (38.1%) were female and 81 (61.8%) were male. The mean age was 54.9 (range, 2–82) years.

Clinical and radiological evaluation

The most common reason for admission was headache (68.7%, n=90). In addition, 30 (22.99%) patients were admitted with dizziness, 19 (14.5%) with seizures, and 3 (2.3%) with vision loss. CT and MRI were performed in all patients.

Radiological examination revealed that 108 (82.4%) patients had a supratentorial tumor, while 23 (17.5%) patients had a tumor at the posterior fossa. In addition, 16 (12.2%) patients had more than one lesion in the intracranial region. To reduce intracranial edema and high intracranial pressure caused by the lesion, dexamethasone (16 mg/day) was started in all patients preoperatively.

Tumor resection was classified as total, gross total, subtotal, and biopsy according to intraoperative surgical observation, and MRI was performed in the early postoperative period. Total resection included complete excision of the tumor and capsule, gross total resection meant excision of nearly all tumor tissues and capsule remnants are left, and subtotal resection was defined as cases where the tumor capsule and <10% of the tumor remained.

Surgical strategy

Neuronavigation (featured MRI) was used in all cases in addition to routine surgical preparations. After induction of anesthesia, the patient's head was positioned in accordance with the localization of the lesion by wearing a head clamp.

After the neuronavigation installation, the skin and subcutaneous tissue were passed through an incision made in accordance with the lesion localization in all cases. Craniotomy and craniectomy were performed in cases with lesions located in the cerebral hemisphere and posterior fossa, respectively. Especially in cases with increased intracranial pressure and tight dura mater, mannitol (1 g/kg) was infused rapidly before dural opening [26]. Tumor resection was performed by endoscopic methods (n=20, 15.2%) by placing a thoracoport in deeply located lesions. In other cases, tumor resection was performed by microscopic methods (n=111, 84.7%). After tumor resection, bleeding control was performed in all cases, and the dura was sutured. A bone flap was placed. The skin was properly closed.

RESULTS

Neuronavigation was used in all cases in addition to routine surgical preparations. Especially, in cases with increased intracranial pressure and tight dura mater, mannitol (1 g/kg) was rapidly infused before dural opening [26]. Antiedema treatment (dexamethasone) was continued in all cases in the early postoperative period. In the postoperative period, pulmonary embolism developed in 2 (1.5%) patients, wound infection in 7 (5.3%), and cerebrospinal fluid fistula in 6 (4.5%). In the postoperative period, 3 (2.3%) patients were lost to follow-up because of various complications during the hospitalization period.

Total resection was performed in 25 (19%) patients, gross total resection in 83 (63.3%), subtotal resection in 18 (13.7%), and biopsy in 5 (3.8%) (Figs. 1–3). The patients were discharged after the improvement of the existing preoperative complaints and the wound had healed. The result of histopathological examination revealed that the most common tumor origin was the lung (n=63, 48%) (Table 1). PET was performed after histopathological diagnosis to detect other possible spread of the primary tumor. Subsequently, chemotherapy and radiotherapy treatments were planned.

Table 1. Clinicopathological and postoperative characteristics

Caracteristics	Number	%
Sex		
Male	81	61.8
Female	50	38.1
Symptoms		
Headache	90	68.7
Dizziness	30	22.9
Seizure	19	14.5
Visual lost	3	2.3
Localization		
Cerebral	108	82.4
Posterior fossa	23	17.5
Primer site		
Lung	63	48
Breast	23	17.5
Lenfoma	12	9.1
Gastrointestinal system	9	6.8
Renal	4	3.05
Melanoma	4	3.05
Others	16	12.2
Surgical methods		
Microscopic	111	84.7
Endoscopic	20	15.2
Resection		
Total	25	19
Gros total	83	63.3
Subtotal	18	13.7
Biopsy	5	3.8
Postoperative Complication		
Pulmonary embolism	2	1.5
Wound infection	7	5.3
CSF fistula	6	4.5
Exitus	3	2.3
Relaps	12	9.1

Eight (6.1%) patients died within the first 3 months because of intracranial and primary tumor complications, and 25 (19%) patients were lost to follow-up. The mean overall survival was 5.3 (range, 1–36) months during the follow-up period, and 12 (9.1%) patients had a recurrence and undergo surgery again.

REPRESENTATIVE CASES

Case #1:

A 70-year-old male patient was admitted to our clinic with balance disorder. Neurological examination is normal. He has a history of surgery for gastric adenocarcinoma. On MRI, a 3.5x4 cm mass lesion was detected in the right cerebellar hemisphere. Gross total resection was obtained in the patient who was operated microscopically (Figure 1). Pathological examination was compatible with gastric adenocarcinoma. The patient was discharged on the 5th postoperative day and was referred to radiotherapy. The patient died in the 11th postoperative month due to complications arising from the gastrointestinal system.

Case #2:

A 69-year-old male patient applied to our clinic with complaints of headache and dizziness. In her neurological examination, her right upper and lower extremities were 2/5 paresis. He has a history of right nephrectomy for renal cell carcinoma. Cranial MRI revealed a 3x4 cm mass in the left parietal region. The patient was operated using endoscopic methods and thoracoport. The tumor was grossly excised (Figure 2). Pathological examination was consistent with renal cell carcinoma metastasis. The patient was discharged on the 5th postoperative day and received whole brain radiotherapy. He died at the postoperative 14th month due to non-intracranial complications.

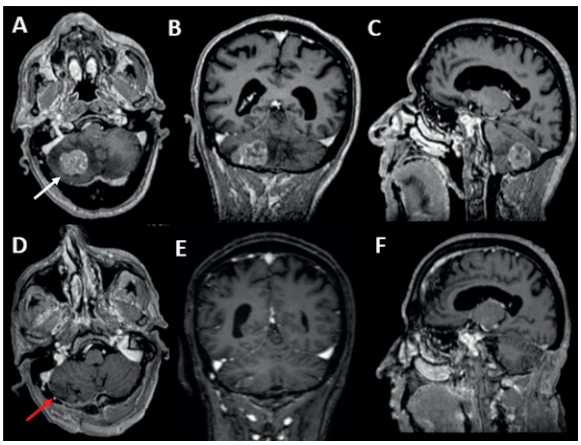

Figure 1. A-C: Preoperative T1-contrast Cranial MRI, D-F: Postoperative sixth month T1-contrast Cranial MRI, White Arrow: Tumor Tıssue, Red Arrow: Tumor cavity

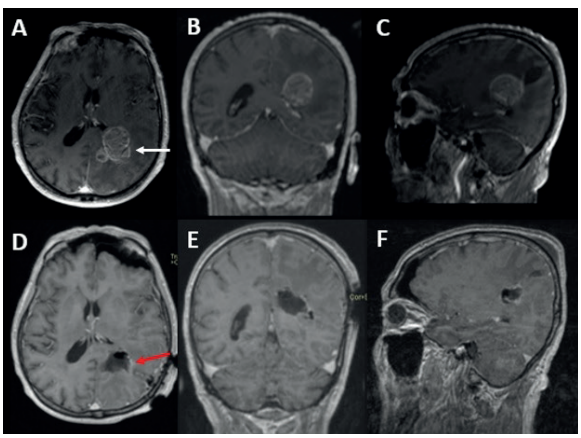

Figure 2. A-C: Preoperative T1-contrast Cranial MRI, D-F: Postoperative 12th month T1-contrast Cranial MRI, White Arrow: Tumor Tıssue, Red Arrow: Tumor cavity

Case #3:

A 61-year-old male patient applied to our clinic with the complaint of dizziness. In her neurological examination, tandem gate was unsuccessful, but other examination findings were normal. There was no significant pathology in his history. Cranial MRI revealed a 3x2.5 cm mass in the left cerebellar hemisphere. The patient was operated with microscopic methods. The tumor was grossly excised (Figure 3). Pathological examination was compatible with high-grade B-cell lymphoma. The patient was discharged on the 4th postoperative day and

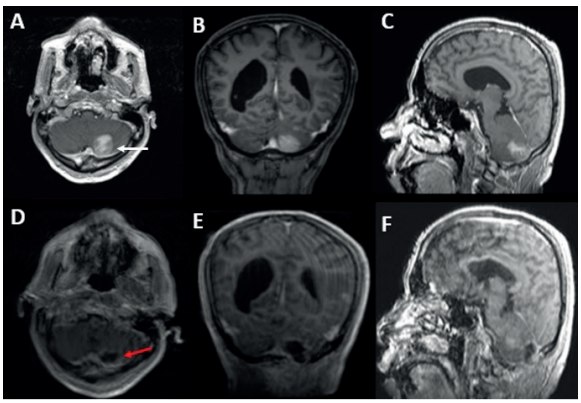

Figure 3. A-C: Preoperative T1-contrast Cranial MRI, D-F: Postoperative 3rd month T1-contrast Cranial MRI, White Arrow: Tumor Tıssue, Red Arrow: Tumor cavity

received whole brain radiotherapy. He died 6 months postoperatively due to complications related to multiple intracranial involvements.

DISCUSSION

Metastasis is the most common type of intracranial neoplasm [39]. Its incidence is 10 times higher than that of primary brain tumors and occurs in approximately 25% of all patients with cancer [24]. This number is expected to increase as more patients develop cancers, imaging technology becomes more common, and there was no progress in finding methods to prevent cancers from metastasizing to the brain [11].

Brain metastases are most commonly detected between ages 50 and 70 years [40]. In this study, the mean patient age was 54.9 years.

The lung is the most common site of origin among all brain metastases. Generally, this is followed by the breast, gastrointestinal tract, lymphomas, renal tumors, and other tumors [5,31,35]. Brain metastases are rare in sarcomas and are more common in undifferentiated sarcomas with previous metastases. The incidence of sarcoma metastasizing to the brain is <1% [14]. In our study, metastases originating from lung cancer (n=63, 48%) were found most frequently. The breast (n=23, 17.5%), lymphoma (n=12, 9.1%), gastrointestinal tract (n=9, 6.8%), kidney (n=4, 3.05%), malignant melanoma (n=3.05%), and other tumors (n=16, 12.2%). The majority of brain metastases (77.7%–85%) are located in the cerebral hemispheres, followed by the cerebellum (15%–20%) and brainstem (2%–5%) (32,38). In this study, similar to the literature, 82.4% (n=108) of the cases were localized in the cerebral hemisphere and 17.5% (n=23) were localized in the posterior fossa.

The most common complaint was headache (49%). Mental changes (32%), focal weakness (30%), and seizures (18%) were other symptoms [32,38]. The most common reason for admission was headache (n=90, 68.7%). Other complaints were dizziness (n=30, 22.9%), seizure (n=19, 14.5%), and vision loss (n=3, 2.3%).

Surgery, Whole Brain RT (WBRT), stereotactic radiosurgery, and chemotherapy are treatment options for brain metastasis [12,36]. Many factors such as age, performance status, number of lesions, and treatment type affect the treatment modality. Aggressive treatment helps improve overall survival. Modi *et al*. reported that resection of metastatic lesions prolongs overall survival [27].

Surgery is an effective treatment modality in increasing survival. Surgical treatment is recommended, especially in brain metastases with large-scale, perilesional edema, neurologic deficits, and unknown histopathological diagnosis [28]. Surgical treatment not only makes adjuvant therapy more effective but also provides benefits such as the alleviation of the mass effect, symptomatic improvement, and histopathological evaluation [21]. However, it is more effective in single lesions [7]. Solitary metastatic lesions have sharp margins and are amenable to surgical resection [23].

Surgery for deep-seated lesions is challenging and postoperative morbidity risk is higher. Such lesions are usually treated to provide palliation [11,21]. Minimally invasive approaches are used to reduce postoperative mortality and morbidity, especially in the surgical intervention of deeply located lesions, but studies on this subject are limited [13,23]. Hong et al. demonstrated the use of minimally invasive methods in 20 patients with deeply located metastatic lesions [23]. Many studies use tubular retractors for minimally invasive approach [6,21,23]. In this study, we also performed tumor resection with endoscopic methods by placing a thoracoport in 20 (15.2%) patients, especially in deeply located cases.

Bakhsheshian et al. reported gross total resection in 80% of 25 patients with deeply located metastatic brain tumors [6]. In the present study, total resection was performed in 25 cases (19%), gross total resection in 83 (63.3%) cases, subtotal resection in 18 (13.7%) cases, and biopsy in 5 (3.8%) cases.

WBRT is a frequently preferred treatment for brain metastases. The role of chemotherapy in the treatment of brain metastases is controversial because of the blood–brain barrier. Most authors argue that most chemotherapeutic drugs are unable to cross the blood–brain barrier; thus, the efficacy of chemotherapy in brain metastatic disease is low or nonexistent [18]. In cases with more than one metastasis, WBRT provided less recurrence in the postoperative period and longer survival than the group that did not receive radiotherapy [18]. In the present study, all (n=98, 74.8%) patients who were followed up in the postoperative period received WBRT.

Five (10%) new cases of neurologic deficits, one case of stroke (2%), and one case (2%) of exitus were reported after resection in a study that included deeply located metastatic brain tumors [21,23]. In another study, new-onset motor weakness and deep-vein thrombosis were reported in one (4%) patient [6]. In this study, pulmonary embolism occurred in 2 (1.5%) patients, wound infection in 7 (5.3%), CSF fistula in 6 (4.5%), and exitus in 3 (2.3%).

Patients with a single metastatic lesion had significantly higher survival rates than patients with multiple metastases [16]. In this study, multiple brain metastases were detected in the intracranial region in 16 (12.2%) patients, and 87.5% (n=7) of the patients who died in the first 3 months after surgery were those with more than one metastasis.

Ekici et al. reported a mean survival of 6.7 months [16]. In the present study, the mean survival during the follow-up period was 5.3 months.

CONCLUSION

Brain metastases are an important cause of morbidity and mortality. The incidence, survival rates, and treatment modalities of brain metastases vary greatly according to the histopathological diagnosis of the primary tumor. Surgical intervention reduces intracranial pressure and eliminates tumor-related edema. Therefore, postoperative survival rates increase. In addition to surgical treatment, adjuvant WBRT reduces recurrence and increases survival in these cases. However, more clinical studies are needed to evaluate the efficacy of single or combined treatments in metastatic brain tumors.

Ethical Approval: This study was approved by the Scientific Research Ethics Committee of the Turkish Republic Health Sciences University (No: 2020-304 / 30.06.2020).
Conflict of interest: There is no conflict of interest in our study.

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Evaluation of Serum Superoxide Dismutase Levels in Lumbar Degenerative Spinal Diseases: A Prospective Meta-analysis

Lomber Dejeneratif Omurga Hastalıklarında Serum Süperoksit Dismutaz Düzeylerinin Değerlendirilmesi: Prospektif Bir Metaanaliz

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ABSTRACT

Background: The aim of this study was to evaluate the correlation between serum superoxide dismutase (SOD) enzyme levels and lumbar degenerative spinal diseases (LDSD).
Materials and Methods: Ninety-four patients with LDSD and 64 patients without LDSD were investigated. Human SOD ELISA kits were used to measure the amount of enzymes in the samples. Serum SOD enzyme levels were determined by Student-t and Mann Whitney-U tests to determine differences between groups.
Results: The patient group was classified according to the characteristics of the disease, clinical symptoms, Visual Analog Scale (VAS) values, and Oswestry Disability Index (ODI) scores. Along with these parameters, serum SOD levels were evaluated statistically. There was no statistically significant difference in serum SOD levels in both groups. However, serum SOD levels were relatively lower in the patient group ($p>0.05$).
Conclusions: Our study could supply objective value for future researchers investigating specific lumbar diseases, should they attempt to find a serum biomarker for the disease. More studies with an increasing number of patients

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are needed to support the results of our study. Doing so may offer more specific insights on the mechanisms of LDSD and its features, which could contribute to the literature.

Keywords: Lumbar degenerative spinal disease, superoxide dismutase enzyme, serum biomarker

ÖZ

Amaç: Bu çalışmanın amacı, serum süperoksit dismutaz (SOD) enzim düzeyleri ile lomber dejeneratif omurga hastalıkları (LDOH) arasındaki ilişkiyi değerlendirmektir.
Gereç ve Yöntem: LDOH'li 94 hasta ve LDOH'siz 64 hasta incelendi. Örneklerdeki enzim miktarını ölçmek için insan SOD ELISA kitleri kullanıldı. Gruplar arasındaki farklılıkları belirlemek için serum SOD enzim düzeyleri Student-t ve Mann Whitney-U testleri ile belirlendi.
Bulgular: Hasta grubu, hastalığın özelliklerine, klinik semptomlara, Visual Analog Scale (VAS) değerlerine ve Oswestry Disability Index (ODI) skorlarına göre sınıflandırıldı. Bu parametrelerle birlikte serum SOD düzeyleri istatistiksel olarak değerlendirildi. Her iki grupta serum SOD düzeylerinde istatistiksel olarak anlamlı fark yoktu, ancak serum SOD düzeyleri hasta grubunda göreceli olarak daha düşüktü (p>0,05).
Sonuçlar: Gelecekte araştırmacılar spesifik lomber hastalıkları incelemek için bir serum biyobelirteci bulmaya çalışırlarsa, çalışmamız nesnel değerler sağlayabilir. Sonuçların desteklenmesi için artan hasta sayısı ile daha fazla çalışmaya ihtiyaç vardır. Bu bilgiler ışığında hastalıkların veya özelliklerin daha spesifikleştirilmesi ile denenebilecek araştırmalar için çalışmamızın sonuçlarının literatüre katkıda bulunacağı düşüncesindeyiz.

Anahtar Kelimeler: Lomber dejeneratif omurga hastalıkları, süperoksit dismutaz enzimi, serum biyobelirteci

INTRODUCTION

Lumbar degenerative spinal diseases (LDSD) are the most common cause of loss in the workforce today. Recently, the average lifetime for someone with LDSD has increased with the advancement of technology and medical information and the frequency of occurrence of degenerative spinal diseases has increased in parallel with this. The spinal degeneration process is multifactorial and irreversible, leading to mechanical dysfunction [(1)]. Thus, progressive intervertebral disc degeneration results in decreased disc height, affecting the biomechanics of the spine, which results in degenerative diseases such as disc herniation, spinal stenosis, and spondylolisthesis [(2)].

Cells are protected against oxidative damage by antioxidant defense systems under normal physiological conditions. These systems include enzymatic antioxidants such as superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), and non-enzymatic antioxidants such as vitamin C and vitamin E.

SOD is a metalloenzyme that catalyzes the reaction of the superoxide radical to hydrogen peroxide and molecular oxygen. The catalyzed reaction of this enzyme is known as the first defense against oxidative stress. Because it is a powerful initiator of superoxide chain radical reactions, oxygen radical levels in cellular compartments are kept under control.

The aim of our study was to evaluate the correlation between the serum SOD enzyme level and LDSD. Since the degeneration processes correlate with the increase of free radicals in terms of a causal relationship, our hypothesis was that an individual's SOD level could be used as a biomarker in the diagnosis and clinical follow-up of LDSD.

METHODOLOGY

A control group of 94 patients with LDSD and 64 patients without LDSD were enrolled in our study. Patient numbers were determined by the power analysis method. The number of patients in our study was determined by the power analysis method as follows:

In studies evaluating the effects of SOD and reactive oxygen radicals in patients with LDSD, the quantitative determination of free

oxygen radicals in the serum of all patients was performed. According to the hypothesis, the SOD levels of patients with LDSD were expected to be lower than those of patients without LDSD.

In the literature, when the calculated effect size (d) for the difference between the level of free oxygen radicals between the patient and control groups is 0.5, the working power of at least 80% according to the design of 5% type-1 error and bidirectional statistical hypothesis testing. In order to achieve this, it was calculated that a total of 128 participants, 64 people in each of the study arms, should be included in the study. See Fig. 1.

Included in this study were adult patients with lumbar disc herniation, spinal stenosis, lumbar spondylolisthesis, and related spinal deformities as well as those who had previously undergone similar degenerative sequelae. Excluded were those who had suffered some form of trauma or who had been diagnosed with a malignancy. The control group consisted of volunteers who had images of lumbar vertebrae in the archive; no complaints of problems with the lumbar spine; no findings of neurological importance; and no lumbar pathology.

Blood samples were taken from patients and control groups; neurological examinations were performed; and radiologic findings and anamnesis were taken into consideration. Serum samples were centrifuged at 5,000 rpm for 15 minutes. SOD levels were determined using ELISA test kits. This was carried out at the central laboratory of molecular medicine.

The amount of SOD enzyme in the samples was measured with human SOD-ELISA kits. The kit, which works on the sandwich ELISA principle, contains two different antibodies, one for fixing the target molecule to the lots on the microplate, and the second for the assay for enzymatic labeling. Serum samples and standards were pipetted into wells on a microplate coated with a specific antibody for surface SOD and ligated with any available SOD immobilized antibody. After removal of unbound material, the HRP-Conjugate Human SOD detection antibody was added to the lots. A chromogen solution was added to the batch after washing to remove unbound HRP reagent. It was observed that the color changed in parallel with the amount of SOD. Color intensity was measured at a wavelength of 450 nm.

Obstacles and limitations during experiments

Reagents from other lots or sources were not mixed. A check was conducted to ensure that the selected calibrator diluent for the standard curve was consistent with the tested samples. Since the samples were expected to produce higher values than the highest standard, the samples were replicated with the diluent under the appropriate calibrator. This analysis was designed to remove the interference of other factors found in biological samples. ELISA did not rule out the possibility of interference until all the factors were tested.

Storage conditions

Kit reagents were stored at (+2) - (+8) ºC. Immediately after use, the remaining reagents were kept in cold storage at +4 °C.

Test procedure

All reagents were prepared before testing. All standards and samples were added to the microplate in duplicate. Sample wells were tested by setting standard lots. A standard 50 µL kit diluted in standard wells was added. A sample

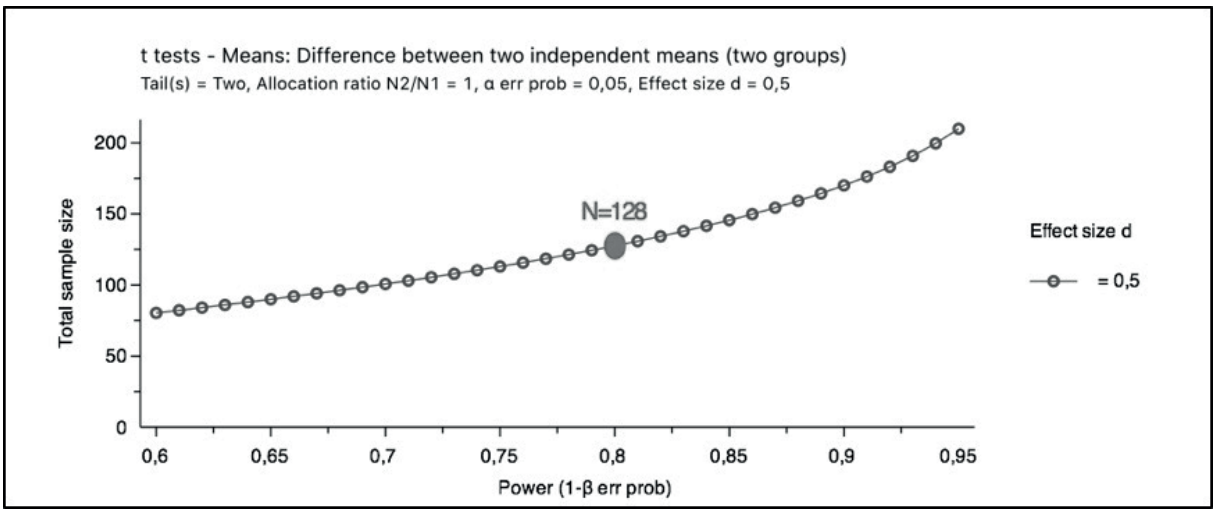

Figure 1. Sample size calculation

diluent of 40 µL was added to test the sample. Then 10 µL samples were added. These were incubated at 37 ° C for 45 minutes after being covered with a plate lid. The procedure was repeated four times for a total of five washes, with each well aspirated and washed. Each hopper was filled with the washing buffer (250 µL) using a bladder, manifold dispenser, and automatic washer. For good performance, care was taken to completely remove the liquid at each step. The remaining buffer after washing was cleaned by aspiration and filtration. After the plate was inverted, it was cleaned with a clean paper towel. Except empty lots (blind), each lota HRP-conjugate detection antibody (50 µL) was added and incubated for 30 minutes at 37°C. The aspiration/washing process was repeated five times. To each lota, chromogenic solution (50 µL) and chromogenic solution B (50 µL) were added and incubated for 15 minutes at 37°C with gentle mixing. Care was taken to protect the system from light. Fifty µL of stop solution were added to each lota. The color in the wells was expected to turn yellow. The solutions in the wells were allowed to mix well when they were green or when the color change was not correct. The optical density at 450 nm was read within 15 minutes using a microtiter plate reader.

Data analysis and calculation of results

For each standard, control and sample, double readings were averaged and the average zero standard optical density was subtracted. A standard curve was generated as a logarithmic curve fit with four parameters, reducing the data. Separately, a curve was drawn from the points on the graph based on the average absorbance for each standard in the x and y axes; a double control was applied. In the diluted samples, the concentration read from the standard curve was multiplied by the dilution factor. A standard curve with a detection range of 12.5 to 200 pg/ml was generated for each sample group tested.

Measures taken for standardization during the experiment

Care was taken to not put the reagents from one kit lot into another. Standard, conjugate,

and microtiter plates were matched for optimal performance. Kit reagents and materials were allowed to reach room temperature (20-25ºC) before use. No water bottles were used to dissolve samples or reagents. Only diluted or distilled water was used to dilute the reagents. Unused strips were stored at (+2) - (+8) ºC in the provided dryer and sachets. New disposable pipette tips were used for each transfer to prevent contamination. Acid and sodium hypochlorite solutions were not mixed. All samples were processed to inactivate viruses. Sodium hypochlorite was added to the liquid waste to a final concentration of 1.0%. The wastes were left for at least 30 minutes to neutralize the viruses before being thrown away.

Statistical analysis

Statistical analyzes of this study were performed using the SPSS 24.0 package program. The statistical significance limit was taken as $p<0.05$. Student-t and Mann Whitney-U tests were used to determine the differences of serum SOD enzyme levels between groups.

RESULTS

The mean age of 94 patients in our study was calculated as 50.11 ± 12.20. In the group of patients with LDSD, the number of males was 39 and the number of females was 55. The mean body mass index (BMI) of this group was 30.79 ± 27.18. The mean age of 64 people in the control group was 41.23 ± 10.36. The number of males in this group was 39 while the number of females was 25. The mean value of BMI in the control group was calculated as 26.68 ± 4.48 (Table 1).

SOD levels were measured and compared by sera from patients and control groups using the ELISA method. No statistically significant difference was found between both groups (Figure 2). After comparing SOD levels of both groups, the group with LDSD was separated according to some features. These features were compared statistically by looking at the SOD levels. The features examined were bulging-protrusion-extrusion number, black disc count, facet joint hypertrophy, listezis, flavum hypertrophy, muscular atrophy, Modic degeneration, and lordosis characteristics in the lumbar disc. These properties are described in detail in Table 2. Based on these characteristics, there was no significant difference in statistical calculations made within patient groups.

Patients' clinical symptoms were classified as back pain (axial pain), leg pain (radicular pain), waist pain, and leg pain. With reference to these symptoms, patient groups were statistically evaluated according to their SOD levels. Results obtained according to clinical features were not statistically significant (Table 3). Patients were compared statistically with SOD level values between Visual Analog Scale (VAS) values and Oswestry Disability Index (ODI) scores

Table 1. Demographic datas, BMI and smoking habits of each patient and control groups

Parameter	Patient (n=94)	Control (n=64)	p value
Age	50,11 ± 12,20	41,23 ± 10,36	0,000*
Gender			
Female/Male	55 / 39	25 / 39	0,016*
BMI	30,79 ± 27,18	26,68 ± 4,48	0,241
Smoking			
Yes/No	23 /71	20 / 44	0,367
Smoking			
(package year)	4,79 ±12,52	5,96 ± 10,06	0,534

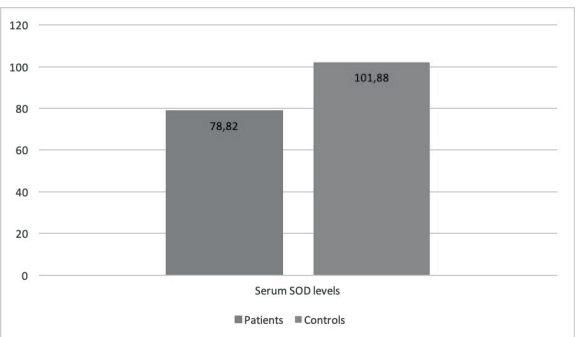

Figure 2. Comparison of serum SOD levels of patients and control groups

Table 2. Patient group, according to the characteristics of the disease

Parameters	Patient Group (n=94)					
Modic Degeneration	**Absent**		**Type 1**		**Type 2**	
(n)	77		5		12	
Lordosis	**Normal**		**Straight**		**Scoliosis**	
(n)	65		28		1	
Facet Joint Hypertrophy	**Absent**			**Exist**		
(n)	18			76		
Lysthesis	**Absent**			**Exist**		
(n)	24			70		
Flavum Hypertrophy	**Absent**			**Exist**		
(n)	30			64		
Muscle Atrophy	**Absent**			**Exist**		
(n)	75			19		
Number of Bulging	**0**	**1**	**2**	**3**	**4**	
(n)	31	39	18	4	2	
Number of Protrusion	**0**	**1**	**2**	**3**		
(n)	37	42	10	5		
Number of Extrusion	**0**	**1**	**2**			
(n)	58	35	1			
Number of Black Disc	**0**	**1**	**2**	**3**	**4**	**5**
(n)	20	43	21	6	3	1

Table 3. SOD levels in patient group according to clinical features

Parameter	Back Pain (n=17)	Leg Pain (n=11)	Back and Leg Pain (n=66)	p Value
SOD level values	54,47 ± 54,92	55,65 ± 27,73	88,96 ± 137,11	p > 0,05

Table 4. ODI values of patients group

ODI	1	2	3	4	5
Number of patients	0	16	32	27	19

ODI Scala: 0% to 20% - minimal disability 20% to 40% - moderate disability 40% to 60% - severe disability 60% to 80% - crippled 80% to 100% - bed bound (or exaggerating symptoms).

themselves. There was no statistically significant difference for either VAS or ODI values (Table 4). In group of patients with LDSD, the average VAS value was 6,5.

DISCUSSION

Symptoms of lumbar disc herniation occur most frequently in people ages 30-50 years and the prevalence is about 1-3% [3]. It is estimated that every year, 2,75 out of every 1000 people with back pain will have a severe attack requiring hospitalization [4]. However, the number of lumbar spine surgeries has also increased over the past two decades. This increase has increased hospital costs and surgical complications [5]. When conservative treatment is unsuccessful, the indication for surgery is on the agenda [6]. Traditionally, the surgical procedure is discectomy [7].

Hou et al. reported that serum and intervertebral disc SOD activity decreased gradually with age. In the geriatric group, the intervertebral disc SOD activity was significantly lower than the young and adult group, and the serum SOD activity in the young group was significantly higher than in the adult and geriatric group [8]. This support that, if the SOD activity is high the disc is healthy.

Ho et al. investigated the effects of age, gender and smoking habits on enzymatic activities. They explained that erythrocytes have antioxidant enzyme activities such as CAT, SOD, GPx. A significant decrease in erythrocyte GPx

activity was detected in smokers compared to non-smokers, while significant increases were observed in erythrocyte CAT and SOD activities. There was no age-related difference in erythrocyte GPx activity between the groups. Erythrocyte CAT and GPx activities were significantly lower at the age of 60 in the smoker group. It was found that women had higher erythrocyte GPx activity than men [9]. In our study, smokers had lower serum SOD levels than non-smokers, but this was not statistically significant.

Silig et al. reported the genotyping of the polymorphism of the SOD1 gene of 494 healthy Turkish individuals. The distribution of SOD1 A251G polymorphism in this population was investigated using a PCR-RFLP method. Genotype and allele frequencies were counted. The expected and observed genotype distributions were assessed using the Hardy-Weinberg equilibrium X2 test. In this study, 494 (278 females, 56.3% and 216 males, 43.7%) A251G polymorphisms in the SOD1 gene were investigated. The average age of the study group was 38.4. The observed genotype frequencies of SOD1 were AA: 86.2%; AG: 13.4%; and GG: 0.4%, respectively (A: Adenine, G: Guanine). This is important because it was the first study on SOD1 A251G polymorphism in the Turkish population [10]. We believe that research on antioxidant systems in different areas, such as our work, will provide values specific to the Turkish community as well as the medical literature as a whole.

Andersen et al. defined the methodological conditions suitable for the analysis of copper-zinc-SOD (CuZn-SOD), GPx, CAT and glutathione reductase (GR) in highly reproducible human erythrocytes. 220 people randomly selected from 20-89 age group were included in the study. CuZn-SOD and GR activities were associated with an age-related decrease, while no significant changes in age were observed for GPx and CAT. These results were consistent with previous studies showing that CuZn-SOD activity in erythrocytes decreases with age [11]. However, age-related changes in SOD activity are controversial. In our study, no statistically significant correlation was found between age and serum SOD levels.

CONCLUSION

Enzyme levels were relatively low in patients with LDSD (p=0.302) as expected. However, there was no statistically significant difference in serum SOD levels between the patient and control groups. We believe that the results of our study will shed light on future studies, so more specific information about LDSD will contribute to the literature.

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Ventrikül Büyüme Paterni Ventriküloperitoneal Şant Cevabını Preop Belirleyebilir Mi?

Can Ventricule Growth Pattern Preop Determinate Ventriculoperitoneal Shunt Response?

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ÖZ

Amaç: Normal Basınçlı Hidrosefali (NBH) kafaiçi basınç artışı olmaksızın ventrikül genişlemesi gösteren ve "yürüyüş bozukluğu, demans ve inkontinans" kardinal bulguları ile ortaya çıkan bir sendrom olarak tarif edilmiştir. Bu klasik triad beyin omurilik sıvısı (BOS) tahliye işlemleri ile düzelme gösterir. Ne var ki tanımının üzerinden yarım asır geçmesine rağmen hastalığın semptomları, fizyopatolojisi, tanı ve tedavi kriterleri, insidans ve prevalansında belirsizlik sürmektedir.
Bu çalışmada ventrikül genişlemesinin radyolojik ve klinik özellikleri ile Ventriküloperitonel "Shunt" (VPS) ameliyatına iyi yanıt veren ve vermeyen hastaların sonuçlarının değerlendirilmesi amaçlandı.
Gereç ve Yöntem: 27 olgudan oluşan bu Normal Basınçlı Hidrosefali (NBH) serisinde ameliyat öncesinde ve 6 ay sonrasında ayrıntılı nörolojik muayene yanında Normal Basınçlı Hidrosefali Derecelendirme Skalası (NBHDS), nöropsikoloji testleri (NPT) ve bilgisayarlı beyin tomografisi (BT), kranyal manyetik rezonans görüntüleme (MRG) yapıldı. Radyolojik olarak mevcut ventrikül genişlemesinin özellikleri ve eşlik eden MRG bulguları değerlendirildi. Bütün olgular ayarlanabilir VPS (Medtronic Strata®) ile tedavi edildiler ve ameliyat sonrasında en az 6 ay takip edildiler.
Bulgular: NBHDS göre 27 hastanın 22 si VPS ameliyatına iyi yanıt verdi, 5 i yanıtsızdı. Ameliyat öncesi ventrikülleri uniform genişleyen hastaların ventriküllerin sadece temporooksipital bölümü geniş olan hastalar karşılaştırıldığında VPS yanıtı ile istatistiksel anlamlı ilişki saptanmadı (p=0.768, p=0.623).
Sonuç: Bu çalışmada VPS cevaplı ve cevapsız hastalar ile ventriküllerin büyüme formu arasında bir ilişki olmadığı gösterildi.

Anahtar Kelimeler: Ventrikül büyüme paterni, normal basınçlı hidrosefali, ventriküloperitoneal shunt cevabı

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ABSTRACT

Objective: Normal Pressure Hydrocephalus (NPH) has been described as a syndrome that shows ventricular enlargement without increased intracranial pressure and presents with cardinal signs of "gait disturbance, dementia and incontinence". This classic triad improves with cerebrospinal fluid (CSF) evacuation processes. However, although half a century has passed since its definition, the symptoms, physiopathology, diagnosis and treatment criteria, incidence and prevalence of the disease remain uncertain.
In this study, it was aimed to evaluate the radiological and clinical features of ventricular enlargement and the results of patients who responded and did not respond to Ventriculoperitoneal Shunt (VPS) surgery.
Materials and Methods: Normal Pressure Hydrocephalus (NPH) series consisting of 27 cases, in addition to detailed neurological examination before and 6 months after surgery, Normal Pressure Hydrocephalus Grading Scale (NPHGS), neuropsychology tests (NPT), and cranial computerized tomography (CT), cranial magnetic resonance imaging (MRI) was done. Radiological features of existing ventricular enlargement and accompanying MRI findings were evaluated. All cases were treated with adjustable VPS (Medtronic Strata®) and were followed up for at least 6 months postoperatively.
Results: According to NNHDS, 22 of 27 patients responded to VPS surgery, 5 were non-responders. When the patients whose ventricles were uniformly enlarged preoperatively, only the temporooccipital part of the ventricles was compared, no statistically significant correlation was found with the VPS response (p=0.768, p=0.623).
Conclusion: In this study, it was shown that there was no relationship between VPS responsive and non-responsive patients and the growth form of the ventricles.

Keywords: Normal pressure hydrocephalus, ventricule growth pattern, ventriculoperitoneal shunt response

GİRİŞ

NBH, ilerleyici ventrikül büyümesi, yürüyüş bozukluğu, idrar inkontinansı ve demansla seyreden, kafa içi basıncının normal olduğu bir ileri yaş hastalığı olarak tanımlanmıştır [1]. NBH, bilinen klasik tanımının yanında üzerinden uzun yıllar geçmesine rağmen hala aydınlatılamamış patogenezi olduğu, üzerinde fikir birliğine varılmamış radyolojik bulguları olduğu, bir takım nörodejeneratif hastalıkların eşlik ettiği düşünülen bir hastalıktır [2]. Nörobilim ve Radyodiagnostik alanda tüm gelişmelere rağmen günümüzde NBH tanısında altın standart hastanın ameliyattan fayda görmesidir [3,4]. Birçok yazar idiyopatik NBH tanısının klinik çalışmalar ve preop tetkiklerle değil, VPS cerrahisinin başarılı sonuçlanmasıyla konulabileceği görüşünü benimsemektedir [3,4]. Hastalardan ameliyat öncesinde VPS ameliyatından fayda görecek olanları saptamak için radyolojik yöntemlerin önemli olduğunu düşünen ve bunun için radyolojik metot öneren birçok çalışma mevcuttur [5-8].

Bu çalışmada VPS ameliyatına iyi yanıt veren ve vermeyen hastaların ameliyattan önce radyolojik görüntüler incelenerek, ventriküler büyüme formunu karşılaştırması planladık.

GEREÇ ve YÖNTEMLER

Ocak 2014 – Haziran 2016 tarihleri arasında hastenemizde NBH tanısı ile opere edilmiş hastalar dahil edildi. Hastaların tamamına NBHDS, NPT, beyin BT ve MR yapıldı. Şikayetleri, klinik özellikleri ve NPT sonuçları NBH ile uyumlu hastalar çalışmaya dahil edildi.

NBHDS, NBH'nin klasik triadının (kognitif bozukluk, yürüme bozukluğu ve üriner inkontinans) her birinin şiddetini ayrı ayrı değerlendirmek için klinisyen tarafından derecelendirilmiş bir ölçektir (Tablo 1). Her alanın skoru 0 ile 4 arasında değişir, yüksek puanlar kötü semptomları gösterir. Toplam skor hastanın tedaviye vermiş olduğu cevabı gösterir. 0 ile 12 arasında puanlanır. Düşük puan iyi cevabı yüksek puan ise kötü cevabı belirtir. Ameliyat öncesi skora göre toplam skorda 1 puanlık düşüş tedaviden fayda gördüğünü göstermektedir [9-11].

Radyolojik inceleme, ameliyat öncesi beyin BT ve MRG görüntülerine bakılarak yapıldı. Hastaların lateral ventriküllerinin genişleme

Tablo 1. Normal Basınçlı Hidrosefali Derecelendirme Skalası (NBHDS)

Puan	Tanım
Kognitif Bozukluk	
0	Normal
1	Amnezi ya da dikkatsizlik şikayetinde bulunmakla birlikte objektif hafıza ve dikkat eksikliği yok
2	Hafıza kaybı veya dikkatsizlik varlığı, ancak zaman ve yer dezoryantasyonu olmaması
3	Zaman ve yer desoryantasyonu varlığı, fakat konuşma mümkün
4	Dezoryante veya anlamlı konuşma mümkün değil
Yürüme Bozukluğu	
0	Normal
1	Başdönmesi var, ancak objektif yürüme güçlüğü yok
2	Dengesiz ancak bağımsız yürüyüs
3	herhangi bir destek ile yürümek
4	Yürüyememek
İdrar İnkontinansı	
0	Normal
1	Sık idrara çıkma veya idrar sıkışma hissi
2	Ara sıra idrar kaçırma (haftada 1-3 veya daha fazla, ancak günde bir defadan az)
3	Sürekli idrar kaçırma (günde 1 veya daha fazla kez)
4	Sürekli mesane disfonksiyonu

paternine bakılarak iki gruba ayrıldı. Grup-1: Uniform ventrikül genişlemesi olan hastalar, Grup-2: Temporooksipital bölüm ağırlıklı genişlemesi hastalar şeklinde gruplandırıldı.

Çalışma için yerel etik kurulu onayı alındı (12.01.2017 tarihli etik kurul onayı protokol no: 18). Hastalardan yazılı ve sözel olarak aydınlatılmış onam alındı.

İstatistiksel Analiz

İstatistiksel analiz için IBM SPSS Statistics sürüm 25.0 (IBM Co., Armonk, NY, ABD) kullanıldı. Demografik verilerin değerlendirilmesinde tanımlayıcı istatistiksel yöntemler (frekans, yüzde, ortalama, standart sapma) kullanıldı. İki grup arasında ilişkililik durumunun belirlenmesine yönelik olarak kategorik değişkenler için X^2 analizi yapıldı. Sonuçlar %95 güven aralığında ve anlamlılık $p < 0.05$ düzeyinde değerlendirildi.

BULGULAR

Çalışmaya 22 hasta dahil edildi. Hastaların 16-83 yaş aralığında ve yaş ortalamasının ($\bar{X}$)=63,48 (Ss.=15,30) olduğu tespit edildi. Eğitim durumlarının, hiç eğitim almayandan 15 yıl eğitim alana değişim gösterdiği; ortalama $\bar{X}$=6 yıl (Ss.=4,98) olduğu görüldü. Hastaların 14'ü kadın (%51,9), 13'ü erkek (%48,1); tümü sağ eli baskın bulunmuştur (Tablo 2).

Hastaların 5 (%19)'i VPS cerrahisine olumlu yanıt vermezken, 22 (%81)'si VPS cerrahisine iyi yanıt verdi. Hastaların 11 (%41)'inin ventriküllerin temporooksipital bölümü genişlerken (Grup-2), 16 (%59)'sında uniform genişleme mevcuttu (Tablo 3). Ventriküllerin genişleme formu ile VPS cerrahinde alınana yanıt arasında istatistiksel anlamlı ilişki saptanmadı (p=0.768, p=0.623).

Tablo 2. Demografik Ölçümler

		$\bar{X}$ / Sıklık	Ss. / %
Yaş		63,48	±15,30
Eğitim (yıl)		6	±4,98
Cinsiyet	Kadın	14	51,90%
	Erkek	13	48,10%
El Dominansı	Sağ	27	100%
	Sol	0	%0.0

Tablo 3. VPS Operasyonu Yanıtı ile Ventrikül Büyüme Formu Arasındaki İlişki

	VPS İyi yanıt vermeyen	VPS İyi yanıt veren	P değeri
Grup-1 Temporooksiptal genişleme	2 (%40)	9 (%41)	0.768
Grup-2 Uniform genişleme	3 (%60)	13 (%59)	0.623
Toplam	5 (%100)	22 (%100	

TARTIŞMA

NPH hastalarında, VPS ameliyatına iyi yanıt vermesini preop dönemde belirlemek henüz mümkün değildir. Literatürde bununla ilgili birçok çalışma mevcutur. Bu çalışmalardan bir kısımı radyolojik verilere bakarak bunu tahmin etmeye çalışmaktadır [8,12-14]. Bazı çalışmalarda ise klinik özelliklere bakılarak hastaların VPS'ye cevabı öngörülmeye çalışılmıştır [15,16]. Bu çalışmalardan net bir sonuç elde edilememiştir. Biz de çalımamızda VPS ameliyatına iyi yanıt verecek ve vermeyecek hastaları preop dönemde belirleyebilmek için bir radyolojik görüntüleme yöntemi kullandık. Bu yönteme göre, hastaların bir kısmında ventriküllerin temporooksipital büyüme paternini hakimken, bir kısmında ise ventriküllerin tamamı uniform halde genişlemektedir. Bu farklı ventrikül büyüme paternlerini hastaların VPS yanıtlarıyla karşılaştırdık. Ancak ventriküllerin büyüme şekli ile VPS yanıt arasında anlamlı ilşkli saptamadık.

VPS cerrahisine yanıt vermeyen hastaların sayının beş olması sonuçların tartışılır olduğunu düşümdürse de daha büyük hasta popülasyonları ile daha büyük çalışmalar yapılması gerektiğini düşünmekteyiz.

SONUÇ

Çalışmamızın sonuçlarına göre ventrikül büyüme şeklinin VPS yanıt cevabını preop belirmek için yetersiz olduğu ortaya çıkmıştır. Ancak daha büyük popülasyonlar ile çalışmanın terarlanmasında fayda olduğunu düşünmekteyiz.

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Nöroşirurjide Yeni Nesil Dura Sızdırmazlık Sağlayıcı Yama (Hemopatch®) ile Klinik Deneyimimiz

Hemopatch®, A New Generation Dural Sealant in Neurosurgery; Our Clinical Experience

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ÖZ

Nöroşirürjide beyin omurilik sıvısı (BOS) fistülü önemli bir komplikasyondur. Hemopatch®'in (Sealing Hemostat – Baxter Healthcare SA, Avusturya) fibrin yapıştırıcı (Tisseel®, Baxter Healthcare SA, İsviçre) ile birlikte kraniyal cerrahide kullanımı ile birlikte literatür değerlendirmesi yapılmıştır. İntrakraniyal kitle nedeniyle ameliyat edilen ve dural kapanma aşamasında fibrin yapıştırıcı ile birlikte Hemopatch® kullanılan 4 hastanın ameliyat sonrası erken ve geç dönem sonuçları irdelendi. Hastaların yaş ortalaması 62.25 ± 10.49 yıl ve ortalama takip süreleri 16.25 ± 3.27 hafta idi. Fibrin ile birlikte Hemopatch® kullanılan hastaların tamamı kraniyal cerrahi (%75 pterional kraniyotomi, %25 retrosigmoid kraniyotomi idi) geçiren hastalardan oluşmaktaydı. Takip sırasında 3 hastada Beyin Omurilik Sıvısı (BOS) kaçağı görülmezken, 1 hastada postoperatif erken dönemde BOS kaçağı gerçekleşti. Kaçağın gerçekleştiği bu hastada, geniş dura insizyonu nedeniyle dural tabaka tamamen çıkarıldıktan sonra fasya ve ksenograft ile duroplasti yapılarak sutür hattını güçlendirmek amacıyla Hemopatch® uygulanmıştır. Sonuç olarak, öncelikle Hemopatch®'in fibrin yapıştırıcılı kraniyal cerrahide dura sızdırmazlık sağlayıcı olarak kullanılmasının uygulanabilirliğini ve güvenliğini ortaya koyduk.

Anahtar Kelimeler: BOS fistülü, dural kapanma, hemopatch

ABSTRACT

Cerebrospinal fluid (CSF) fistula is an important complication in neurosurgery. A literature review was performed with the use of Hemopatch® in cranial surgery together with fibrin glue. Early and late postoperative results of 4 patients who were operated for an intracranial mass and used Hemopatch® with fibrin glue in the dural closure of

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CSF leak stage were evaluated. The mean age of the patients was 62.25 ± 10.49 years and the mean follow-up period was 16.25 ± 3.27 weeks. All of the patients who used fibrin glue Hemopatch® consisted of patients who had undergone cranial surgery (75% was pterional craniotomy, 25% was retrosigmoid craniotomy). Cerebrospinal Fluid (CSF) leakage occurred in the early post-operative period in 1 patient who underwent Hemopatch® by completely removing the dural layer due to extensive dural invasion and performing duraplasty with fascia after the follow-up. Hemopatch was applied and CSF leakage was not observed in the other 3 patients with small dural defects. In conclusion, we first demonstrated the feasibility and safety of using Hemopatch® as a dural sealant in fibrin glued cranial surgery.

Keywords: CSF fistula, dural closure, hemopatch

GİRİŞ

BOS fistülü kraniyal ve omurilik cerrahisi sonrasında, yüksek enfeksiyon riski, hastanede kalış süresinin uzaması ve bir çok durumda yeniden ameliyat ihtiyacına neden olan ve böylece sağlık bakım maliyetlerini artıran önemli bir komplikasyondur [2,8]. Bu nedenle, sıvı geçirmez bir şekilde dural kapanma sağlamak için birçok teknik ve kapatıcı materyal geliştirilmiştir. Bu amaçla geliştirilen malzemelerden biri, polietilenglikol (PEG) kaplı kolajen yama olan Hemopatch'tir. Dural sızdırmazlık sağlayıcı özelliğinin yanı sıra Hemopatch, hemostat olarak da kullanılabilmektedir [1]. Hemopatch®, kendinden yapışan bir yüzeye ve tabaka benzeri bir arkalığa sahip bir peddir. Bu kolajen pedin aktif tarafında yeni, kendinden yapışkanlı yüzey kullanılmıştır. Aktif ajan, polietilenglikol (PEG) ile doku proteinleri ve kolajen arasındaki kovalent amid bağları yoluyla dokuya bağlanan, hızlı protein reaktif monomerdir. Çalışmamızın amacı, kraniyal cerrahide fibrin yapıştırıcı ile Hemopatch® kullandığımız vakalardaki deneyimimizi literatür eşliğinde sunmaktır.

MATERYAL ve METOD

Bu çalışmada, Nisan 2022 ile Haziran 2022 tarihleri arasında SBÜ Gaziosmanpaşa Eğitim ve Araştırma Hastanesinde intrakraniyal yolla elektif ameliyat edilen ve dural kapanma aşamasında Hemopatch® kullanılan hastalar irdelendi. Kraniyal cerrahi uygulanan 4 hastanın (2 erkek, 2 kadın) klinik verileri geriye dönük olarak toplandı (Tablo 1). Ortalama yaş 62.25 ± 10.49 yıl ve ortalama takip süresi 16.25 ± 3.27 hafta idi. Çalışmamıza yalnızca kraniyal cerrahi uygulanan hastalar dahil edildi. Tüm işlemler tek bir cerrrah (O.B.) tarafından yapıldı. Kısa dönemli çalışmamızdaki hasta sayısı istatistiksel olarak yeterli sonuç vermeyeceğinden dolayı tüm ameliyatların kapanma aşaması yazımıza resim olarak eklendi.

Duranın kapanma tekniği ve Hemopatch uygulaması

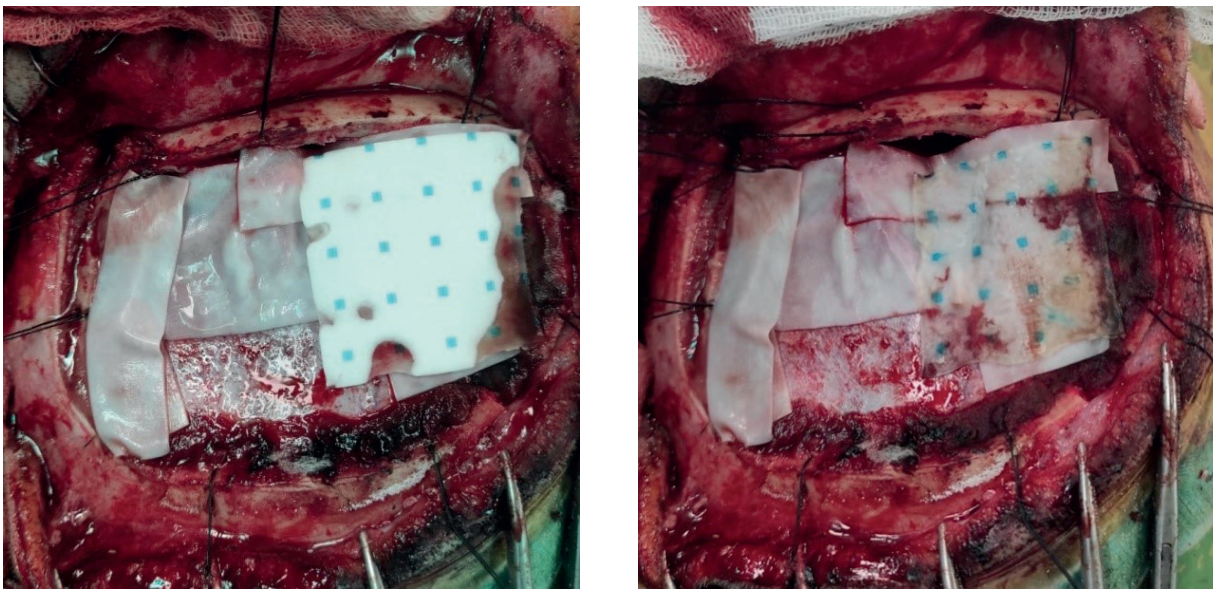
Kraniyotomi yapılarak opere edilen ve dura (4-0 vicyrl) primer olarak kapatılan (1 hastaya ise fasya ve ksenogreft geniş duraplasti yapıldı) hastalara duraplasti yapıldı ve ardından sütur hattına PEG kaplı ve kolajen bazlı sızdırmaz hemostatik yama olan Hemopatch®, üreticinin kullanım talimatlarına göre uygulandı. Kolajen pedin aktif tarafı dura yüzeyine uygulandı, ardından kuru bir gazlı bezle 2 dakika hafif basınç uygulandı. İkinci aşamada, kapamanın bütünlüğü değerlendirildikten sonra fibrin yapıştırıcı Hemopatch'in etrafına damlatma yöntemi ile uygulandı.

Tablo 1. Temel Veriler ve Sonuçlar

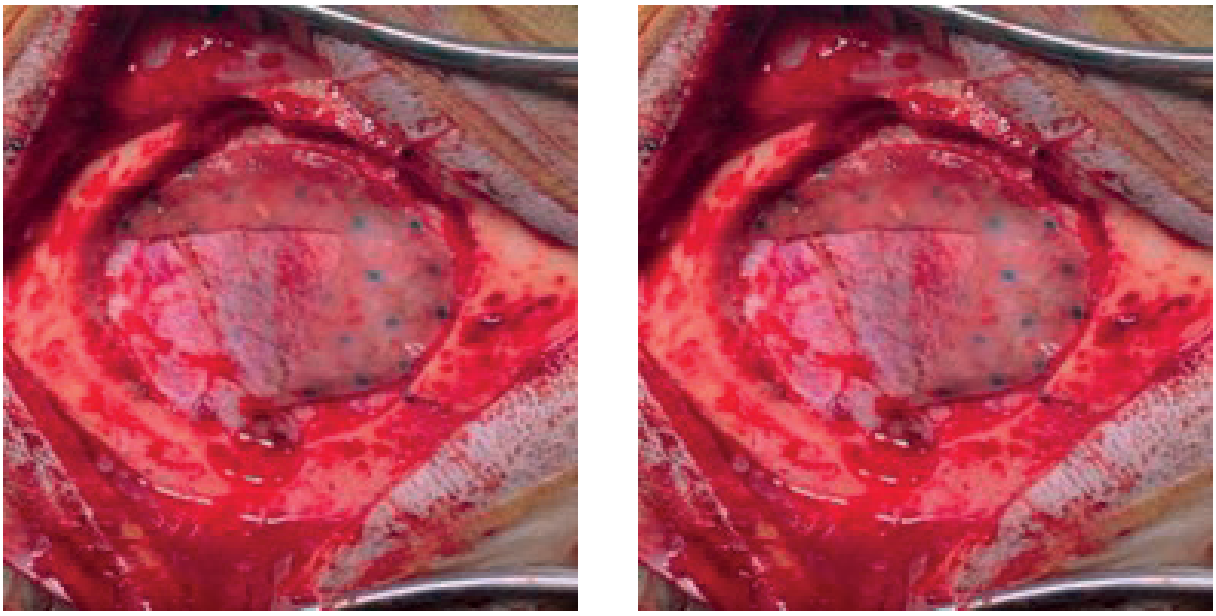
Hasta	Cinsiyet	Yaş	Lokasyon	Patoloji	Yöntem	Dural kapanış	Komplikasyon
1	E	47	Sol Frontotemporal	Menenjiom Grade 1	Pterional	Geniş Defekt (7 mm)	BOS fistülü
2	K	72	Sağ Frontal	Menenjiom Grade 1	Pterional	Küçük açıklık	Yok
3	K	72	Sağ Temporal	Menenjiom Grade 1	Pterional	Küçük açıklık	Yok
4	E	58	Sol Serebellopontin	Vestibüler Schwannoma	Retrosigmoid	Görünen açıklık yok	Yok

BULGULAR

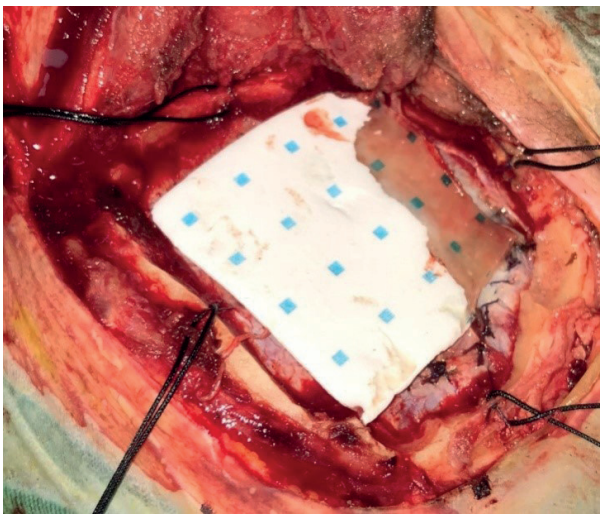
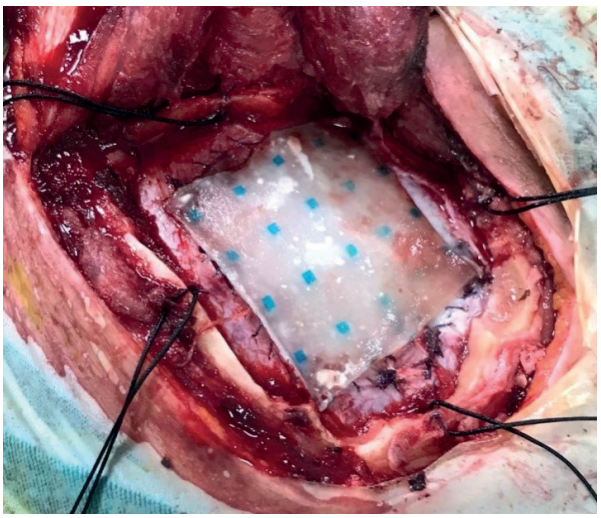
Dört (4) kraniyal cerrahi (1 retrosigmoid kraniyotomi) gerçekleştirildi. Bir (%25) hasta haricinde tüm hastaların (%75) duraları primer olarak kapatıldı. Cerrahi prosedür gereği duranın çıkartılmasıyla oluşan geniş defekte fasya ve ksenogreft ile sekonder duraplasti yapılan bir hasta dışında takip sırasında BOS fistülü olmadı. BOS fistülü olan hastanın yara yeri ponksiyone edilerek bandaj ile sarıldı. Hastanın cerrahi revizyona ihtiyacı olmadı. Hastalar post-operatif erken dönemde mobilize edildi. Yine hastaların takiplerinde fibrin yapıştırıcı ile Hemopatch® kaynaklı herhangi bir yara enfeksiyonu veya yan etki meydana gelmedi. Tüm hastalarda erken mobilizasyon ve taburculuk sağlandı (Resim 1-4).



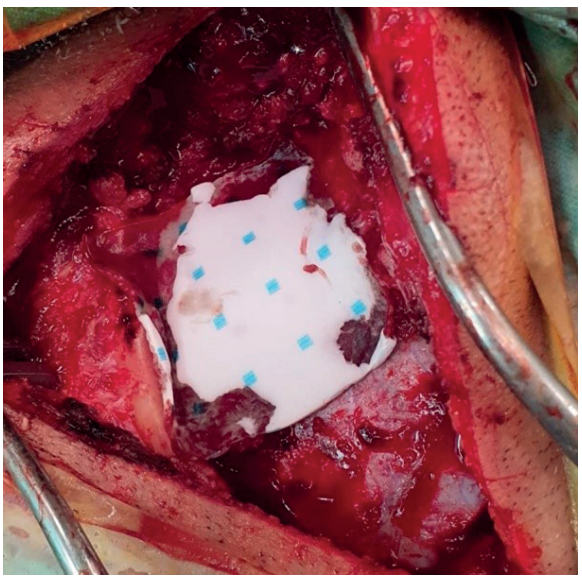
Resim 1. Hasta 1: Sol frontotemporal kitle nedeniyle opere edilen 47 Y/E hasta, Tanı: DSÖ Menengioma, Derece 1. Geniş defekt nedeniyle fasya ve ksenogreft ile sekonder duraplasti yapıldı.



Resim 2. Hasta 2: Sol frontal kitle nedeniyle opere edilen 72 Y/K hasta, Tanı: DSÖ Menengioma, Derece 1.

Resim 3. Hasta 3: Sağ semporal kitle nedeniyle opere edilen 72 Y/K hasta, Tanı: DSÖ Menengioma, Derece 1.



Resim 4. Hasta 4: Sol serebellopontin kitle nedeniyle opere edilen 58Y/E hasta; Tanı: DSÖ Vestibüler Schwannoma.

TARTIŞMA

İntrakraniyal kitle nedeniyle opere edilen küçük retrospektif seride cerrahi revizyon oranı oldukça düşüktü. Duranın primer olarak su geçirmez bir şekilde kapatılması kraniyal nöroşirürjinin vazgeçilmez bir parçasını oluşturur, çünkü revizyon cerrahisi hastalar için ek riskler getirmektedir [5]. İkinci bir ameliyat hastanede kalış süresinin uzamasına neden olup ve dahili ve cerrahi komplikasyon olasılığını önemli ölçüde artırarak ek maliyetler yaratmaktadır [6,7]. Ayrıca özelikle tümör cerrahisi uygulanan hastalarda, hastaların planlanan ek tedavilerinin başlama sürelerinin uzamasına neden olmaktadır.

Literatürde de posterior fossa prosedürleri dahil olmak üzere, 3 mm açıklıklara kadar dural defektlerde sutür hattına uygulanarak BOS sızdırmazlığı sağlamada Hemopatch başarılı bulunurken, 3 mmden geniş dural defekti olan 3 hastanın 1'inde BOS kaçağı görüldüğü belirtilmiştir [9].

Çalışmamızda da aldığımız hasta grubumuzda, bir hasta dışında BOS fistülü olan hasta olmadı. BOS fistülü gelişen hastanın fistül bölgesi ponksiyone edilerek sarıldı ve ikinci bir operasyona gerek kalmadan fistülü düzeldi. Serimizdeki hasta sayısının az olması bu sonucu göreceli hale getirse de; Hemopatch® gibi kolay uygulanabilen sızdırmazlık sağlayıcıların uygulanması, yara enfeksiyonları ve BOS fistüllerine bağlı revizyon cerrahisi riskini azaltmaya yardımcı olabilir.

Polietilen glikol ile kaplı kolajen matris olan Hemopatch®, genel cerrahi ve kalp cerrahisinde de değerlendirilmiştir [3,13,14]. Bildirilen klinik sonuçların iyi olmasının yanında hayvan testlerinde de hiç bir nörotoksik komplikasyon

bildirilmemiştir [12]. Doğru dural kapama, büyük defektlerin otolog doku ile desteklenmesi ve kemik flebinin dikkatli bir şekilde yeniden yerine konması kraniyal cerrahi prosedürün her zaman temelini oluşturmaktadır. Bununla birlikte, Hemopatch® uygulaması su geçirmezliği desteklemektedir [4,11]. Ayrıca, kranial operasyonlardan sonra cerrahi alan enfeksiyonlarının oranını önemli ölçüde azaltır [10]. Hasta grubumuzda yara enfeksiyonu dahil Hemopatch® ile ilgili herhangi bir yan etki veya alerjik reaksiyona rastlamadık. Bu nedenle Hemopatch®'in kraniyal cerrahi sonrasında dura defektlerini kapatmak için güvenli ve uygulanabilir bir materyal olduğu sonucuna vardık. Dura sızdırmazlığında kısmen yeni bir materyal olan Hemopatch®'in etkinliğini açıkça değerlendirmek için büyük ve ileriye dönük klinik çalışmalar yapmak gerekliliği vardır.

SONUÇ

Yapmış olduğumuz küçük çaplı retrospektif çalışmada, primer dural onarımın mümkün olmadığı durumlarda bile dura sızdırmazlığı amacıyla kullanılan Hemopatch®'in kullanımının etkili, güvenli ve uygulanabilir olduğu görülmektedir. Nöroşirürji alanında dura sızdırmazlığı açısından Hemopatch®'in umut verici sonuçlarını doğrulamak için ileri kontrollü ve ileriye dönük çalışmalar ile farklı dura sızdırmazlığı sağlayıcıların etkinliği karşılaştırılmalı olarak değerlendirmelidir.

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Unexpected Intratumoral Bleeding during Surgery Decision: Gliosarcoma

Cerrahi Kararı Verme Aşamasında Gerçekleşen İntratümöral Kanama ve Klinik Bozulma: Gliosarkoma

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ABSTRACT

Introduction: Gliosarcoma is a rare central nervous system tumor and shows genetic, clinical, and prognostic similarities Glioblastoma multiforme. It presents with progressive neurological deficits such as increased intracranial pressure, seizures, and hemiparesis.
Case Report: We report an 81-year-old female patient was consulted from internal medicine clinic with severe headache and weakness on her right side.
Conclusion: Gliosarcoma may be accompanied by intra-tumor bleeding. It is not possible to predict when the bleeding would occur. Hematoma may mask tumoral lesion.

Keywords: Intracranial tumor, gliosarcoma, intratumoral hemorrhage

ÖZ

Giriş: Gliosarkom, nadir görülen bir merkezi sinir sistemi tümörüdür ve Glioblastoma multiforme ile genetik, klinik ve prognostik benzerlikler gösterir. Artmış kafa içi basıncı, nöbetler ve hemiparezi gibi ilerleyici nörolojik defisitlerle kendini gösterir.
Olgu Sunumu: Sağ tarafta şiddetli baş ağrısı ve güçsüzlük şikayeti ile iç hastalıkları kliniğinden konsülte edilen 81 yaşında kadın hastayı sunuyoruz.
Sonuç: Gliosarkoma tümör içi kanama eşlik edebilir. Kanamanın ne zaman olacağını tahmin etmek mümkün değildir. Hematom tümör lezyonunu maskeleyebilir.

Anahtar Kelimeler: İntrakraniyel tümör, gliosarkoma, intümöral kanama

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INTRODUCTION

Gliosarcoma (GSM) is a rare central nervous system tumor and contains both gliomatous and sarcomatous components. It shows genetic, clinical, and prognostic similarities with Glioblastoma multiforme (GBM) as an uncommon variant [1]. However, GSM has distinct clinical behaviors such as the tendency to settle in the periphery of the cerebral lobes, showing dural connections similar to meningiomas, intra/extracranial metastasizing, and worse prognosis compared to GBM [1,2]. Although the treatment strategy of GSM is similar to GBM, there is no consensus on the effect of chemotherapy on the survey since GSM is rare and the literature consists of small case series showing different findings [1].

The clinical presentation is also similar to GBMs, including progressive neurological deficits such as increased intracranial pressure, seizures, and hemiparesis [1]. A gliosarcoma case presenting with acute hemorrhage has also been reported as well [3].

CASE REPORT

An 81-year-old female patient was consulted from internal medicine clinic with severe headache and weakness on her right side. Her medical history included asthma and congestive heart failure. She was not using any antiplatelet or anticoagulant drug. She was conscious, alert, and oriented, but the muscle strength on the right was 3/5 on the upper and lower extremities, both proximally and distally. No speech impairment or neck stiffness was noted. In her physical examination, only bilateral leg edema was seen. She underwent cranial magnetic resonance imaging MRI showed a space-occupying lesion in the left frontotemporal area, revealed peripheral contrast enhancement (Figure 1). Surgical intervention for both diagnosis and decompression purposes was recommended to the patient. During the decision-making process of the patient and her relatives, the patient suddenly experienced loss of consciousness one day after offering surgery. Her GCS was 6 (E2V1M3). No remarkable change was seen on her vitals or ECG. Intubation was performed. A control non-contrast and contrast cranial CT were

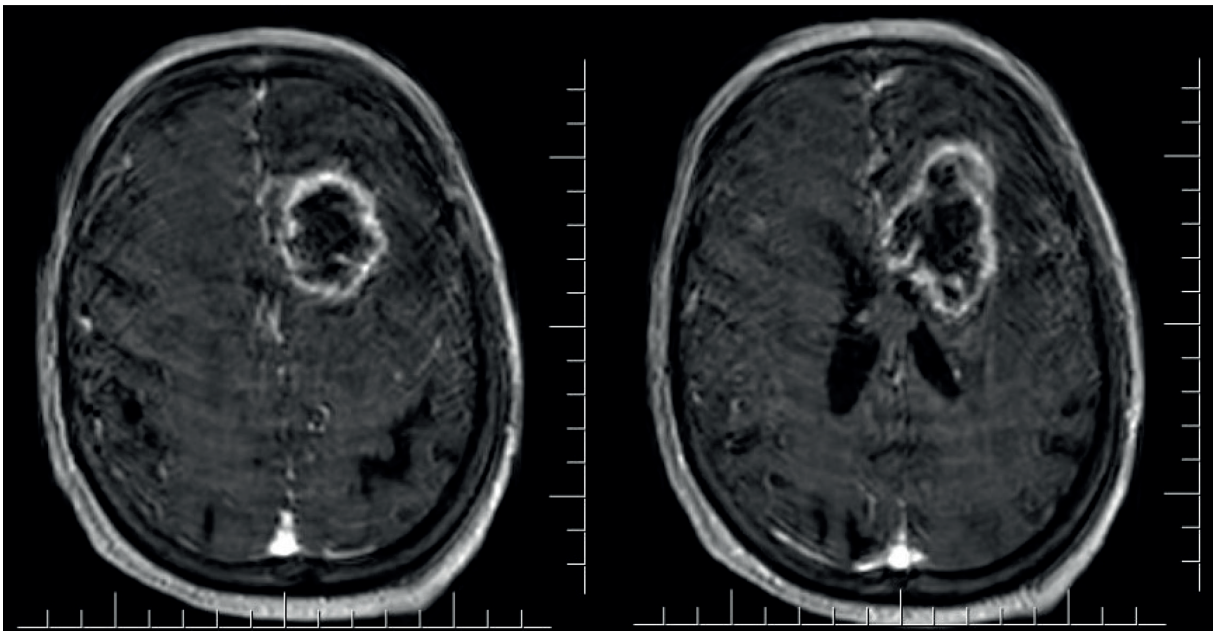

Figure 1. Contrast-enhanced axial MR images of brain showing peripherally contrast-enhanced lesion

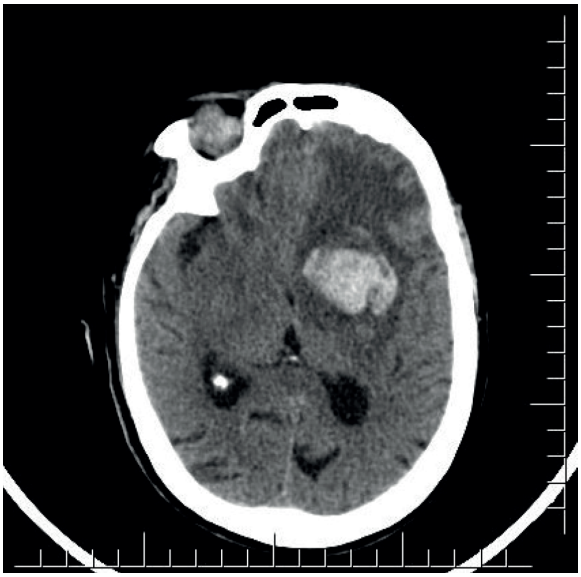

Figure 2. CT image of brain showing hematoma masking the tumor

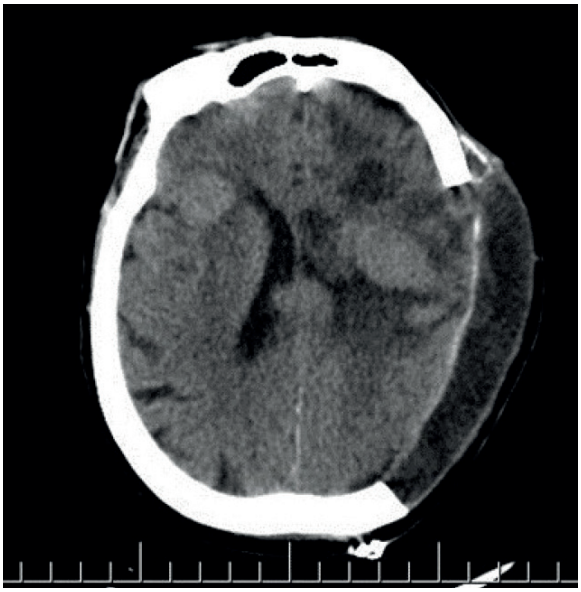

Figure 3. Postoperative CT image showing no hematoma or tumor

ordered, and a re-consultation with neurosurgery was planned. The examinations revealed 35x37 mm intracerebral hemorrhage into the previously detected lesion in the left frontotemporal area and a remarkable midline shift (8 mm) (Figure 2). The patient underwent urgent surgery to evacuate the hematoma and tumor. The post-operational tomography revealed that the midline shift was recovered, and the hematoma was evacuated entirely (Figure 3). The pathology examination was reported as "gliosarcoma". The patient died after a 4-month intensive care unit (ICU) follow-up with intubated state. As our patient did not have a chance to be extubated during her ICU follow-up, she did not receive any adjuvant chemo or radiotherapy.

DISCUSSION

GSM accounts for 1-8% of all GBM cases and less than 0.5% of all intracranial tumors [4,5]. Singh et al. reported the incidence as 5.2% in their study in 2015 [1]. GSM can be primary or secondary. In the same study, secondary GSM cases were detected in 2 of 16 patients. Generally, it is common in older males. The clinical characteristics and treatment approaches are very similar to GBM. However, it tends to settle in the temporal lobe compared to GBM [2,6-9]. It can also be found in frontal, parietal, and occipital lobes [9,10]. Cases with peritrigonal, corpus callosum, ventricle, brainstem, and cerebellum involvement have been reported in the literature [1,11]. Although rare, GSM can present with multifocal lesions mimicking metastatic disease [12]. The tumor location in our case was the temporal lobe in accordance with the literature, but the patient was an elderly female patient.

The most common symptoms are focal neurological deficit, tonic/clonic seizures, location-specific and increased intracranial pressure presentations such as weakness, headache, nausea, vomiting, visual disturbances, confusion, lethargy, ataxia, or altered mental status [3]. So it is not surprising GSM can be an ischemic stroke mimic [13]. Hemorrhage has been reported very rarely in GBM cases in the literature. One report has a similar patient profile with acute hemorrhage accompanied by sudden consciousness impairment in 2019 [3]. It has been suggested that the predisposing factor of

spontaneous hemorrhage in such cases is intense and abnormal vascularity. Singh et al. mentioned intracranial hemorrhage in 2 patients of 16 [1]. Duan et al. reported a GSM case presenting with rapid tumor growth in the cerebellopontine corner and intratumoral hemorrhage [14]. In cases presenting with hemorrhage, the tumor mass is often masked by bleeding on radiological imaging like our case. A case of GBM with extensive pachymeningeal dissemination mimicking a chronic subdural hematoma has also been reported recently [15].

CONCLUSION

GSM often causes gradual neurologic symptoms depending on tumor location and size. Gliosarcoma may be accompanied by intra-tumor bleeding. It is not possible to predict when the bleeding would occur. As in our patient, it may bleed during the decision of surgery. It should be remembered that hematoma may mask tumor.

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Case Report / *Olgu Sunumu*

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The Treatment of Advanced Cubital Tunnel Syndrome in a Patient with Hemophilia and Its Postoperative Results

Bir Hemofili Hastasında İleri Evre Kübital Tünel Sendromunun Tedavisi ve Postop Sonuçları

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ABSTRACT

We would like to inform and guide other hand surgery physicians by sharing the results of a patient with ulnar nerve compression due to hemosiderin accumulation due to hemophilia. We operated a hemophilia patient who applied late and had ulnar nerve compression and we achieved a successful result. In this publication, the patient we operated on was presented as a case report and discussed in the light of literature.

Keywords: Ulnar nerve entrapment, hemophilia, nerve entrapment, claw hand, neuropathy

ÖZ

Kas-iskelet sistemi hemorajileri homofili hastalarında sık görülür. Hemofili hastalarında ulnar nöropati ile ilgili son yıllarda literatürdeki yayın sayısı çok sınırlıdır. Hemofilide periferik nöropatilerin en sık femoral sinirde görüldüğü belirtilmiş olsa da diğer periferik sinirlerde de görülebilmektedir.

Anahtar Kelimeler: Ulnar sinir sıkışması, hemofili, sinir sıkışması, pençe el, nöropati

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INTRODUCTION

Musculoskeletal hemorrhages are common in patients with hemophilia. In this publication, we will describe the pre- and post-operative clinical condition of a patient with severe ulnar nerve compression around the elbow region due to hemophilia-related accumulation of hemosiderin and significant atrophy in areas innervated by the ulnar nerve.

PATIENT

A 25-year-old right-handed 55 kg 172 cm male patient presented with complaints of numbness, tingling, numbness and loss of strength in his left hand. He had claw hand deformity in the 4th and 5th fingers. There was no abduction-adduction in the fingers and there was atrophy of the interosseous and hypothenar muscles innervated by the ulnar nerve. Tinel, Wartenberg, Jeanne and Froment sign findings were positive. Two point discrimination measurements increased in the ulnar region, especially on the 5th finger and it was measured as 9mm.

Figure 1

Figure 2

While MR and USG images showed a mass lesion formation due to accumulation in the ulnar nerve region at the level of the medial epicondyle, on USG it was found that the diameter of the ulnar nerve increased compared to the measurements of the healthy side, the mass was outside the nerve at the beginning, but the nerve could not be observed due to the compression of the mass after it passed through the medial epicondyle.

In EMG, ulnar motor conduction block was observed in the elbow segment. In addition to the ulnar neuropathy findings, there was a 50-degree limitation of extension in the elbow due to hemophilic arthropathy, and the flexion was 135 degrees. The patient with hemophilia A had factor VIII deficiency. Early surgery decision was made owing to the advanced complaints and findings. Factor VIII was given at 2500-unit doses before the operation. The patient underwent ulnar nerve neurolysis, anterior transposition and excision of the mass. The operation was performed under tourniquet control. He continued to take factor VII for 3 days after the operation. There was no abnormal bleeding in the dressing or

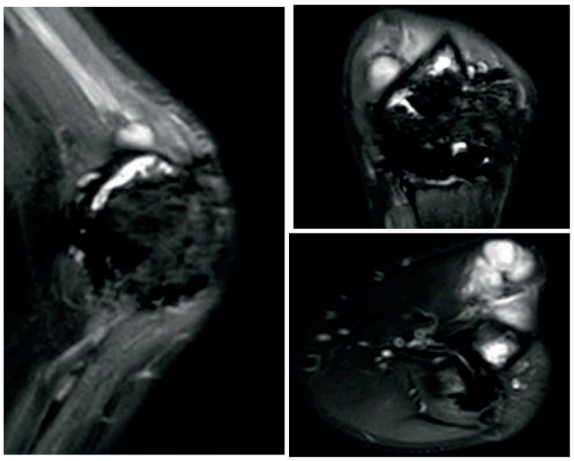

Figure 3

hematoma in the wound area. It was determined that ulnar neuropathy findings regressed on the 2nd postoperative day. In the follow-ups, the numbness disappeared, the loss of sensation and the claw hand deformity regressed. In the third month follow-up, the patient's complaints regressed significantly. VAS pain score decreased from 7/10 to 1/10. The atrophies were still partially ongoing, but the Wartenberg and Froment findings were negative. The two-point separation was 4mm. While Gabel and Amadio's Ulnar Nerve Rating Scale preoperatively was 2/9, on the second day post-operatively it was 3/9 and on the 3rd month it was 7/9.

METHODS

In tourniquet hemostasis, a longitudinal incision extending 8 cm proximal and 4 cm distal to the medial epicondyle was entered, and the subcutaneous mass was reached immediately. The ulnar nerve was separated from the mass and freed, its motor branches were exposed, and the mass was excised while preserving them. A part of the medial intermuscular septum was excised, and the ulnar nerve was transposed anteriorly to the subcutaneous tissue. In order to keep the ulnar nerve at the transposed site, a pocket was made from the surrounding soft tissue and covered loosely. No compression or folding was observed along the liberated nerve trace.

DISCUSSION

In recent years, the number of publications in the literature about ulnar neuropathy in patients with hemophilia is very limited. Therefore, we think that our case will contribute to the current literature. Although it has been stated that peripheral neuropathies are most commonly seen in the femoral nerve in hemophilia, they can also be seen in other peripheral nerves. In the study of Ehrmann L. et al., the number of patients with ulnar nerve lesion was shown as 4 among 36 hemophilia patients with peripheral nerve lesions [(1)]. Besides, cases of carpal tunnel syndrome due to compression in the median nerve in patients with hemophilia have also been shown [(2)].

In peripheral nerve compression due to acute bleeding, if the symptoms are mild, coagulation factor supplementation and immobilization of the joint can be tried first to ensure bleeding control. In patients with severe symptoms, surgical decompression is recommended. Debkowska MP et al. stated that in this case, there was no response to medical treatment alone. In such cases, they recommended the prevention of hematoma with minimal dissection to provide decompression of the nerve [(3)].

Cases caused by chronic compression are well treated with surgical treatment. Peripheral nerve compressions are usually seen secondary to intramuscular hematoma or hemarthrosis, but intraneural hemorrhages have also been reported [(4)]. Although we saw neural edema in our case, we did not observe intraneural hemorrhage. According to a study by Mortazavi SM et al. in 2010, a high rate of HIV and HCV positivity was

shown depending on the possible frequency of transfusion. In this publication, 6/6 patients were positive for HCV and 4/6 patients were HIV positive [5]. In our case, HIV and HCV serology was negative, but we think that surgeons planning such operations should pay maximum attention to viral serology results.

Arthropathy is also a very important problem in hemophilic patients. We think that advanced arthropathy due to recurrent intra-articular hemarthrosis, in addition to restriction of movement in the joint, compresses the nerve. Hogh J. et al. found in their study that 87% of hemophilic patients had radiographic evidence of elbow arthropathy [6]. The pathological mechanism underlying the development of hemophilic arthropathy is quite complex and is not yet fully understood. The two main processes that play a role in the pathogenesis of arthropathy are inflammation of the synovial membrane and cartilage degeneration [7,8]. The presence of blood in the joint induces chondrocyte apoptosis and has a direct corrosive effect. As a result of recurrent bleeding in the same joint, erythrocyte-derived hemosiderin accumulates in synovial macrophages and triggers synovial inflammation, causing the synovium to become hypertrophied [9]. The joint is deformed and range of motion is limited with a tendency to flexion contracture. These changes lead to joint destruction known as "chronic hemophilic arthropathy". In our case, flexion contracture continues even though the patient's ulnar neuropathy findings regressed.

CONCLUSION

We would also like to point out that although the complaints and findings of this patient were obvious, the patient visited the clinic very late so that clinical findings like nerve compression was in advanced stage. This patient's complaints had regressed significantly after the operation, if he had visited or been noticed earlier, he could have been treated before findings such as atrophy occurred. It carries an important role for physicians who frequently follow hemophilia patients, carefully examine neuropathy findings and be alert, in order to diagnose and intervene in such patients earlier. With early intervention, the results will be better.

Conflict of interest: There is no conflict of interest in our study.
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