

Our Results of Clivus Chordoma with Endoscopic Endonasal Surgery-Our Clinical Experiences

Murat Samet Ateş¹ , Duygu Durusoy¹ , Sevinç Eraslan¹, İsa Kaya¹ , Hüseyin Biçeroğlu² , Sercan Göde¹ , Erkin Özgiray² , Raşit Midilli¹ , Sedat Çağlı² , Bülent Karıcı¹ 

¹Department of Otolaryngology, Ege University School of Medicine Hospital, İzmir, Turkey

²Department of Neurosurgery, Ege University School of Medicine Hospital, İzmir, Turkey

Abstract

Objective: Chordoma is a rare, primary malignant bone tumor derived from primitive notochord remnants in the skull base. Chordomas are slow-growing, low-grade neoplasms that are more likely to cause local recurrence, but distant metastases are uncommon. The aim of this study was to report the preoperative and postoperative results of chordoma patients who underwent endoscopic endonasal surgery.

Material and Methods: This study included 10 patients (8 female and 2 male) who underwent endoscopic endonasal pituitary surgery due to chordoma in the Neurosurgery and Otolaryngology Departments of a tertiary medical center between May 2014 and August 2017. All data were obtained from patients' folders and hospital information system retrospectively by evaluating complaints, operation notes, pathology results, radiological images, and postoperative control notes. Patients were evaluated in the postoperative period for a relapse or residual tumor, additional treatment, postoperative complications, and complaints which is regressed or not.

Results: The mean age was 51 years (range, 16-79). Patients were admitted to the Otolaryngology Clinic with headache reported in 2 patients, vision loss in 1 patient, vision loss with headache in 6 patients, and nasal obstruction and headache in 1 patient. A physical examination showed the abducens paralysis in 3 patients and oculomotorius paralysis in 1 patient due to tumor indentation. All patients underwent endoscopic endonasal transethmoid and transsphenoid surgery. Complete gross tumor removal was achieved with the transsphenoidal approach in 9 patients, and the transsphenoidal and far-lateral transcondylar approach in 1 patient.

Conclusion: Considering the local aggressive nature of tumor, radical surgery and adjuvant radiotherapy are the main treatments modalities of chordomas located in the skull base. The endoscopic endonasal transsphenoidal approach has become the gold standard method in daily practice due to its reliability and minimal morbidity.

Keywords: Endoscopic endonasal surgery, transsphenoidal approach, skull base chordomas, clivus

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Address for Correspondence: Duygu Durusoy

E-mail: duygudurusoy8@gmail.com

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INTRODUCTION

Chordomas are primary bone tumors arising from the primitive notochord remnants (1). The incidence of the disease accounts for 1%-4% of all malign bone tumors (1, 2). It occurs along the axial axis, mostly in the sacrococcygeal (50%) and the sphenoid-occipital region (35%), and rarely in mobile vertebrae (15%) (3-5). Chordomas are considered to be a slowly growing tumor, characterized by bone destruction and rarely distant metastatic spread (6). They mainly show local recurrence (6). The recurrence rates are highly frequent, and a 5-year survival rate is estimated in approximately 65% to 79% of cases (4). Chordomas are more frequently seen in men aged between 40 and 70 years (2). They are rarely seen in children (7). Chordomas located in the skull base may cause symptoms depending on the compression of the cranial nerves (1). The most common symptoms are diplopia and headache (1). Following gross total resection, radiotherapy (RT) is considered as the standard treatment mode of clival chordomas (8). The reasons that make the gross total resection difficult are the midline location of the tumor, the infiltrative-destructive nature of the tumor, its proximity to neurovascular structures, and a large size at the time of diagnosis (9-11). Gross total resection can be achieved with lower complication rates by the endoscopic endonasal transsphenoidal surgical method, which can be applied with a newly emerging surgical technique and equipments and the advantage of multidisciplinary approach (6, 9, 11). Even when the gross total resection is performed, microscopic residues may remain in the surrounding tissue due to chordomas' infiltrative nature, and recurrence is more frequent than expected (1, 8). After surgical treatment, majority of patients need additional therapy because of the macroscopic and microscopic residue (12). The response

of chordomas to conventional RT is known to be poor (8). The proton-beam RT and gama knife radiosurgery methods are reported to be effective in the treatment of residual and recurrent tumor (4, 13, 14). Although there is a wide consensus on the necessity of adjuvant therapy after surgical treatment, several treatment methods might be seen. The purpose of our study is to reveal the outcomes of the endonasal endoscopic surgical approach in chordoma patients.

MATERIAL AND METHODS

We retrospectively evaluated the preoperative and postoperative outcomes in 9 patients with radiological pre-diagnosis of chordoma and 1 patient diagnosed with chordoma pathologically, who were treated with the endoscopic endonasal surgical approach method in cooperation with the Ege University Otorhinolaryngology Clinic at the Ege University Brain and Nerve Surgery Clinic between May 2014 and August 2017. Necessary information was obtained by reviewing the patient file. Clinical symptoms, the size and location of the tumor, resection degree, the cerebrospinal fluid (CSF) leakage rate developed postoperatively, development of cranial nerve paralysis, and recovery rates of clinical symptoms were reviewed. Pre- and postoperatively performed cranial computed tomography (CT) and cranial magnetic resonance imaging (MRI) of all patients were investigated. Only 1 patient had chordoma diagnosis made pathologically in the preoperative period. The endonasal endoscopic transsphenoidal surgical approach was primarily performed on all patients.

Written informed consent was obtained from all participants. The patients were laid in the supine position, slightly rotating the head to the right, under general anesthesia. Then, the middle turbinate was gently pushed laterally by passing the nasal cavity with endoscope assistance, and sphenoid sinus ostium was aimed to be detected. After specifying the sphenoid ostium, the ostium was enlarged with the Kerrison assistance, starting from the medial and inferior side. Posterior septal bone and intersinus septum, if present, were gently removed by forceps. Thus, a wide view of the sphenoid sinus, which is easily accessible from both cavities, was provided. This wide view helped us to detect freely both carotid arteries and optic nerve lines. The bone on the wall of sella tursica was removed by forceps or Kerrison, and the elevation of the remanent of bone structures gently by elevator revealed all boundaries of the sella. The clivus was reached transsphenoidally. The mass in the clival region was removed by forceps, aspirator, and round curettes.

Tissue samples taken from the tumor were sent to pathology for sampling. The presence of residual tumor was investigated with 0-, and if necessary, 30- and 45-degree telescopes. An intraoperative navigation system was used to determine the surgical margin in case of the vertical or ventricular and cavernous growth of the tumor. Upon detecting the residue in 1 patient, the surgical procedure was completed with the far lateral transcondylar approach on the postoperative Days 5 and 10. All patients were evaluated with early postoperative period (24-48 hours) cranial MRI and cranial CT (Figure 1, 2 and 3). MRIs of the follow-up

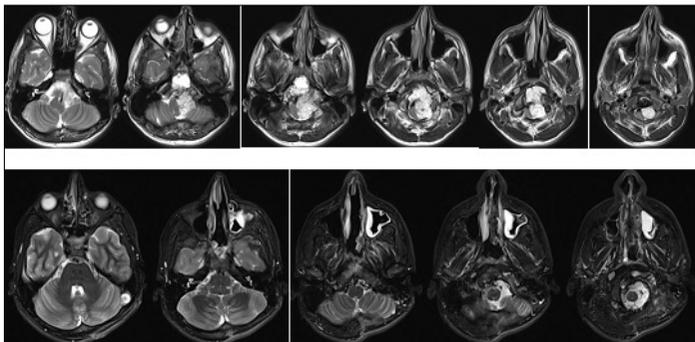


Figure 1. Pre- and postoperative MRI imaging of a patient diagnosed with clivus chordoma

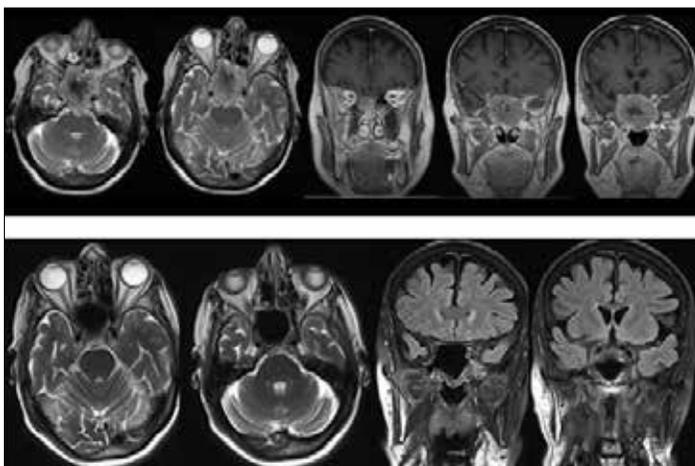


Figure 2. Pre- and postoperative MRI imaging of a patient diagnosed with C1 and clivus chordoma

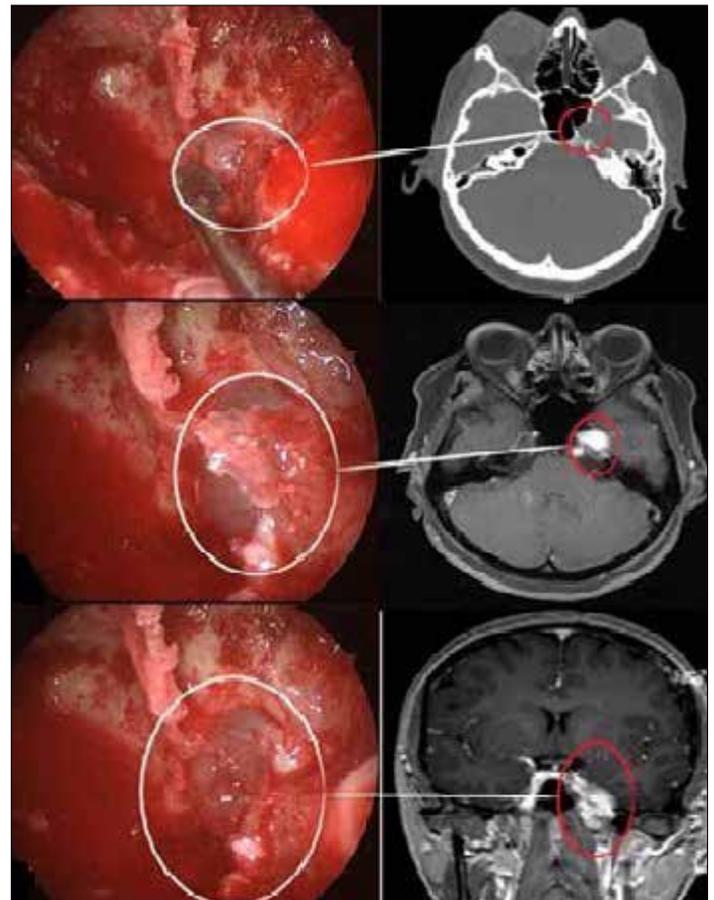


Figure 3. Matching of preoperative endoscopic imaging in a patient who was operated for chordoma located in the meckel cave with CT and MRI imaging

Table 1. Preoperative data of the patients

Age	Sex	Complaint	Additional neurologic deficit	Tumor diameter	Tumor localization
42	M	Visual loss	6 th cranial nerve paralysis	4.5 cm	Sphenoid sinus, suprasellar fossa
66	M	Headache	None	6 cm	Clivus, nasopharynx, sphenoid sinus, ethmoid sinus, maxillary sinus
49	M	Visual loss+headache	None	6.9 cm	Suprasellar region, clivus
42	F	Headache+nasal congestion	6 th cranial nerve paralysis	2.3	Meckel cave, clivus, petrous apex
16	M	Visual loss+headache	None	7 cm	Clivus, foramen magnum, cervical vertebra 1, cervical vertebra 2
64	M	Visual loss+headache	3 rd cranial nerve paralysis	4 cm	Clivus, sphenoid sinus, ethmoid sinus
79	M	Visual loss+headache	None	5 cm	Sella, sphenoid sinus, clivus
53	M	Visual loss+headache	None	3.9	Clivus, sphenoid sinus, ethmoid sinus
48	F	Visual loss+headache	6 th cranial nerve paralysis	4	Clivus, cavernous sinus, parasellar region, sella
61	M	Headache	None	2	Clivus, sphenoid sinus

**Figure 4.** Basilar artery imaging in a patient who underwent dura resection due to clivus chordoma**Figure 5.** Repair was performed with nasoseptal flap and left inferior turbinate flap in a patient who underwent clivus chordoma surgery and developed CSF rhinorrhea twice
Arrow, Nasoseptal flap, Star, Inferior turbinate flap

patients were evaluated at the 3rd and 12th month of the postoperative period and annually. The mean follow-up duration was 15 months (ranging between 3 and 39 months).

RESULTS

The mean age of the patients (n=10) was 51 (ranged between 16 and 79 years). The study group included 8 male and 2 female patients. 20% (n=2) of patients were admitted to our clinic complaining of headache, 10% (n=1) of vision loss, 60% (n=6) of visual loss and headache, and 10% (n=1) of nasal congestion and headache. In 30% (n=3) of patients, n. abducens paralysis was observed, and restriction in the eye movement due to n. oculomotorius paralysis during diagnosis in 10% (n=1). The largest diameter of the tumor size was detected as 4.27 cm (range between 2 and 7 cm) (Table 1). A gross total resection with endoscopic endonasal transtentorial transsphenoidal approach was performed in all

patients in cooperation with the Brain and Nerve Surgery Clinic. The gross total resection was completed with far lateral transcondylar approach on postoperative Days 5 and 10 because of detecting the residue in 1 patient in the early period. Reconstruction using the nasoseptal flap was performed in all patients. Large dura mater and arachnoid resection were performed in 6 patients, and a high flow of CSF was observed (Figure 4). Clival defect was repaired with nasoseptal pedicled flap in all patients. Reconstruction with fascia lata was performed on 2 of the patients due to CSF flow seen in their follow-ups. Upon continuation of the CSF flow also in 2 patients, 1 of the patients underwent the repair of the skull base defect with fascia lata received from the other leg, and the other patient underwent the repair of skull base defect with inferior turbinate flap (Figure 5). Hydrocephalus was observed on control cranial MRI in 1 patient due to the complaint of headache on the

Table 2. Postoperative data of the patients

Surgery	Recurrence	Additional therapy	Follow-up duration	Pathology	Complication
Endoscopic endonasal transsphenoidal	13 th month	RT	20 months	Conventional	Visual loss-embolism of the retinal artery, hydrocephalus
Endoscopic endonasal transsphenoidal	30 th month	RT	39 months	Chondroid	Hydrocephalus
Endoscopic endonasal transsphenoidal	None	None	17 months	Chondroid	BOS fistula
Endoscopic endonasal transsphenoidal	None	None	12 months	Conventional	None
Endoscopic endonasal transsphenoidal	None	None	18 months	Kondroid	BOS fistula
Endoscopic endonasal transsphenoidal +bilateral far lateral transcondylar approach	None	None	21 months	Conventional	None
Endoscopic endonasal transsphenoidal	3 rd month	Proton beam RT	11 months	Dedifferentiated	None
Endoscopic endonasal transsphenoidal	None	None	5 months	Conventional	None
Endoscopic endonasal transsphenoidal	None	None	4 months	Conventional	None
Endoscopic endonasal transsphenoidal	None	None	3 months	Conventional	None

postoperative Day 4, and lumbar puncture was performed. Tissue culture study was performed on the CSF material, and growth was found. Intravenous antibiotherapy was regulated as 120 mg/kg/day meropenem, 600 mg linezolid q12h, and 200 mg fluconazole q24h as recommended by Infectious Diseases and Clinical Microbiology. Clinical improvement was observed on the postoperative Day 8 during follow-ups. A regression in hydrocephalous was detected on control cranial MRI, performed on the postoperative Day 9. Embolism of the retinal artery was determined on the postoperative Day 10 in 1 patient who developed vision loss, and anticoagulant therapy was initiated. Upon the development of headache on the follow-ups of the same patient, ventriculoperitoneal shunt was inserted following the detection of hydrocephalous on control cranial MRI performed on the postoperative Day 20. Clinical improvement was observed during the follow-ups of 2 patients with n. abducens paralysis and 1 patient with n. oculomotorius paralysis, whilst no clinical improvement was seen in 1 patient with n. abducens paralysis. The mean follow-up duration was 15 months (ranged between 3 and 39 months). Two patients were referred for RT in the postoperative period due to the residual tumor, and 1 patient was referred for proton-beam RT. Reoperation was performed in 1 patient receiving RT and 1 patient receiving proton-beam RT due to detection of recurrence in their follow-ups. When examined histopathologically, 3 of patients were diagnosed with chondroid chordoma, 1 of patients with dedifferentiated chordoma, and the rest of patients with conventional chordoma (Table 2).

DISCUSSION

Clival chordomas are midline tumors in the anterior skull base. They are diagnosed pathologically. Even though a fine-needle aspiration biopsy or tru-cut biopsy is a recommended method for preoperative pathologic sampling in the chordomas of the sacral and axial region, it is hard to make a pathological sampling of the skull base chordomas (14, 15). Therefore, the diagnosis is usually made using CT and MRI during the preoperative period (3). On CT, chordomas are pursued as a soft tissue mass infiltrating the clivus and causing destruction of the bone tissue. On MRI, they are detected as homogenous, hypointense lesions originating from the clivus and causing expansile bone destruction (3, 15). The literature review revealed that chordomas are frequently diagnosed radiologi-

cally (8, 15-18). In our study, 1 patient was diagnosed with chordoma as the pathologic diagnosis in the preoperative period. Nine patients had a pre-diagnosis of chordoma following radiologic examination.

Chordomas and chondrosarcomas are similar because of their clinical symptoms, location, and features in the radiological imaging. However, differential diagnosis should be formulated pathologically since their clinical behaviors and responses to treatment are substantially different, and the treatment should be planned according to pathology results (19, 20).

There have been several opinions expressed about the treatment management of the clival chordomas. There is a consensus that the ideal treatment management should provide maximal and safe resection (3, 16, 20). Due to high complication rates, radical surgery is not preferred by many surgeons in the surgical treatment of clival chordomas in which en bloc resection is impossible (3, 8, 16). Under the circumstances, maximal safe resection is performed as the first treatment step in most medical centers (15). Some studies have indicated that the complication rate is less frequently observed in non-radical surgery, but the recurrence rate is more frequent due to the residual tumor (3). Some studies have stated that the gross total resection is not possible in most cases because of its location, proximity to the important neurovascular structures, local aggressive behavior, and even though subtotal resection is applied, the residual tumor in small sizes can be controlled by a high-dose RT in the postoperative period (8, 15).

There are difficulties in surgical resection because of the chordomas location, local aggressive behavior, and proximity to carotid artery and cranial nerve pairs (12). There are various surgical approaches and techniques in the surgical treatment of the clival chordomas (8, 12, 15). The surgical approach to be selected is determined by considering the localization of the tumor, extension, growth pattern, and adjacency to surrounding vital tissues and dura (3). The extradural and midline origin of clival chordomas highlight the midline approach among surgical techniques (8). The development of endoscopic techniques has made endonasal transsphenoidal approach the golden standard in the surgical treatment of the clival chordoma (5, 6, 8, 11, 22). In anterior approaches, the access to lateral surgical structures such as n. abducens and petrous apexes is limited (3, 16). However, with the aid of angled endoscopes, the access to anatomi-

cal regions constituting the lateral boundaries is easier, and an increase in controlling of the operation cavity and a reduction in residual tumor and complication rate are observed.

In the study conducted by Jägersberg et al. (1), it was stated that gross total resection (8%) was performed in 2 of 13 patients, and incomplete resection and debulking surgery (92%) in 11 patients. In the study of Förander et al. (8), it was indicated that the gross total resection (13%) was performed in 3 of 22 patients, subtotal resection (55%) in 12 patients, partial resection (28%) in 6 patients, and biopsy (4%) in 1 patient. In the study by Taniguchi et al. (5), it was pointed out that all 4 patients underwent gross total resection (100%). In the study carried out by Fatemi et al. (22), it was stated that gross total resection (43%) was performed in 6 of 14 patients, near-total resection (43%) in 6 patients, and subtotal resection (14%) in 2 patients. In our study, gross total resection was applied in 9 patients with the endoscopic endonasal transsphenoidal approach, and 1 patient with endoscopic endonasal transsphenoidal and far lateral transcondylar approach. When compared to literature findings, our gross total resection rate was similar to data in the study conducted by Taniguchi et al. (5), and it was observed to be high compared to gross total resection rates in other series.

In some studies, a combined or staged surgery implementation is recommended to provide gross total or subtotal resection. In a study conducted by Förander et al. (8), 8 of 22 patients underwent staged surgery. In our study, gross total resection was applied to 9 patients with the endoscopic endonasal transsphenoidal approach. Following performing the endoscopic endonasal transsphenoidal approach in 1 patient, gross total resection was completed with far lateral transcondylar approach due to detection of residual tumor tissue in the postoperative cranial MRI.

When comparing surgical methods, endoscopic endonasal transsphenoidal surgical approach is less invasive compared to other methods, and less complication is observed (3, 8, 23). The complication seen in intra- and postoperative period include carotid artery injury, CSF leak, n. abducens and oculomotorius paralysis, cavernous sinus hemorrhage, and hydrocephalus (16). Studies have shown that the complication rate has increased in recurrent operations due to residue or recurrence (8, 12, 16). In the literature review, it was reported that new neurological deficit developed in 0% to 80% cases after surgery, vascular injuries in 9% to 12%, and CSF fistula in 8.3% to 30% (4, 10, 11, 20, 24, 25). In the study by Walcott et al. (15), newly developed cranial nerve paralysis (63%) was observed in 7 of 11 patients who underwent clival chordoma surgery, and cranial nerve paralysis was reported to be completely regressed in all patients at the end of the follow-up period. In the study by Fatemi et al. (22), it was stated that complete regression or recovery in cranial nerve paralysis was observed in 8 of 10 patients.

In our study, on the other hand, newly developed cranial nerve paralysis was not seen, but the most frequently observed symptom was the CSF leak. To prevent the CSF leak, the repair of skull base defect with a nasoseptal flap was performed on all patients following the resection. However, the CSF leak was persistent in 2 patients. After performing the repair of the skull base defect with fascia lata and inferior turbinate flap on this patient, complete regression was observed in the CSF leak.

In our study, 2 of 3 patients with n. abducens paralysis and 1 patient with n. oculomotorius paralysis had a complete resolution in the postoperative follow-ups, and no improvement was detected in 1 patient with n. abducens paralysis. The study of Pettersen et al. revealed that a regression in n.

abducens paralysis was observed in 3 (60%) of 5 patients after the operation (7). Frank et al. (26) stated in their study that a regression of 75% was observed in n. abducens paralysis after the endoscopic endonasal transsphenoidal approach. In the study by Maira et al. (27), this rate was reported to be 71%. These rates are similar to the ones in our study.

One of the most controversial issues in the treatment management is the timing of the adjuvant therapy. RT is effectively used as such in clival chordomas. The aim of the adjuvant therapy of the clival chordoma with RT is to have an impact upon the target lesion without harming the surrounding critical structures (15). With new developments in the radiation technology it is possible to provide to be given high-dose RT to the target tissue, while reducing the toxic effects caused by RT in the surrounding tissues. Nowadays, the proton-beam RT is frequently preferred because of its effect on the target tissue in the clival chordomas and less harmful impact on the surrounding tissues (1, 19).

Some researchers suggest an early RT planning for postoperative residual management since the radical surgery is not possible in most cases (8, 16). In cases where postoperative RT is not planned, it is reported that the recurrence rates in the first 3 years may vary between 12% and 60% (22).

As another opinion, it has been argued that patients showing no progression in clinical symptoms or MRI can be followed-up untreated. RT can be performed along with the surgery in the planning of residual management if progression is determined (18).

Recurrences are one of the difficulties encountered in the treatment management of the clival chordomas. Even though an aggressive surgery is performed in primary cases, the rates of recurrence and progression are observed to be high. Different treatment methods were defined in the recurrent cases. RT or RT following surgery can be performed in the recurrent cases (15, 28). Although it can change according to the location of the lesion, extension status, age, and performance status of the patient, re-RT planning for the same region that was previously exposed to RT may pose a problem in the planning of the effective dose. Sekhar et al. indicated that RT treatment should not be used in primary cases if possible, and RT should be retained for recurrent cases as an alternative therapy (18, 25, 29, 30). In our study, gross total resection was performed only in primary cases. Two of the patients who developed recurrence in their follow-ups received conventional RT, and one received the proton-beam RT. Re-resection was performed in 2 patients who received RT since the progression was detected during the treatment. This treatment management is similar to the one described by Sekhar et al. (30).

The mean postoperative follow-up duration was 15 months (between 3 and 39 months). No mortality was seen in the follow-ups. It has been specified in the literature that the mean survival time ranged between 3.6 and 6.6 years, and this time could be increased by appropriate surgical treatments and adjuvant therapies (31). The results of the study will be re-evaluated and re-analyzed when the patients reach 5- to 10-year follow-up time. Nowadays, the use of the endoscopic endonasal transsphenoidal method in the treatment of clival chordoma has opened new horizons; however, the best management is still controversial.

CONCLUSION

Chordomas, which are frequently located in the skull base, are locally aggressive tumors. The aim of the surgical treatment approach is to ensure safe resection. As the skull base defects can be repaired safely, surgery with the endoscopic endonasal approach has become the stan-

standard treatment method for clivus chordomas. It is possible to apply it safely even in the anatomical regions located in the lateral boundary, which are hard to access with the endonasal transsphenoidal surgical approach using angled endoscopes. The resection of the posterior septum allows four-hand surgery so that surgical maneuvers are easier to perform. Four-hand surgery enables the use of an endoscope, aspirator, and cautery at the same time, and it also ensures bleeding control. Experienced doctors from the Neurosurgery and Otorhinolaryngology departments working as a team improve the quality of surgery. Chordoma surgery is a maximally invasive surgical procedure with minimal intervention, and chordomas require a close follow-up due to their morbidity rate and complications.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Ege University (Karar No: 17-4.1/9).

Informed Consent: Written informed consent was obtained from the patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - H.Ö.; Design - H.B.; Supervision - S.G., H.B.K.; Data Collection and/or Processing - M.S.A.; Analysis and/or Interpretation - S.G., E.Ö., S.Ç.; Literature Search - D.D., S.E.; Writing Manuscript - D.D.; Critical Review - İ.K.

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