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ORIGINAL ARTICLE

Endoscopic Endonasal Surgery of Clival Chordomas: Preliminary Results

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Abstract Chordomas are rare malignant tumors, often affecting the clival region. Traditionally, they are removed via craniotomic approach but the introduction of the endoscopic endonasal technique (EEA) allowed to control this area. This article shows a series of patients affected by clival chordomas treated with endoscopic approach. Patients who underwent EEA or transoral approach (TO) for clival chordomas at our Skull Base Referral Center, have been retrospectively examined. Clinical symptoms, preoperative neuroradiological evaluation, surgical approach, complications and postoperative results were evaluated. Nine patients (4 females and 5 males; age range 45–82 years, mean 61 years) were included. Chordomas involved upper clivus in 4/9 cases, with (2) or without (2) extension to the middle clivus, middle clivus alone in 2/9, lower clivus in 2/9, and the whole clivus in 1/9. Tumors were totally (4/9) or subtotally (5/9) removed. Skull base reconstruction was performed with a multilayer technique (6/9) or a gasket-seal closure (1/9), using pedicled nasoseptal flaps, middle turbinate and mucoperichondrial grafts, fascia lata and synthetic fascia. No reconstruction was performed in 2 cases. Recurrence occurred in 4 cases, who underwent a new operation. All the other patients underwent proton-beam radiotherapy with no documented tumor growth at the last follow-up (median: 24.9 months; range: 7–36 months). EEA and TO resulted to be safe procedures for treatment of clival chordomas. These approaches may be used as an alternative to the traditional approaches, according to the extension of the pathology.

Keywords Chordomas · Clivus · Endoscopic approach · Pedicled flaps · Radiotherapy

Introduction

The neoplastic pathologies involving the clivus can range from immune to endocrine neoplasms [3], but the most frequently encountered lesions are chordomas and chondrosarcomas [2]. Chordomas are defined as rare (incidence: 0.08 per 100,000) slow growing tumors deriving from embryonic notochordal tissue, and often develop within bone. All ages may be affected, but mainly these lesions arise during the third to the fifth decade of life, with a slight male predominance [4]. They are tumors with low to intermediate malignancy, and are characterized by a propensity for local aggression. Metastases are rare and usually occur after recurrence. In particular, they are generally localized at sacrum, clivus, or cervical vertebrae, as these lesions often involve the spine within its distal and proximal ends. Caudal chordomas occur in 50% of cases, while cranial chordomas involving the clival region affect a third of cases, generally as extradural midline masses. Involvement of cranial nerves, especially the abducens nerve, can be seen at presentation [4]. Chordomas of the cervical spine represent from 3 to 7% of cases, and usually they arise as parapharyngeal or paravertebral masses [15, 17].

The clivus is known for its complex anatomy, representing a surgical challenge for its proximity to vital neurovascular structures [13]. Anatomically, this area can be divided into three regions: the upper clivus, the midclivus and the lower clivus. Each portion has been traditionally

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approached via different surgical routes, including the orbitozygomatic and the transpetrosal routes [18].

Recently, new approaches have been designed to reach the clivus through an endoscopic EEA [11], with improvements in the reduction of complications' rate thanks to the avoidance of brain retraction and the chance to use local reconstructive flaps [13].

The first experiences of EEA and TO for clival lesions have been presented in a previous article, showing surgical outcomes and post-operative complications of patients treated by the Skull Base Team at Verona University Hospital [7]. This paper focuses only on patients affected by clival chordomas, showing new cases and enlarging the previously presented follow-up.

Materials and Methods

Patients with diagnosis of clival chordoma, surgically treated with EEA and TO between September 2015 to February 2018 at our Referral Skull Base Center, were included in the study. A retrospective review of charts and videos was made. Patients affected by chordomas, treated with open approaches, alone or combined with endoscopic approaches, were excluded.

Radiological Assessment

Preoperative CT scan and MRI with contrast were performed to all patients, in order to make the diagnosis, to perform staging of the pathology and plan the surgical approach. Images obtained with the first radiological procedure allowed to guide the neuronavigation system during the surgical operation. Further CT scans were also performed after 6 h since the end of the intervention to check the surgical field.

Surgical Technique

The endoscopic approach was performed with a 0° endoscope. First, any flap or graft was collected. Then, removal of the posterior part of the nasal septum and opening of the sphenoid sinus were achieved. Drilling of the clivus allowed to isolate and remove the tumor. Reconstruction was performed with the previously collected flaps or grafts, and with reinforcement with absorbable material or a Foley catheter.

The 0° endoscope was used also to perform one TO through the oral cavity; the lower clivus was dissected to treat the lesion and, at last, an absorbable suture was used.

The 4-hands endoscopic EEA and the TO have already been described in a previous paper [5].

Surgical procedures were performed by the senior surgeons (D.M. and A.M.). The patients layed in a supine position for 48 h after surgery. After that period, they gradually reached a standing position. Clinical controls were conducted postoperatively after 2, 6 and 12 months during the first postoperative year. If needed, any additional controls were made after a further 6 or 12 months.

Results

Resection of clival tumors was performed in a total of 9 patients. Histological report confirmed the diagnosis of "clival chordoma" for all cases. There were 4 males and 5 females. Patients' mean age at time of operation was 61 years, ranging from 45 to 82 years. A preoperative diagnosis of obesity was present in 1 patient, with a BMI index equal to 38. Hypertension was present in 4 cases. Four patients had been previously treated for a chondroid chordoma, a pituitary macroadenoma, a clival chordoma, with a craniotomic approach, and a clival chordoma resected with EEA at another institution. The last three patients underwent also adjuvant radiotherapy.

Overall, 4 patients had the lesion involving the upper clivus with (2) or without (2) extension to the middle clivus. Middle clivus alone was involved in 2 cases, while tumors located in the lower clivus were found in other 2 patients. At last, 1 patient had a condroid chordoma relapse extending from the upper to the lower clivus.

EEA was performed in 8 patients. A total resection was achieved in 3 cases. In other 5 cases, complete tumor removal could not be obtained since the lesion was strictly adherent to the internal carotid artery and the optic nerve.

One 73-year-old female patient had previously been operated on for a clival chordoma at another institution, with EEA. She underwent adjuvant Proton-beam radiotherapy, but due to a relapse of the lower clivus, documented by MRI, she was then re-operated on at our institution via TO. During intervention, a cystic lesion of the posterior pharyngeal wall was noticed and totally removed.

Concerning complications, one case of intraoperative bleeding from the clival plexus occurred and was successfully controlled with bipolar forceps and hemostatic gel. After the operation the patient was admitted to the ICU for 2 days. Then, she returned to the ENT department without any further complication.

Skull base reconstruction after disease removal was achieved with different techniques. In 3 patients the multilayer technique was accomplished by using a double pedicled nasoseptal flap [8], one of which was reinforced with fascia lata. The multilayer technique was performed also in other 3 patients with mucoperichondrium and

synthetic fascia (1), with mucoperichondrium and fascia lata (1), and with a single Hadad-Bassagasteguy's flap reinforced with a middle turbinate graft (1). The gasket-seal technique [10] was accomplished in 1 patient by harvesting and using a double nasoseptal flap and fascia lata. In 1 case a small defect of the ethmoid roof was repaired with mucoperichondrial graft and fibrin glue. No reconstruction was needed after TO; in this case, absorbable suture was enough to close the defect.

After surgery, a brain CT scan was performed after 6 h and 5 days in order to check the surgical field. No major complications were noticed and patients were discharged at a median of 11 days (range: 4–23 days).

One patient was re-operated on after 18 months: a sub-total removal of the middle cranial fossa lesion was achieved with the same approach as the first operation; residuals infiltrating the right abducens nerve and the carotid artery were left in place; skull base was reconstructed with the previously used double Hadad-Bassagasteguy's flap, fascia lata and left middle turbinate flap, without postoperative complications. Proton beam radiotherapy was administered after discharge and, to date, follow-up MRI and CT scans reveal no residual growth.

Despite post-operative proton therapy, 1 patient needed re-intervention after 21 months, due to a residual regrowth, that had been left in place due to deep infiltration of the cavernous sinuses. With the new operation, the residual was completely removed using the same approach. Fascia lata and autologous fat graft were used to reconstruct skull base. During follow-up, the patient complained vision worsening on the left eye, and the last MRI showed a fragment of tumor invading the left optic nerve canal and the dura of the frontal lobe, so she underwent fronto-pterional craniotomy to accomplish optic nerve decompression and sub-total resection of the tumor (Figs. 1, 2).

After 11 months, despite the previous total removal procedure of chordoma extending to the left infratemporal fossa, 1 patient was re-admitted to our unit due to a bulky relapse of the tumor involving the nasal cavity, the right petrous apex and the basilar artery region, as documented by the follow-up imaging. With the same EEA, the lesion was sub-totally removed, leaving residuals in the basilar artery region. The nasal cavity was then filled with absorbable material. After 7 months, a further admission to our department was needed due to a posterior nasal massive bleeding, that was controlled with posterior packing. An urgent Angio-MRI showed right internal carotid artery dissection with a small pseudoaneurysm, so embolization was performed. Four months later, the patient experienced a new massive nose bleeding deriving from the contralateral internal carotid artery, thus he needed EEA for nasal packing. To date, the patient is still alive, even if blood loss determined neurological deficits.

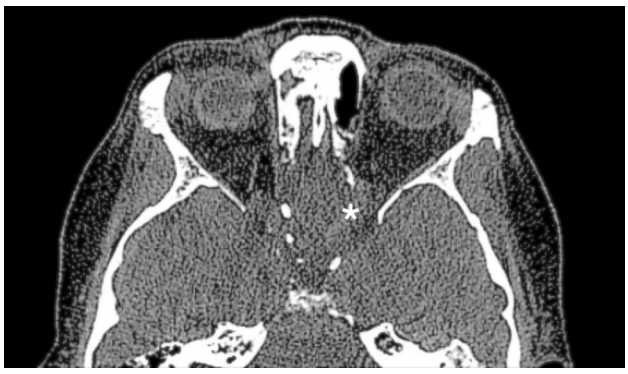

Fig. 1 Follow-up CT scan of Patient no. 8. Tumor relapse (white star) was noted in the ethmoidal roof and extending into the left optic nerve canal, and involving the frontal dura

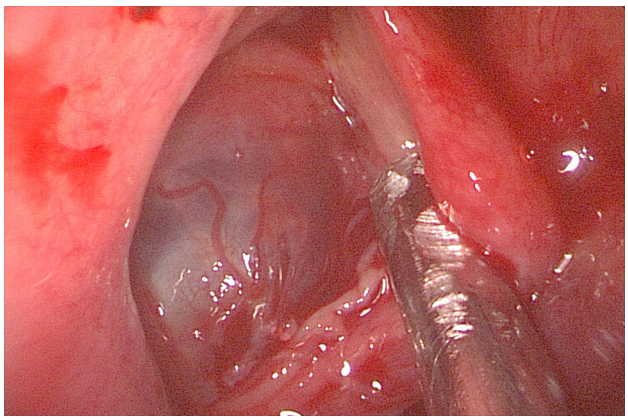

Fig. 2 Intra-operative endoscopic trans-nasal finding during last revision. The tumor was located in the ethmoidal roof and invaded the left optic nerve canal. Due to extension of the lesion, a craniotomic approach was chosen

Histological examination confirmed the diagnosis of "clival chordoma" relapse in the three above-mentioned patients.

Re-operation was performed even in another patient, despite total removal procedures, due to a suspect relapse documented with imaging. She was re-operated on with EEA for removal of a middle clivus lesion and reconstruction was accomplished with Lyodura®, autologous fat graft and fibrin glue. Histological examination was negative for malignant lesions.

One 55-year-old woman was seen at our outclinic 1 month after the operation. She had been subtotally treated with EEA for a lesion extending to the middle cranial fossa. The post-operative imaging showed a massive residual regrowth, extending to the posterior cranial fossa, the sphenoid sinus and the left orbit.

All of the other patients underwent proton beam therapy, due to fragments of the tumor infiltrating the carotid

arteries and/or the optic nerves. No documented growth of the residuals was noticed at the follow-up MRI scans.

The median follow-up since the first operation was 24.9 months (ranging from 7 to 36 months).

Patient characteristics and surgical results are summarized in Table 1.

Discussion

Clival chordomas are known to be the lesions most frequently arising from this anatomical region, deriving from notochord residues [14]. They grow slowly, but can lead to complications causing erosion and compression of close nerves and vessels [10], as well as intradural extension [9]. Curative excision is very rarely achieved, since the association of the complex anatomy of the clivus and the spreading pattern of the tumor make aggressive treatment a potential cause of relevant comorbidities [16]. Also, a high percentage of recurrent disease is observed even in case gross total resection is achieved [7]. For these reasons, adjuvant radiation therapy is indicated for the treatment of clival chordomas [6].

Regarding surgery, various surgical approaches have been developed over the years, all based on the concept that the path chosen to reach the tumor should be oriented by its lateral extension and relationship with the clivus. Based on the anatomical subdivision of this region, the orbitozygomatic approach has been utilized to reach its upper portion, while the midclivus and the lower clivus have been reached respectively through transpetrosal and lateral routes [18].

The treatment of clival chordomas has been changed over the last decades by the introduction of transnasal endoscopy and its variants, allowing to achieve maximum exposure of the tumor to grant the highest degree of removal as possible, while minimizing comorbidities, all thanks to the angled and magnified view given by the endoscopes as opposed to the traditional microscopic straight view. There are obviously also disadvantages to the endoscopic technique, including the need for dedicated instruments, a narrower field of operation, and the use of a single hand (easily overcome by the "4 hands" technique). It should also be noted that the learning curve is a relevant factor in the planning of this surgery [10].

In our case series, 8 patients underwent EEA due to chordomas involving the upper or middle clivus, and 1 patient underwent TO for removal of a lower clivus lesion. In some of them, as reported, a sub-total excision could be accomplished, since the tumor was strictly adherent to the carotid artery or the optic nerve. Thus, a further operation was needed due to a residual regrowth. Four patients underwent adjuvant proton beam therapy, testifying that, to date, 44.4% of surgical treatment combined with adjuvant therapy is effective.

As reported in Table 1, reconstruction techniques were various in our series. The main technique used was the multilayer reconstruction with pedicled naso-septal flaps, whereas, depending on the extension of the tumor and consequently on the dural defect, also mucoperichondrium, lyodura and fascia lata have been used. These reconstruction materials and techniques resulted to heal correctly the dural defect, and no cases of CSF leakage were encountered during follow-up. In particular, even the patient suffering from obesity (considered as a possible risk factor [1]), did not experience CSF leak, reason being that the dural defect was small and it was covered with a mucoperichondrial graft. Even if our case series is relatively small, our results confirm the importance of the appropriate reconstruction method and, in particular, the use of pedicled flaps for skull base repair [12].

In our record, EEA and TO has been confirmed as a viable option for the treatment of clival lesions in general, and clival chordomas in particular. Consistently with the results reported in literature, low postoperative comorbidities and recurrence rates were observed. It can thus be said that endoscopy has claimed its role in the treatment of clival lesions, not as a replacement for traditional approaches, but as a safer and equally effective surgical technique. Nonetheless, it shall not be forgotten that patient selection is a crucial part of the planning of endoscopic surgery: in our opinion, clival lesions of the midline with lateral extent within the limits accessible to the endoscopic approach should electively be treated with such approach, as it shows lower rates for mortality and morbidity when compared to traditional microscopic approaches. Indeed, none of our patients experienced major complications during the post-operative period, neither at the last follow-up.

Regrowth was observed in 4 patients, but it must be said that with a second operation, the pathology was controlled in 3/4 (75%). Since chordomas have a high probability for regrowth and recurrence [7], our rate (44.4%) is in accordance with results of the literature.

Conclusions

Depending on the extension of the pathology and the eventual involvement of other structures, clival chordomas may be approached with the endoscopic treatment. This technique represented a valid alternative to the traditional open approaches. Further studies and cases should be achieved in order to confirm the feasibility of EEA and TO.

Table 1 Patients' characteristics and surgical details

Patient no.	Gender	Age at first operation (years)	Co-morbidities	Previous surgery	Tumor location	Approach	Resection	Technique	Type of flap	Post-operative treatment	Follow-up (months)
1	M	73	Hypertension	No	Lower clivus	EEA	Subtotal	Multilayer	Double H-B	PB	32
2	F	55	No	No	Upper clivus	EEA	Subtotal	Multilayer	Double H-B + Fascia lata	None	33
3	M	49	No	Yes	Upper-middle clivus	EEA	Subtotal	Multilayer	Single H-B + Middle turbinate	PB	15
4	F	45	No	No	Middle clvus	EEA	Total	Multilayer	Double H-B	PB + surgery[a]	36
5	M	55	No	Yes	Upper-middle-lower clivus	EEA	Subtotal	Gasket-seal	Double H-B + Fascia lata	Sub-total removal of chordoma relapse after 18 months + PB	32
6	F	73	Hypertension	Yes	Lower clivus	TO	Total	None	None	PB	7
7	M	71	Hypertension, obesity	Yes	Middle clivus	EEA	Total	None	Mucoperichondrium	PB + surgery[b]	22
8	F	49	No	No	Upper-middle clivus	EEA	Subtotal	Multilayer	Mucoperichondrium + Fascia lata	PB + surgery[c]	32
9	F	82	Hypertension	No	Upper clivus	EEA	Debulking	Multilayer	Mucoperichondrium + Cook fascia	PB	15

M male, *F* female, *EEA* endoscopic endonasal approach, *TO* transoral approach, *H-B* pedicled nasoseptal flap, *PB* proton beam radiotherapy

[a]A second operation was performed due to a suspect relapse. Histological examination resulted to be negative for malignancies

[b]A second operation was needed due to a chordoma relapse after 11 months since the previous intervention. After further 7 months the patient was re-admitted to our institution due to posterior nasal bleeding, treated with packing and embolization. After further 4 months a new massive bleeding due to a rupture of the contralateral internal carotid artery occurred, determining neurological deficits

[c]The patient underwent total removal of chordoma regrowth after 21 months. Due to a relapse, she underwent fronto-pterional approach for optic nerve decompression and sub-total removal of the tumor

Compliance with Ethical Standards

Conflict of interest All authors declare that they have no conflict of interest.

Human and Animal Rights This research involved human participants, who all signed an informed consent before any further treatment.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee.

Informed Consent Informed consent was obtained from all individual participants included in the study.

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