Endoscopic transsphenoidal approach in resection of intracranial clivus chondrosarcoma: A case report

HAO TIAN JIANG[1,2], PAN WANG[1,2], JUN WEI WANG[1], JIE LIU[1,2], CHAO TANG[1,2], GANG ZHANG[1,2], JIN YU PAN[1], HAO FEI GENG[3] and NAN WU[1]

[1]Department of Neurosurgery, Chongqing General Hospital, Chongqing 401147; [2]Graduate Institute, Chongqing Medical University, Chongqing 400016; [3]Department of Radiology, Southwest Hospital, Third Military Medical University (Army Medical University), Chongqing 401147, P.R. China

Received March 15, 2023; Accepted September 7, 2023

DOI: 10.3892/ol.2023.14085

Abstract. Intracranial primary chondrosarcomas are rare, accounting for <0.15% of all intracranial tumors, but exhibit a high risk of recurrence. Due to the rarity of this condition, it has proven difficult to establish efficacy-based treatment guidelines. The present study details a case of clivus chondrosarcoma exhibiting no recurrence following surgical resection using an endoscopic transsphenoidal approach and postoperative adjuvant radiotherapy. A 41-year-old female presented with primary symptoms of left eye esotropia, scotoma of the left nasal visual field and double vision. Preoperative cranial magnetic resonance imaging revealed a lesion on the clivus, which was initially diagnosed as chordoma. However, clivus chondrosarcoma was ultimately diagnosed based on intraoperative findings and postoperative histopathology. The tumor was totally resected and 25 doses of adjuvant radiotherapy with planning gross tumor volume (60 Gy) and planning clinical target volume (50 Gy) were administered for 5 weeks. The patient was discharged at 12 days post-surgery with no obvious postoperative complications. Over the 28-month follow-up period, there was no evidence of recurrence, which may be due to the successful use of combined gross total resection and adjuvant radiotherapy. Therefore, surgical resection using an endoscopic transsphenoidal approach and postoperative adjuvant radiotherapy is an effective method for treating intracranial clivus chondrosarcoma.

Introduction

Intracranial primary chondrosarcomas are considered to arise from residual embryonic cartilage tissue or chondrocytes following endochondral ossification (1). While these tumors are rare, accounting for ~1% of all chondrosarcomas and <0.15% of all intracranial tumors (2,3), the recurrence risk is high; the 5-year recurrence rate for patients with chondrosarcoma treated with surgery alone is 44%, so a timely diagnosis is essential to effectively treat these patients. However, an accurate diagnosis is challenging, as this condition may manifest with diverse and non-specific symptoms. Patients frequently present with chronic headache and various symptoms caused by tumor compression of brain tissues, blood vessels and nerves, but these symptoms also occur in patients with chordoma and other brain tumors (4-6). Furthermore, characteristics on computed tomography (CT) and magnetic resonance imaging (MRI) scans typically resemble those of meningioma and chordoma, further hampering an accurate preoperative diagnosis (7-11).

The gold standard for identification of intracranial primary chondrosarcoma is pathological examination and immunohistochemistry (11). The World Health Organization (WHO) divides chondrosarcoma into three histological grades. Grade I tumors, also known as atypical cartilaginous tumors, are well differentiated and appear similar to normal cartilage or benign chondroma, with mild cellular atypia, small nuclei and rare mitoses. Grade II primary chondrosarcomas are moderately differentiated and malignant, with greater cellular atypia, larger nuclei, higher cell density and more frequent mitoses. Finally, grade III tumors are poorly differentiated, with obvious cellular atypia, frequent mitoses and lobules with cells that become less differentiated and spindled at the periphery (4). In addition, a fourth type, grade IV or dedifferentiated chondrosarcoma, can be defined histologically by the presence of a high-grade, often spindled or pleomorphic tumor without significant cartilaginous matrix (12). However, there are also immunohistochemical similarities among chondrosarcoma, meningioma, chordoma and chondromyxoid fibroma that may complicate the postoperative diagnosis (13). Intracranial chondrosarcomas often occur in the skull base, accounting for 6% of all skull base neoplasms (2,14), which increases the difficulty of surgical management, particularly complete resection, due to a close proximity with cranial nerves and vessels.

In the present study, the case of a 41-year-old female with WHO grade II chondrosarcoma of the clivus who was treated

Correspondence to: Professor Nan Wu, Department of Neurosurgery, Chongqing General Hospital, 118 Xingguang Boulevard, Liangjiang New Area, Chongqing 401147, P.R. China
E-mail: wunan881@tmmu.edu.cn

Key words: endoscopy, chondrosarcoma, intracranial tumor, transsphenoidal approach, adjuvant radiotherapy

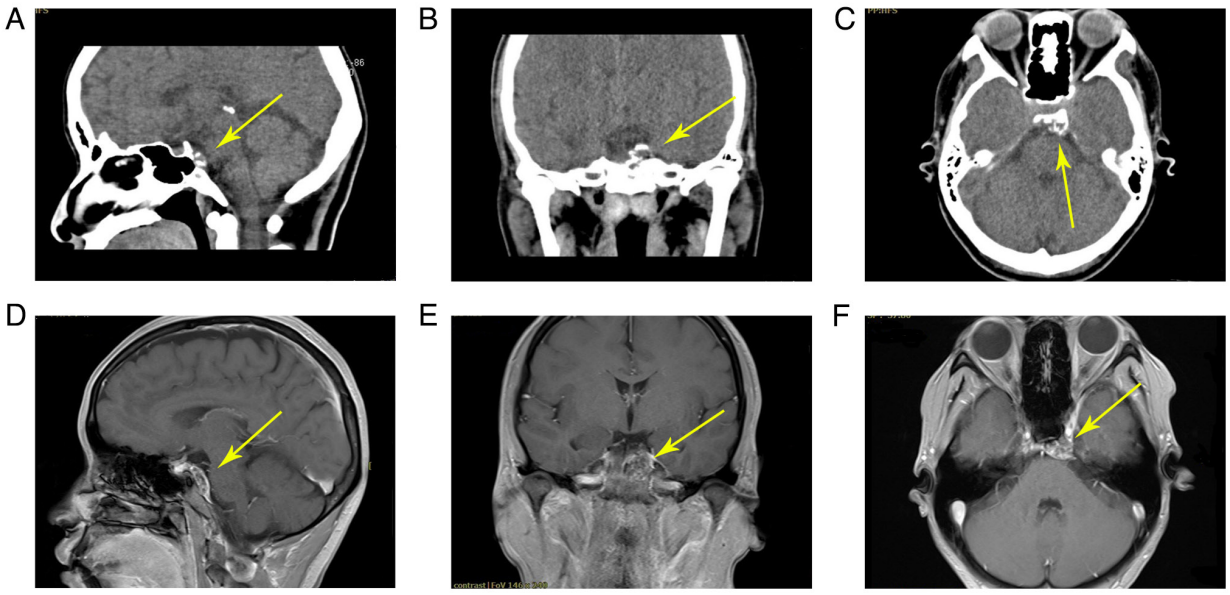

Figure 1. Preoperative CT and MRI images. (A) Sagittal image of the preoperative CT. (B) Coronal image of the postoperative CT. (C) Axial image of the preoperative CT. The preoperative CT showed calcification with a clear margin and enhancement on the clivus. (D) Sagittal image of the preoperative MRI. (E) Coronal image of the postoperative MRI. (F) Axial image of the preoperative MRI. The MRI revealed a mass on the left side of the midline. Yellow arrows indicate the location of the lesion. CT, computed tomography; MRI, magnetic resonance imaging.

surgically through an endoscopic transsphenoidal approach was reported. In order to prevent tumor recurrence, adjuvant radiotherapy [25 doses of 60 Gy planning gross tumor volume (PGTV) and 50 Gy planning clinical target volume (PCTV), over 5 weeks] was performed after the operation. Therefore, surgical resection using an endoscopic transsphenoidal approach and postoperative adjuvant radiotherapy is an effective method for treating intracranial clivus chondrosarcoma.

Case report

In November 2018, a 41-year-old female was admitted to Chongqing General Hospital (Chongqing, China) with esotropia of the left eye, visual impairment of the left nasal field and double vision for the previous 2 months. The patient received a comprehensive examination, including routine blood analyses and evaluations of liver, kidney, immune and blood coagulation functions, but all parameters were within the expected ranges. Neurological examination results were also as expected and there were no obvious signs of pathology. Furthermore, the patient had no history of trauma and no family history of hereditary illness. Visual acuity of the left eye was 0.8 and the extent of left eye esotropia was 10˚, while the visual acuity and visual field of the right eye were normal. Preoperative CT scan images (Fig. 1A-C) demonstrated evidence of a calcified lesion with clear margins and enhancement in the left clivus region. This mass appeared hypo- or isointense on T1-weighted images (T1WI) and heterogeneously hyperintense on T2WI, with heterogeneous enhancement (Fig. 1D-F). The mass demonstrated swelling growth but did not break through the dura and there were no necrotic areas.

Based on preoperative imaging, chordoma was suspected, and the patient underwent tumor resection using the endoscopic transsphenoidal approach. After removing the mucosa at the slope, the lesion was exposed (Fig. 2A) and resembled a chordoma. However, further exposure by removal of the surrounding normal bone revealed a complete capsule, which ruled out a chordoma. Puncture with a fine needle did not induce the outflow of cystic fluid or cerebrospinal fluid. After cutting the capsule, a white, jelly-like, shiny and clear lesion free of bone was observed (Fig. 2B and C). The dura was observed intact over the clivus after gross total resection (Fig. 2D). Surgically resected tumor tissues were analyzed by routine pathological examination using H&E staining. Tumor specimens were first fixed with 4% formaldehyde solution at room temperature for 24 h and then embedded and fixed in paraffin. The specimens were then cut into 4-μm sections and deparaffinized in xylene at 60˚C for 2 h. Subsequently, at room temperature, the sections were stained with 0.5% hematoxylin for 3 min, followed by 0.5% eosin for 3 min. Subsequently, the stained sections were observed under a light microscope to obtain microphotographs of the histopathology. Postoperative histopathological analysis demonstrated that the mass was composed of undifferentiated round or spindle-shaped cells and mature cartilaginous tissue with detectable mitoses, which ruled out dedifferentiated chondrosarcoma (Fig. 3). Immunohistochemical analysis was performed using the DAB substrate kit (cat. no. 8059; Cell Signaling Technology, Inc.) according to the manufacturer's instructions. Immunohistochemical analysis results of the excised tumor were as follows: Vimentin(+), S100(+), stabilin 2(+), integrase interactor 1(+), smooth muscle actin(focal +), desmin(-), calponin(-), cluster of differentiation 34(vascellum +) and brachyury(-). In total, 8% of cells were Ki-67 (MIB-1)-positive. Based on these histopathological and immunohistochemical features, the mass was identified as a grade II chondrosarcoma. Postoperative MRI confirmed that the entire tumor was removed and the patient was discharged at 12 days post-surgery with no obvious postoperative complications. After 1 month, the patient began adjuvant γ-knife treatment with 25 doses

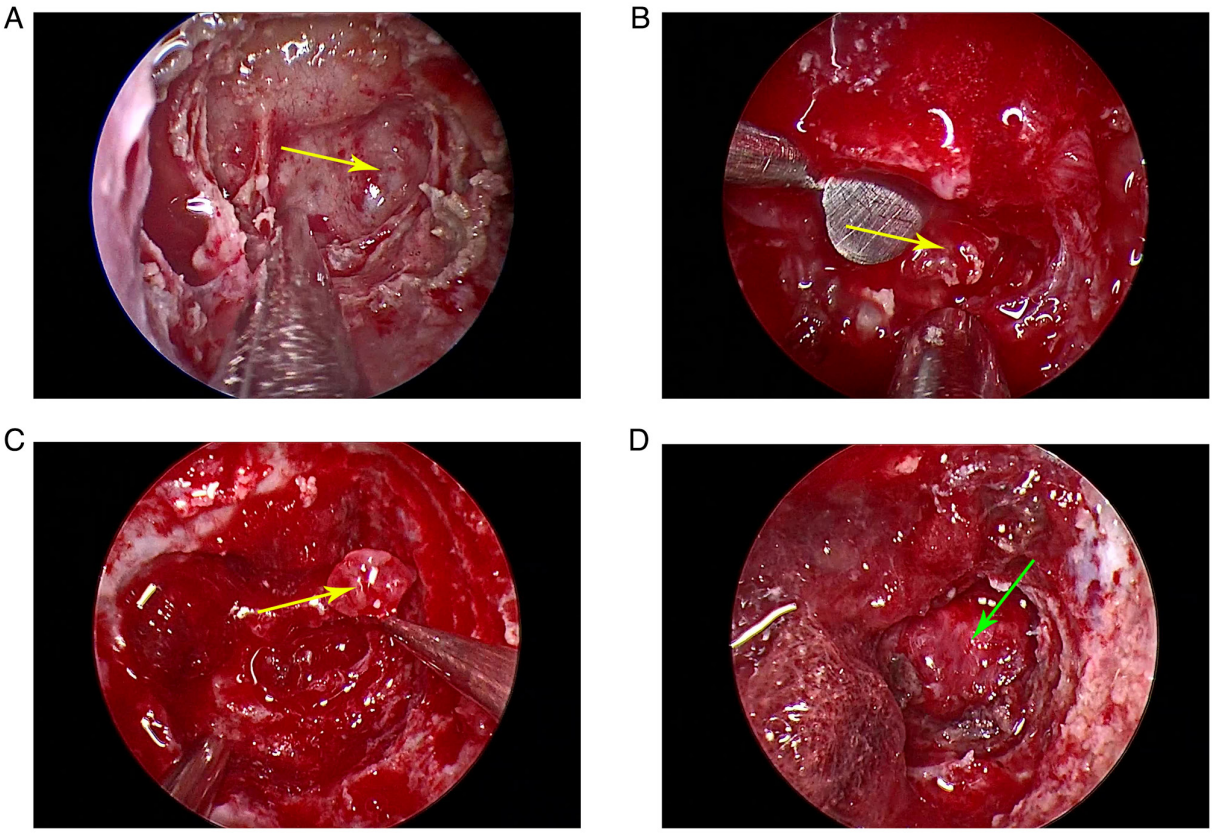

Figure 2. Endoscopic surgical images. (A) After removing the mucosa at the slope, the lesion was exposed. (B) Further exposure by removal of the surrounding normal bone revealed a complete capsule, and puncture with a fine needle did not induce the outflow of cystic fluid or cerebrospinal fluid. (C) Cutting the capsule, a white, jelly-like, shiny and clear lesion free of bone was observed. (D) The dura was observed to be intact over the clivus after gross total resection. Yellow arrows indicate the location of the lesion. The green arrow indicates the dura in the clivus.

of PGTV 60 Gy and PCTV 50 Gy over 5 weeks (Fig. 4). A 3-month postoperative MRI scan demonstrated no evidence of recurrence. There was no evidence of tumor recurrence during the 28-month patient follow-up.

Discussion

Intracranial chondrosarcoma is a rare type of malignant cartilage tumor first described by Mott in 1899 (15). The vast majority of these tumors originate from the skull base, including the petrous, clival, occipital, sphenoid and parietal bones (16-19), while a number of these tumors have also been reported in the brain parenchyma, peripatellar region and spine (20-22). The clinical manifestations of intracranial chondrosarcoma are non-specific, although most patients present with a long-term history of headache and other symptoms of increased intracranial pressure (such as headache, nausea and papilledema) resulting from tumor growth and compression or invasion of local intracranial structures (19,23,24). Neuroimaging is thus essential for preoperative planning. In most cases, intracranial chondrosarcoma appears as high-density or iso-intense lesions on CT, with uneven enhancement, calcification and osteolytic destruction (14,25-28). Compared with CT, MRI can better reveal the focus boundary and tumor characteristics for diagnosis of chondrosarcoma. In general, these lesions appear as low-intensity signals on T1WI, but possibly as mixed high- and low-intensity signals on T2WI with honeycomb enhancement, resembling the typical heterogeneous enhancement of malignant tumors (14,25,26,28-31). However, chordoma and chondrosarcoma exhibit similar imaging characteristics, so a differential diagnosis is difficult prior to surgery.

One possible distinguishing feature between chordomas and chondrosarcomas is the anatomical location of the tumor, as most chordomas occur in the midline of the brain, while chondrosarcomas are usually found on one side (4). In addition, calcification is common in chondrosarcoma (32,33), but not in chordoma, which may aid the diagnosis before surgery. Immunohistochemistry results have shown that chondrosarcoma is cytokeratin (CK)(-), epithelial membrane antigen (EMA)(-) and S100 (+), while chordoma is CK(+), EMA(+) and S100(+) (14). Therefore, immunohistochemistry of excised tumor tissue provides essential information for diagnosis.

There are three histological types of chondrosarcoma: Classic, myxoid or mesenchymal type (23), each with distinct frequencies and prognoses. Chandler *et al* (34) reviewed a series of chondrosarcoma cases and reported that the classic type accounted for 62%, the mesenchymal type for 30% and the myxoid type for only 8%. Bloch *et al* (23) found that prognosis was strongly related to histological type, with the lowest mortality rate among patients with classic chondrosarcoma (5%), followed by myxoid chondrosarcoma (10%) and mesenchymal chondrosarcoma (25%). Moreover, mesenchymal type tumors also exhibited a much higher recurrence rate (63%) compared with the classic type (16%) (35). Therefore,

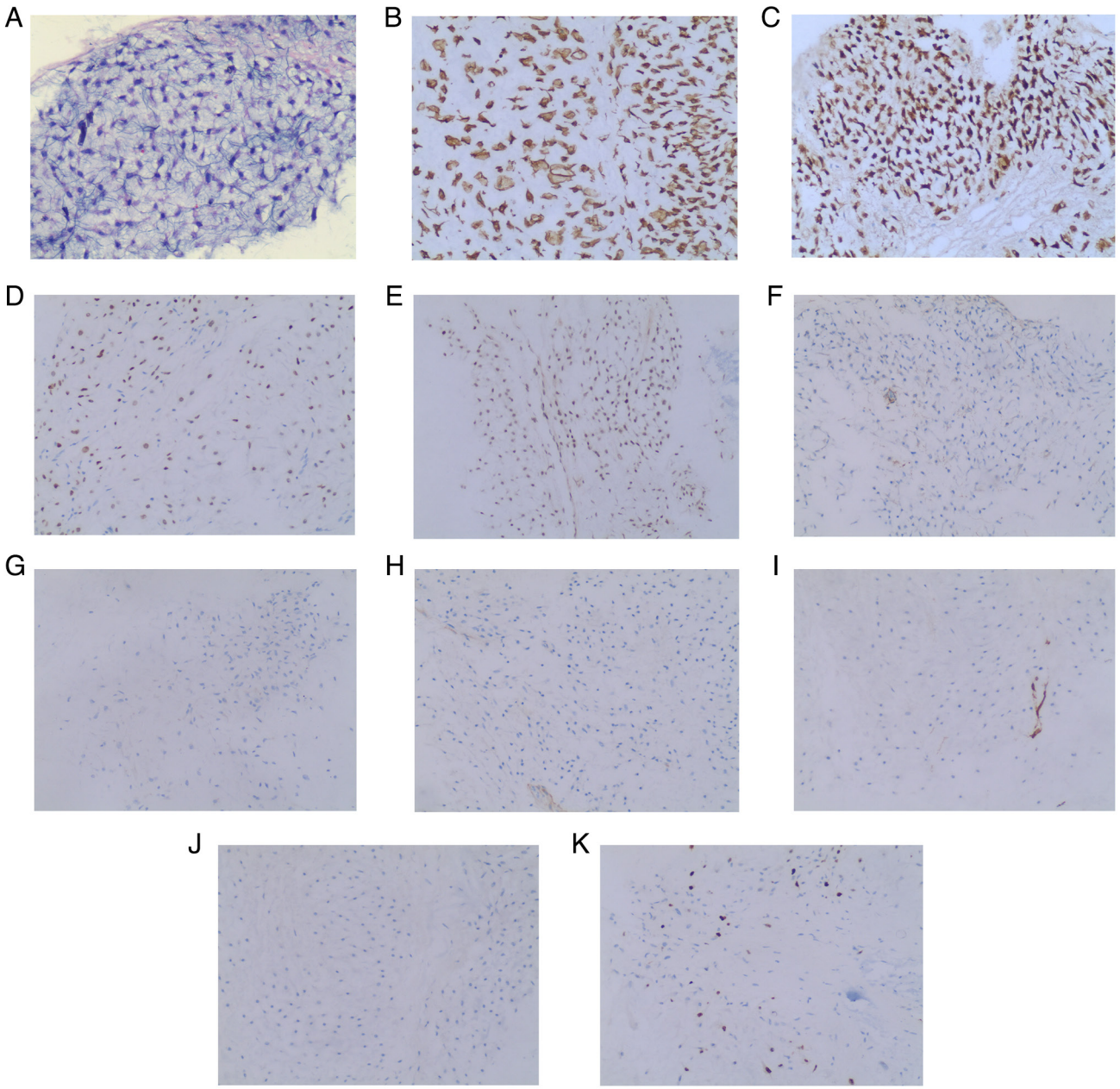

Figure 3. Histological and immunohistochemical staining results. (A) Histopathological analysis of hematoxylin and eosin-stained tissue demonstrated that the mass was composed of undifferentiated round or spindle-shaped cells and mature cartilaginous tissue. Immunohistochemical staining of the mass revealed the following results: (B) vimentin(+), (C) S100(+), (D) stabilin 2(+), (E) integrase interactor 1(+), (F) smooth muscle actin(focal +), (G) desmin(-), (H) calponin(-), (I) cluster of differentiation 34(vascellum +), (J) brachyury(-) and (K) Ki-67(MIB-1 +) (magnification, x20).

mesenchymal chondrosarcoma has a substantially poorer prognosis compared with classic and myxoid chondrosarcoma.

Surgical resection is the preferred first-line treatment for intracranial chondrosarcoma due to aggressive growth, clear boundaries and few metastases. Most resection surgeries are conducted using either a traditional transcranial approach or an endoscope-assisted transsphenoidal approach, as these lesions are most frequently located at the skull base (4). The most common transcranial approaches are frontotemporal, orbital, zygomatic and pterional (36). However, these skull base tumors are often close to cranial nerves and blood vessels, so certain transcranial resection surgeries carry a high risk of nervous system complications. As an alternative, endoscope technologies are growing in popularity for skull base surgery due to the wider field of vision, superior lighting and lack of visual obstruction (16,17,37-41). Hasegawa *et al* (42) reported that of 19 transnasal endoscopic surgeries performed for intracranial chondrosarcoma, 15 resulted in total resection, while only four resulted in subtotal resection due to tumor invasion of important nerves and vessels. Further, only 1 patient experienced tumor recurrence over 5 years of follow-up. These findings suggest that endoscopic skull base surgery can yield a resection rate similar to classical transcranial approaches but with fewer neurological complications. A systematic analysis of 33 studies, including 1,307 patients with intracranial chondrosarcoma, concluded that endoscopic transsphenoidal surgery can safely expose the focus and involved nerves and vessels, enhancing the probability of good surgical results (36).

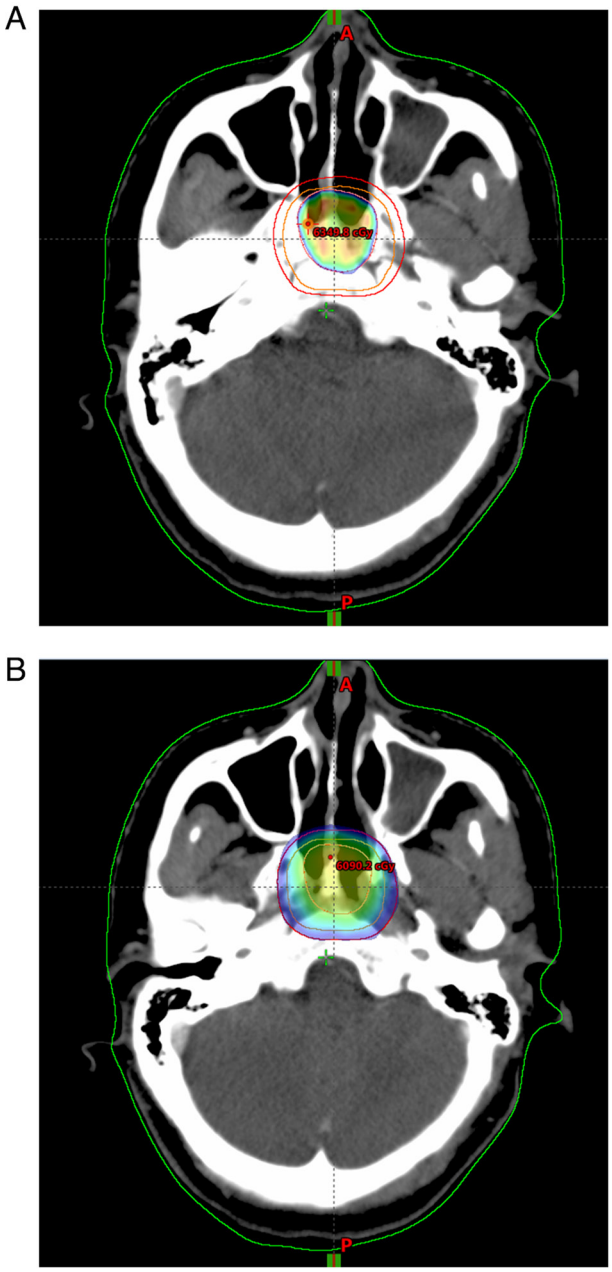

Figure 4. Dose distribution images of adjuvant radiotherapy. (A) Radiation therapy to a dose of 60.0 Gy (planning gross tumor volume). (B) Radiation therapy to a dose of 50.0 Gy (planning clinical target volume).

Therefore, endoscopic transsphenoidal surgery is a good choice for the treatment of intracranial chondrosarcoma. By contrast, for large tumors that cannot be removed in a single operation, staged surgery is recommended (43-45). However, if surgery alone is performed for chondrosarcoma, the prognosis is not ideal and the tumor may recur.

In such cases, adjuvant therapy may improve patient outcomes as chondrosarcoma is considered relatively radiosensitive (46-51). For instance, Bloch *et al* (23,35) reported significant reductions in the 5-year recurrence rate and mortality rate among patients with intracranial chondrosarcoma receiving surgery combined with postoperative adjuvant radiotherapy compared with surgery alone (9 vs. 44% and 4 vs. 26%, respectively). Similarly, Rosenberg *et al* (49) reported 5- and 10-year local control rates of 99 and 98% respectively and 5- and 10-year survival rates as high as 99% in a cohort of 200 patients with intracranial chondrosarcoma receiving combined surgery and radiotherapy. Therefore, adjuvant radiotherapy should be recommended after maximum-achievable tumor resection for patients with large and complex intracranial chondrosarcomas and for tumors in close proximity to vital neural and neurovascular structures. Chemotherapy is not recommended for patients with intracranial chondrosarcoma, as most chemotherapeutic drugs act selectively on rapidly dividing cells and the mitosis rate is low in most tumors of this type (14). Ultimately, continued developments in targeted therapies exploiting specific molecular expression profiles hold the greatest promise for numerous patients with intracranial chondrosarcoma.

In the present study, the case of a 41-year-old female with WHO grade II chondrosarcoma of the clivus who was treated surgically through an endoscopic transsphenoidal approach was reported. In order to prevent tumor recurrence, adjuvant radiotherapy (25 doses of 60 Gy PGTV and 50 Gy planning clinical target volume PCTV, over 5 weeks) was performed after the operation. The prognosis of patients with intracranial chondrosarcoma may be affected by the degree of tumor resection, histological type, choice of postoperative adjuvant radiotherapy and previous treatment, such as surgery or radiotherapy. Therefore, surgery should be the first choice for patients with intracranial chondrosarcoma and endoscopic transsphenoidal surgery is a good surgical option given that these lesions are usually in close proximity to critical nerves and blood vessels. In addition to maximal surgical resection, early adjuvant radiotherapy is recommended for preventing recurrence.

Acknowledgements

Not applicable.

Funding

No funding was received.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

NW, JWW, PW, HTJ, JL, CT, GZ, JYP and HFG participated in the conception, design and data acquisition of the article. HTJ drafted the manuscript. HTJ, JYP and HFG revised the manuscript. NW critically revised the article. NW ensured that questions related to the integrity of any part of the work were appropriately investigated and resolved. HTJ, JL, CT and GZ confirm the authenticity of all the raw data. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

The Ethics Committee of Chongqing General Hospital (Chonqing, China) waived the requirement for additional

ethical review, as this report is retrospective and not based on any specific patient priorities, experiences or preferences. Informed consent for participation in the study or use of the medical data was obtained from the patient.

Patient consent for publication

Written informed consent was obtained from the patient for the publication of anonymized data and any accompanying images.

Competing interests

The authors declare that they have no competing interests.

References

1. Oghalai JS, Buxbaum JL, Jackler RK and McDermott MW: Skull base chondrosarcoma originates from the petroclival junction. Otol Neurotol 26: 1052-1060, 2005.
2. Cianfriglia F, Pompili A and Occhipinti E: Intracranial malignant cartilaginous tumors. Report of two cases and review of literature. Acta Neurochir (Wien) 45: 163-175, 1978.
3. Richardson MS: Pathology of skull base tumors. Otolaryngol Clin North Am 34: 1025-1042, 2001.
4. Kremenevski N, Schlaffer SM, Coras R, Kinfe TM, Graillon T and Buchfelder M: Skull base chordomas and chondrosarcomas. Neuroendocrinology 110: 836-847, 2020.
5. Edem I, DeMonte F and Raza SM: Advances in the management of primary bone sarcomas of the skull base. J Neurooncol 150: 393-403, 2020.
6. Alamer OB, Haider AS, Haider M, Sagoo NS, Robertson FC, Arrey EN, Aoun SG, Yu K, Cohen-Gadol AA and El Ahmadieh TY: Primary and radiation induced skull base osteosarcoma: A systematic review of clinical features and treatment outcomes. J Neurooncol 153: 183-202, 2021.
7. Oot RF, Melville GE, New PF, Austin-Seymour M, Munzenrider J, Pile-Spellman J, Spagnoli M, Shoukimas GM, Momose KJ and Carroll R: The role of MR and CT in evaluating clival chordomas and chondrosarcomas. AJR Am J Roentgenol 151: 567-575, 1988.
8. Müller U, Kubik-Huch RA, Ares C, Hug EB, Löw R, Valavanis A and Ahlhelm FJ: Is there a role for conventional MRI and MR diffusion-weighted imaging for distinction of skull base chordoma and chondrosarcoma? Acta Radio 157: 225-232, 2016.
9. Welzel T, Meyerhof E, Uhl M, Huang K, von Deimling A, Herfarth K and Debus J: Diagnostic accuracy of DW MR imaging in the differentiation of chordomas and chondrosarcomas of the skull base: A 3.0-T MRI study of 105 cases. Eur J Radiol 105: 119-124, 2018.
10. Doucet V, Peretti-Viton P, Figarella-Branger D, Manera L and Salamon G: MRI of intracranial chordomas. Extent of tumour and contrast enhancement: Criteria for differential diagnosis. Neuroradiology 39: 571-576, 1997.
11. Fu LY, Han Q, Cheng P, Yang HJ and Zhao Y: Rare case report and literature review of intracranial mesenchymal chondrosarcoma. Ann Palliat Med 10: 12012-12017, 2021.
12. Limaiem F, Davis DD and Sticco KL: Chondrosarcoma. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing, 2023.
13. Paulus W, Slowik F and Jellinger K: Primary intracranial sarcomas: Histopathological features of 19 cases. Histopathology 18: 395-402, 1991.
14. Zhang Y, Huang J, Zhang C, Jiang C, Ding C, Lin Y, Wu X, Wang C, Kang D and Lin Z: An extended endoscopic endonasal approach for sellar area chondrosarcoma: A case report and literature review. World Neurosurg 127: 469-477, 2019.
15. Mott FW: Chondrosarcoma springing from the sella turcica. Arch Neurol Psychiat 1: 432-433, 1899.
16. Abhinav K, Acosta Y, Wang WH, Bonilla LR, Koutourousiou M, Wang E, Synderman C, Gardner P and Fernandez-Miranda JC: Endoscopic endonasal approach to the optic canal: Anatomic considerations and surgical relevance. Neurosurgery 11 (Suppl 3): S431-S445, 2015.
17. Arbolay OL, González JG, González RH and Gálvez YH: Extended endoscopic endonasal approach to the skull base. Minim Invasive Neurosurg 52: 114-118, 2009.
18. Oghalai JS, Buxbaum JL, Jackler RK and McDermott MW: Skull base chondrosarcoma originating from the petroclival junction. Otol Neurotol 26: 1052-1060, 2005.
19. Korten AG, ter Berg HJ, Spincemaille GH, van der Laan RT and Van de Wel AM: Intracranial chondrosarcoma: Review of the literature and report of 15 cases. J Neurol Neurosurg Psychiatry 65: 88-92, 1998.
20. Marshman LA, Gunasekera L, Rose PE and Olney JS: Primary intracerebral mesenchymal chondrosarcoma with rhabdomyosarcomatous differentiation: Case report and literature review. Br J Neurosurg 15: 419-424, 2001.
21. Li YH and Yao XH: Primary intradural mesenchymal chondrosarcoma of the spine in a child. Pediatr Radiol 37: 1155-1158, 2007.
22. Sindou M, Daher A, Vighetto A and Goutelle A: Parasellar chondrosarcoma: Report of a case operated on through a pteriono-temporal approach and review of the literature. Neurochirurgie 5: 186-190, 1989 (In French).
23. Bloch OG, Jian BJ, Yang I, Han SJ, Aranda D, Ahn BJ and Parsa AT: A systematic review of intracranial chondrosarcoma and survival. J Clin Neurosci 16: 1547-1551, 2009.
24. Güneş M, Günaldi O, Tuğcu B, Tanriverdi O, Güler AK and Cöllüoğlu B: Intracranial chondrosarcoma: A case report and review of the literature. Minim Invasive Neurosurg 52: 238-241, 2009.
25. Chen F, Chen B, Wang H, Xu W, Li W and Chen D: Intracranial nonskull-based chondrosarcoma arising from the sagittal sinus: A case report and review of the literature. World Neurosurg 120: 234-239, 2018.
26. Abele TA, Yetkin ZF, Raisanen JM, Mickey BE and Mendelsohn DB: Non-pituitary origin sellar tumours mimicking pituitary macroadenomas. Clin Radiol 67: 821-827, 2012.
27. Chu J, Ma H, Wang Y, Li K, Liao C and Ding Y: CT and MRI findings of intracranial extraskeletal mesenchymal chondrosarcoma-a case report and literature review. Transl Cancer Res 11: 3409-3415, 2022.
28. Cho BK, Chi JG, Wang KC, Chang KH and Choi KS: Intracranial mesenchymal chondrosarcoma: A case report and literature review. Childs Nerv Syst 9: 295-299, 1993.
29. Lee YY, Van Tassel P and Raymond AK: Intracranial dural chondrosarcoma. AJNR Am J Neuroradiol 9: 1189-1193, 1988.
30. Bingaman KD, Alleyne CH Jr and Olson JJ: Intracranial extraskeletal mesenchymal chondrosarcoma: Case report. Neurosurgery 46: 207-211, 2000.
31. Kothary N, Law M, Cha S and Zagzag D: Conventional and perfusion MR imaging of parafalcine chondrosarcoma. AJNR Am J Neuroradiol 24: 245-248, 2003.
32. Tauber M, van Loveren HR, Jallo G, Romano A and Keller JT: The enigmatic foramen lacerum. Neurosurgery 44: 386-391, 1999.
33. Rich TA, Schiller A, Suit HD and Mankin HJ: Clinical and pathologic review of 48 cases of chordoma. Cancer 56: 182-187, 1985.
34. Chandler JP, Yashar P, Laskin WB and Russell EJ: Intracranial chondrosarcoma: A case report and review of the literature. J Neurooncol 68: 33-39, 2004.
35. Bloch OG, Jian BJ, Yang I, Han SJ, Aranda D, Ahn BJ and Parsa AT: Cranial chondrosarcoma and recurrence. Skull Base 20: 149-156, 2010.
36. Palmisciano P, Haider AS, Sabahi M, Nwagwu CD, Bin Alamer O, Scalia G, Umana GE, Cohen-Gadol AA, El Ahmadieh TY, Yu K and Pathmanaban ON: Primary skull base chondrosarcomas: A systematic review. Cancers (Basel) 13: 5960, 2021.
37. Adappa ND, Learned KO, Palmer JN, Newman JG and Lee JY: Radiographic enhancement of the nasoseptal flap does not predict postoperative cerebrospinal fluid leaks in endoscopic skull base reconstruction. Laryngoscope 122: 1226-1234, 2012.
38. Cavallo LM, de Divitiis O, Aydin S, Messina A, Esposito F, Iaconetta G, Talat K, Cappabianca P and Tschabitscher M: Extended endoscopic endonasal transsphenoidal approach to the suprasellar area: Anatomic considerations-part 1. Neurosurgery 61: 24-33, 2007.
39. Kassam AB, Prevedello DM, Carrau RL, Snyderman CH, Gardner P, Osawa S, Seker A and Rhoton AL Jr: The front door to meckel's cave: An anteromedial corridor via expanded endoscopic endonasal approach- technical considerations and clinical series. Neurosurgery 64: on71-82, 2009.
40. Jho HD and Carrau RL: Endoscopy assisted transsphenoidal surgery for pituitary adenoma. Technical note. Acta Neurochir (Wien) 138: 1416-1425, 1996.

41. Osawa S, Rhoton AL Jr, Seker A, Shimizu S, Fujii K and Kassam AB: Microsurgical and endoscopic anatomy of the vidian canal. Neurosurgery 64 (5 Suppl 2): S385-S411, 2009.
42. Hasegawa H, Shin M, Kondo K, Hanakita S, Mukasa A, Kin T and Saito N: Role of endoscopic transnasal surgery for skull base chondrosarcoma: A retrospective analysis of 19 cases at a single institution. J Neurosurg 128: 1438-1447, 2018.
43. Tzortzidis F, Elahi F, Wright DC, Temkin N, Natarajan SK and Sekhar LN: Patient outcome at long-term follow-up after aggressive microsurgical resection of cranial base chondrosarcomas. Neurosurgery 58: 1090-1098, 2006.
44. Kano H, Sheehan J, Sneed PK, McBride HL, Young B, Duma C, Mathieu D, Seymour Z, McDermott MW, Kondziolka D, *et al*: Skull base chondrosarcoma radiosurgery: Report of the North American gamma knife consortium. J Neurosurg 123: 1268-1275, 2015.
45. Feuvret L, Bracci S, Calugaru V, Bolle S, Mammar H, De Marzi L, Bresson D, Habrand JL, Mazeron JJ, Dendale R and Noël G: Efficacy and safety of adjuvant proton therapy combined with surgery for chondrosarcoma of the skull base: A retrospective, population-based study. Int J Radiat Oncol Biol Phys 95: 312-321, 2016.
46. Suit HD, Goitein M, Munzenrider J, Verhey L, Urie M, Gragoudas E, Koehler A, Gottschalk B, Sisterson J and Tatsuzaki H: Increased efficacy of radiation therapy by use of proton beam. Strahlenther Onkol 166: 40-44, 1990.
47. Coltrera MD, Googe PB, Harrist TJ, Hyams VJ, Schiller AL and Goodman ML: Chondrosarcoma of the temporal bone. Diagnosis and treatment of 13 cases and review of the literature. Cancer 58: 2689-2696, 1986.
48. Castro JR, Linstadt DE, Bahary JP, Petti PL, Daftari I, Collier JM, Gutin PH, Gauger G and Phillips TL: Experience in charged particle irradiation of tumors of the skull base: 1977-1992. Int J Radiat Oncol Biol Phys 29: 647-655, 1994.
49. Rosenberg AE, Nielsen GP, Keel SB, Renard LG, Fitzek MM, Munzenrider JE and Liebsch NJ: Chondrosarcoma of the base of the skull: A clinicopathologic study of 200 cases with emphasis on its distinction from chordoma. Am J Surg Pathol 23: 1370-1378, 1999.
50. Austin-Seymour M, Munzenrider J, Goitein M, Verhey L, Urie M, Gentry R, Birnbaum S, Ruotolo D, McManus P and Skates S: Fractionated proton radiation therapy of chordoma and low-grade chondrosarcoma of the base of the skull. J Neurosurg 70: 13-17, 1989.
51. Suit HD, Goitein M, Munzenrider J, Verhey L, Davis KR, Koehler A, Linggood R and Ojemann RG: Definitive radiation therapy for chordoma and chondrosarcoma of base of skull and cervical spine. J Neurosurg 56: 377-385, 1982.