

Sellar chondrosarcoma presenting with amenorrhea

A case report

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Abstract

Rationale: Intracranial chondrosarcomas are rare entities and most of which arise off the midline. Chondrosarcomas that occur in the sellar region are extremely rare, and to the best of our knowledge, there is no reporting about sellar chondrosarcoma with amenorrhea as the onset symptom.

Patient concerns: A 45-year-old woman presented with a 7-month history of amenorrhea and a 3-month history of progressive visual loss in the left eye.

Diagnosis: The patient was diagnosed with recurrent sellar chondrosarcoma arising from intrasellar with extensive tumor invasion into bilateral sphenoid sinuses.

Interventions: Twice endonasal transsphenoidal tumorectomies were performed followed with a stereotactic radiotherapy and hormone replacement therapy.

Outcomes: The patient's condition was stable and her visual symptoms improved, the hormones returned to normal, and no recurrence was noted on MRI after six months.

Lessons: Sellar chondrosarcomas with the onset of endocrine dysfunctions are extremely rare, which may be misdiagnosed as pituitary adenoma and the definitive diagnosis depends on histopathological and immunohistochemical evidence. The first choice of treatment is surgery with the goal of complete resection, and postoperative adjuvant radiotherapy should be highlighted.

Abbreviations: CK-pan = creatine kinase pancytokeratin, EMA = epithelial membrane antigen, IDH = isocitric dehydrogenase, LH = luteinizing hormone, MRI = magnetic resonance imaging, PLR = prolactin, TSH = thyroid stimulating hormone.

Keywords: amenorrhea, chondrosarcoma, radiotherapy, sellar tumor, surgical resection

1. Introduction

Intracranial chondrosarcomas are rare neoplasms, accounting for approximately 0.15% of all primary intracranial tumors and 6% of all skull base tumors.^[1] These entities can occur at any age, with a peak incidence between 30 and 50 years of age, and there is no significant sexual predominance.^[2] Furthermore, >75% of intracranial chondrosarcomas are located in the skull base, of which only 14% involve the anterior fossa, and the most common location is the petroclival junction.^[3] The majority of these tumors arise from the dura off the midline, but those occurring in the sellar region are extremely rare. Since the first case of sellar chondrosarcoma was described by Allan et al in 2001,^[4] only 7 cases have been reported. Patients

with sellar chondrosarcoma usually present with headaches, diplopia, eye movement disorder and/or visual impairment. Owing to its rarity, the symptom spectrum, diagnosis, and treatment, as well as its prognosis, have yet to be well-understood.

In the present study, we report a case of sellar chondrosarcoma with the onset of amenorrhea. In addition, relevant literatures were reviewed.

2. Case report

This study was approved by the Ethics Committee and institutional Review Board of the First Hospital of Jilin University.

2.1. History and examinations

A 45-year-old woman presented with a 7-month history of amenorrhea and a 3-month history of progressive visual loss in the left eye. Ophthalmological examination revealed left-sided visual impairment and temporal visual field defect. Neurological examination revealed decreased muscle strength (grade 4/5) and tone. Furthermore, there was no galactosia, diabetes insipidus, or headache. The medical history was unremarkable. Brain magnetic resonance imaging (MRI) demonstrated a 3.2 × 2.7 × 2.0 cm oval mass in the intrasellar and suprasellar region with heterogeneous hypointensity on T1-weighted imaging and heterogeneous hyperintensity on T2-weighted imaging. After administering the contrast medium, the lesion exhibited a heterogeneous enhancement-like flower ring (Fig. 1). Laboratory examination revealed elevated prolactin (777.81 mIU/mL,

Editor: N/A.

Consent: The patient has provided informed consent for publication of the case.

The authors report no conflicts of interest.

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Medicine (2018) 97:27(e11274)

Received: 1 April 2018 / Accepted: 4 June 2018

<http://dx.doi.org/10.1097/MD.00000000000011274>

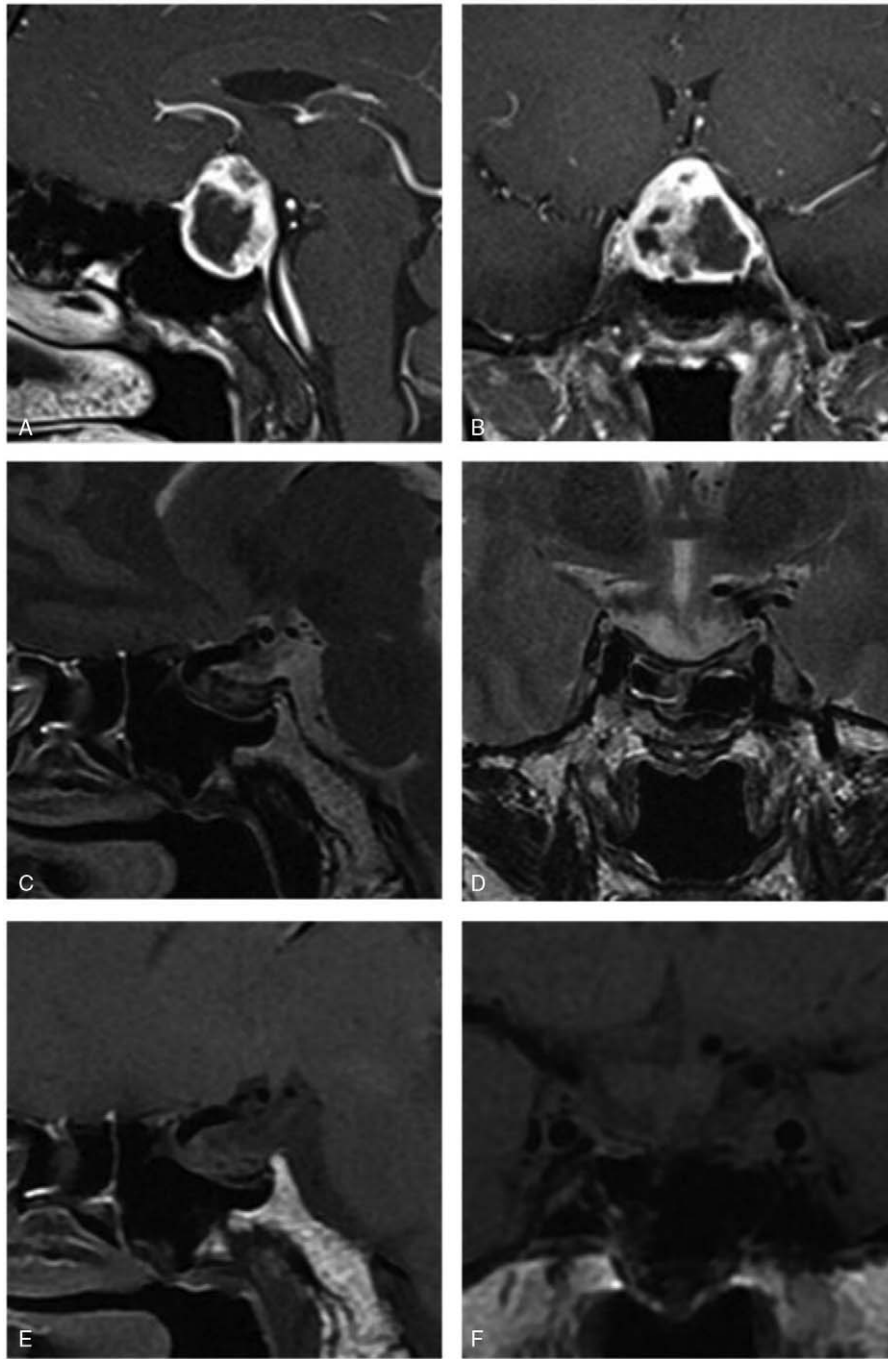


Figure 1. Brain magnetic resonance imaging (MRI) on the first admission. Preoperative MRI revealed a remarkably enhanced (A: sagittal contrasted T1-weighted imaging; B: coronal contrasted T1-weighted imaging) lesion in the intrasellar and suprasellar region. Postoperative MRI revealed that the tumor was totally resected (C: sagittal T1-weighted imaging; D: coronal T1-weighted imaging; E: sagittal contrasted T1-weighted imaging). After a 9-month follow-up, MRI revealed no recurrence (F: coronal contrasted T1-weighted imaging).

normal range: 70.81–566.5 mIU/mL), reduced thyroid-stimulating hormone (0.21 uIU/mL, normal range: 0.27–4.2 uIU/mL), reduced luteinizing hormone (LH; 0.54 mIU/mL; normal range: follicular phase 2.12–10.89 mIU/mL, ovulatory period 19.18–103.0 mIU/mL, and luteal phase 1.20–12.86 mIU/mL), and reduced 24-hour urinary free cortisol (93.13 nmol/L; normal range: 108–961 nmol/L). Growth hormone and thyroid hormone levels were normal. A diagnosis of nonfunctional pituitary adenoma was suspected.

2.2. First operation

A tumorectomy was performed via the endonasal transsphenoidal approach. Intraoperatively, it was found that the tumor was grey-white in color, solid and crisp in nature, and encapsulated, with nodular calcification and a rich blood supply. The diaphragma sellae was involved, whereas the dura mater was intact. A gross total resection was achieved. Pathological examination revealed a highly differentiated chondrosarcoma. Considering its highly differentiated characteristics and complete surgical excision, no adjuvant

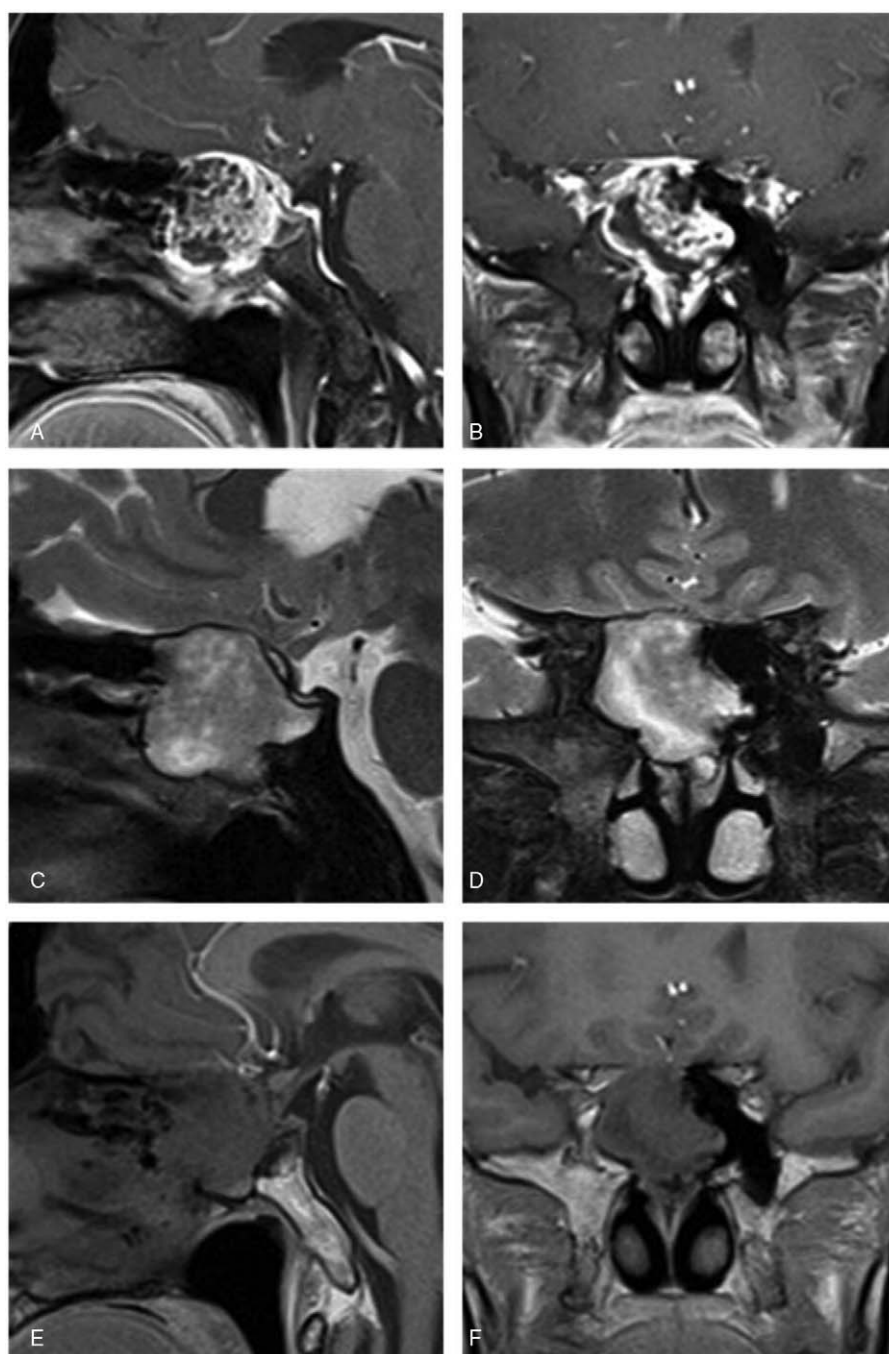


Figure 2. Brain magnetic resonance imaging on the second admission. Sagittal (A) and coronal (B) enhanced T1-weighted imaging revealed an irregular sellar lesion that involved the sphenoid sinuses, which wrapped the right internal carotid artery. The lesion was heterogeneously iso- to hyperintense on T2-weighted imaging (C: sagittal; D: coronal) and heterogeneously hypointense on T1-weighted imaging (E: sagittal; F: coronal).

radiotherapy was performed. Postoperatively, the visual impairment was gradually returned to normal, whereas the amenorrhea remained. Three months after surgery, endocrinal examination revealed normal hormones and her menstrual pattern was regular throughout that period on the oral contraceptive pill. After a 9-month follow-up, no recurrence was noted on MRI (Fig. 1).

2.3. Tumor recurrence and the second operation

Fourteen months after the first operation, the patient developed headache and visual loss in the left eye. Physical examination

revealed severe left-eye visual loss and temporal visual field defect. Brain MRI revealed a $2.8 \times 3.1 \times 2.8$ cm irregular sellar lesion with heterogeneous hypointensity on T1-weighted imaging and heterogeneous iso- to hyperintensity on T2-weighted imaging, and the right internal carotid artery was wrapped. Following administration of the contrast medium, the lesion exhibited a heterogeneous enhancement (Fig. 2). A diagnosis of recurrent chondrosarcoma was made, and a second endonasal transsphenoidal tumorectomy was performed. Intraoperatively, it was found the tumor involved bilateral sphenoid sinuses. The tumor was partially resected. Postoperatively, the headache was

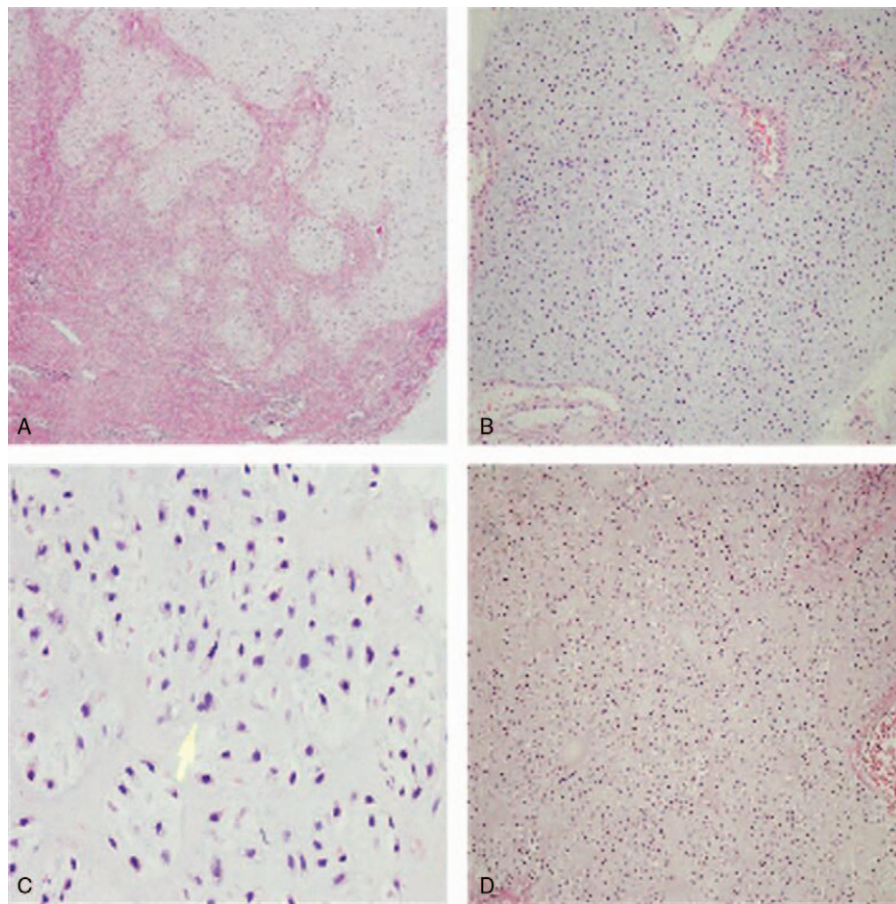


Figure 3. Hematoxylin and eosin staining. Microscopically, the hematoxylin and eosin staining of the resected specimens revealed an abundant hyaline cartilage matrix arranged in a lobulated pattern (A: 40 \times ; B: 100 \times). The chondrocytes were hyperchromatic with binucleation and mitotic figures (C: 400 \times). The histopathological features of the recurrent tumor were consistent with the primary chondrosarcoma (D: 100 \times).

relieved, whereas the patient developed hypopituitarism, necessitating hormone replacement therapy.

2.4. Histopathological findings

Microscopically, the hematoxylin-eosin staining of the resected specimens revealed an abundant hyaline cartilage matrix arranged in a lobulated pattern, and hyperchromatic chondrocytes with binucleation and mitotic figures (Fig. 3). Immunohistochemistry revealed positive staining for vimentin, S-100, and lysozyme, but negative for pancytokeratin (CK-pan), epithelial membrane antigen (EMA), cytokeratin 19, and cytokeratin 5. The Ki-67 labeling index was approximately 10% (Fig. 4). The histopathological features of the recurrent tumor were consistent with the primary chondrosarcoma.

2.5. Adjuvant treatment and prognosis

The patient refused a second-stage craniotomy designed for resecting the residual tumor, and a stereotactic radiotherapy was performed. There was no radiation-related adverse reaction. After a follow-up period of 6 months, the visual symptoms improved, the hormones returned to normal, and no recurrence was noted on MRI.

3. Discussion

The majority of neoplasms in the sellar and parasellar regions originate from the pituitary, and only 10% originate from

nonpituitary tissues, which include benign and malignant neoplasms, primary or secondary vascular malformations, and infective or inflammatory lesions.^[5] Among the cartilaginous tumors that arose from the skull base, chordomas are the most common pathological variant, whereas chondrosarcomas are relatively rare.^[6] In patients with cartilaginous tumors in the sellar region, the common clinical manifestations include headache, diplopia, and visual loss. Nevertheless, endocrine dysfunctions are infrequent.^[3] In the present case, the laboratory findings (elevated prolactin and reduced follicle-stimulating hormone and LH) were consistent with hypogonadotropic hypopituitarism, which can explain the amenorrhea. To the best of our knowledge, this is the first case of sellar chondrosarcoma with amenorrhea as the onset symptom.

There have been several theories postulated regarding the pathogenetic mechanisms of intracranial chondrosarcomas. These entities are malignant tumors that comprise of undifferentiated small cells and islands of atypical hyaline cartilage. In addition to chondroid tissues or chondroid bone, noncartilaginous tissues, such as dura mater, arachnoid, and brain parenchyma, can also be the origin of intracranial chondrosarcomas. Moreover, there are also sparse reports of intracranial chondrosarcomas secondary to deformed osteitis, osteofibrous dysplasia, or cancerated chondroma.^[7] The most common location is bone-and-cartilage junctions in the skull base, suggesting that chondrosarcomas may originate from chondrocytes or remnant mesenchymal stem cells.^[8,9] Previous studies

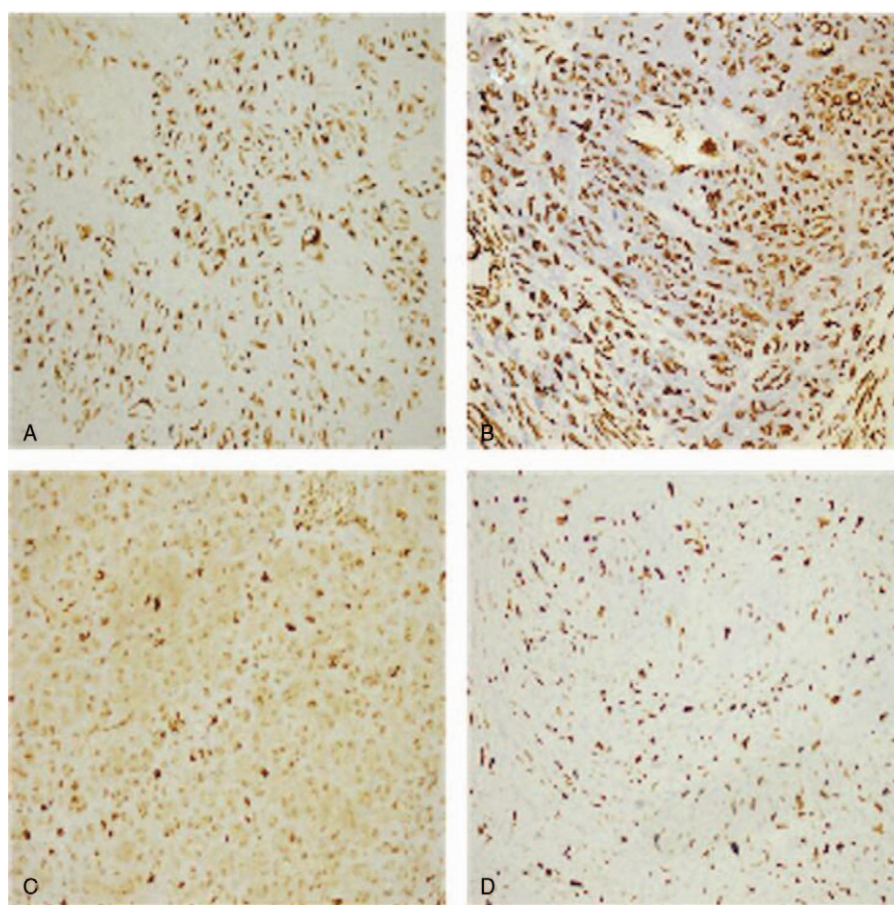


Figure 4. Immunohistochemistry. Immunohistochemical staining revealed positive staining for S-100 (A: 200×), vimentin (B: 200×), and lysozyme (C: 200×). The Ki-67 labeling index was approximately 10% (D: 200×).

have also found that fracture-related ischemia, stress, and shear force can promote the proliferation of osteoblasts, and thereby induce chondrogenesis. As the cranial bone and dura mater share a similar histologic source, dural chondrosarcomas may arise from the remnant of the embryological dural cartilage matrix.^[9] Meanwhile, some scholars have proposed that dural chondrosarcomas may arise from dural fibroblasts or primitive pluripotent mesenchymal stem cells.^[10] In some cases, neither bone nor dura mater are involved, and the chondrosarcomas may arise from pluripotent mesenchymal stem cells in the perforated blood vessels between the pia mater and arachnoid.^[8] In the present case, the sellar chondrosarcoma was located in the hypophyseal fossa. It was speculated that the tumor may have originated from the remnant of the embryological cartilage matrix or pluripotent mesenchymal stem cells.

Radiologically, intracranial chondrosarcomas usually occur off the midline.^[11] Its characteristic imaging features include calcification and osteolytic destruction, which may be present in 45% to 60% and 50% to 75% of all chondrosarcoma cases, respectively.^[3] On computed tomography, irregular destruction of the adjacent bone can be noted, and the soft-tissue component is iso- or hypodense with granular, nodular, or patchy hyperdense calcification. On MRI, intracranial chondrosarcomas show a heterogeneous iso- or hypointensity on T1-weighted imaging and a heterogeneous hyperintensity on T2-weighted imaging, whereas contrast-enhanced imaging reveal a heterogeneous enhancement.^[1] In addition, low-grade malignant tumors are

usually well-demarcated with calcification and pseudocapsule, whereas high-grade malignant tumors are often associated with osteolytic destruction and capillary hyperplasia. In the present case, the tumor exhibited heterogeneous hypointensity on T1-weighted imaging and heterogeneous hyperintensity on T2-weighted imaging with heterogeneous annular enhancement, which was consistent with a chondrosarcoma.

Histopathologically, chondrosarcomas can be classified into 4 subtypes: conventional, mesenchymal, clear cell, and dedifferentiated. The conventional type of chondrosarcoma is the most common.^[12] According to differentiation characteristics, chondrosarcomas can be further divided into 3 histological grades: grade I (well-differentiated), grade II (moderately-differentiated), and grade III (poorly-differentiated). Grade I and II chondrosarcomas have good prognosis, whereas grade III chondrosarcomas are associated with high recurrence rate and metastasis.^[13] Immunohistochemistry facilitates its diagnosis, showing a positive reaction for S-100, but a negative reaction for cytokeratin and EMA. The main differential diagnosis is chordoma, which is positive for cytokeratin and EMA.^[14] The histopathological examination in the present case revealed a highly differentiated chondrosarcoma, whereas the high Ki-67 labeling index (10%) may suggest a malignant nature. On molecular pathology, previous studies have found that more than half of intracranial chondrosarcomas have isocitric dehydrogenase (IDH)1/2 gene mutations, which may be a specific biomarker for differentiating chondrosarcomas and chordomas.^[15]

Surgical resection is the mainstream therapeutic modality for chondrosarcomas, and resection extent is a crucial factor associated with its prognosis. Noteworthily, as skull basal chondrosarcomas are closely adjacent to the hypothalamus, brain stem, and cranial nerves, gross total resection is often not possible. The surgical approaches for these tumors include the transpterional approach and endonasal transsphenoidal approach. The selection mainly depends on the location, size and growth pattern of the individual tumor.^[16,17] According to previous evidences, the 5-year survival rate and recurrence rate of chondrosarcomas following surgery alone were 74% and 56%, respectively.^[18] The role of postoperative adjuvant radiotherapy (including proton radiation, gamma knife, and stereotactic radiotherapy) in the management of chondrosarcoma remains to be well-elucidated, but it appears to be beneficial in several studies.^[19,20] Most chondrosarcomas are resistant to chemotherapy, whereas molecular targeted therapy such as mutant IDH inhibitors remain under research.^[21] In the present case, considering its highly differentiated characteristics and complete surgical excision, no adjuvant radiotherapy was performed following the first operation. Nevertheless, the tumor relapsed 14 months later. Thus, postoperative radiotherapy should be emphasized.

4. Conclusions

Chondrosarcomas in the sellar region with the onset of endocrine dysfunctions are extremely rare, which may be misdiagnosed as pituitary adenoma. The perioperative diagnosis of these entities remains challenging, and the definitive diagnosis depends on histopathological and immunohistochemical evidence. The first choice of treatment is surgery with the goal of complete resection, and postoperative adjuvant radiotherapy should be highlighted.

Author contributions

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