



# Intracranial Extraskeletal Myxoid Chondrosarcoma in Fourth Ventricle

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We present an extremely rare case of intracranial extraskeletal myxoid chondrosarcoma. A 36-year-old male presented with dizziness persisting for 2 weeks. MRI of the patient showed well-enhanced mass of fourth ventricle. The tumor was totally removed under telovelar approach. Pathology results confirmed an intracranial extraskeletal myxoid chondrosarcoma. Adjuvant radiotherapy was initiated one month after the surgery, and MRI followed 3 months after initial operation and showed no evidence of tumor recurrence.

**Keywords** Chondrosarcoma; Brain neoplasms; Extraskeletal; Myxoid; Fourth ventricle.

## INTRODUCTION

Intracranial extraskeletal myxoid chondrosarcoma (EMC) is an extremely rare disease, with only 13 cases reported since its first description in 1972 [1-13]. However, due to lack of precise diagnostic criteria and histologic/genetic evidence of previously reported cases, it is uncertain if all reported cases are true intracranial EMC [14]. We hereby present a new case of intracranial EMC in fourth ventricle. We reviewed previously reported cases of intracranial EMCs to validate their diagnosis and to find out if there are clinical similarities among them.

## CASE REPORT

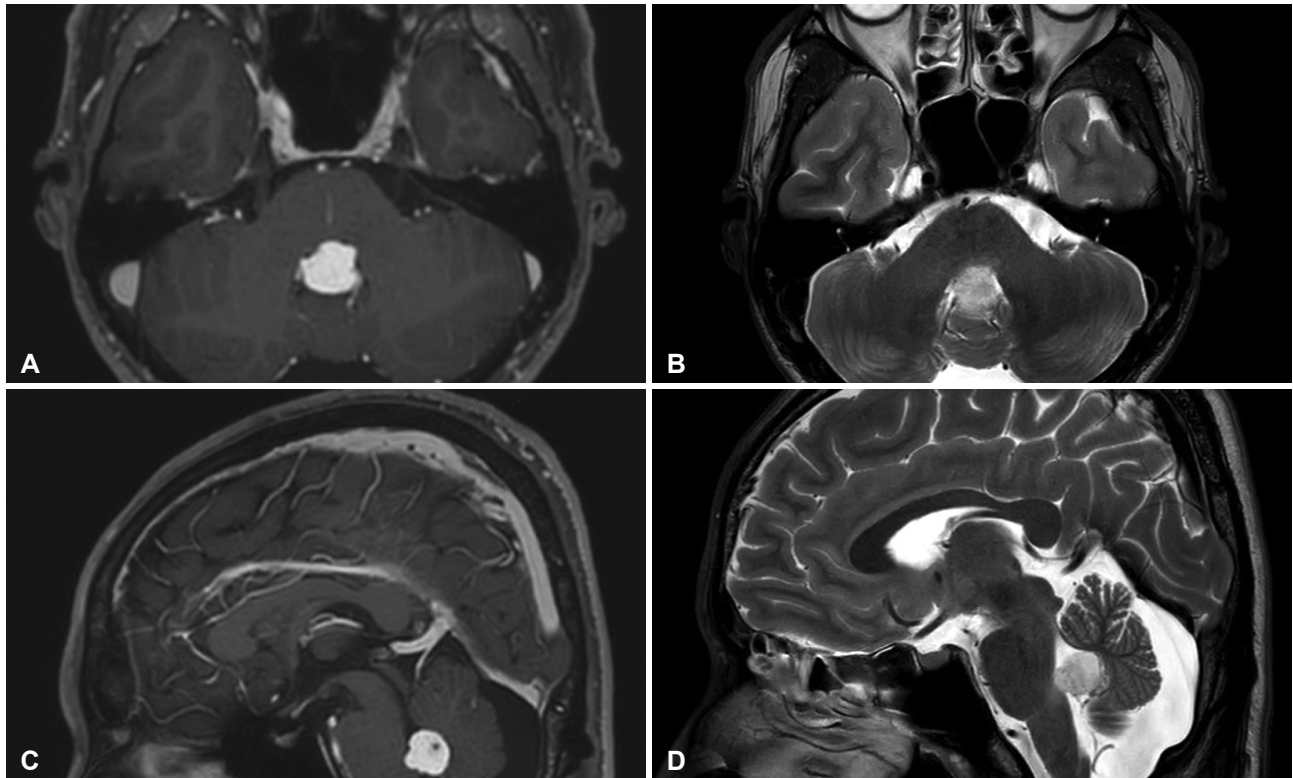
A 36-year-old male presented with 2 weeks of dizziness. MRI of the brain showed approximately 1.6 cm sized intraventricular tumor of fourth ventricle. The tumor showed low signal

intensity on T1, high signal intensity on T2-weighted image and showed homogenous enhancement on contrast enhanced T1-weighted image (Fig. 1). Initial impression of diagnosis was hemangioblastoma, but preoperative angiography did not show any staining of the tumor. The tumor was approached with midline suboccipital craniotomy and telovelar approach. The tumor was attached to the choroid plexus of the rhomboid fossa; there was no other attachment to adjacent structures. The tumor was completely removed *en bloc* (Fig. 2). The whole operation was done under MRI navigation guidance and facial motor evoked potential monitoring.

Microscopic examination of the specimen showed spindle shaped cells with scant eosinophilic cytoplasm on basis of abundant myxoid stroma. Overall pathologic morphology resembled that of a mesenchymal tumor (Fig. 3). Immunohistochemistry (IHC) staining results showed negative in glial markers isocitrate dehydrogenase 1 and glial fibrillary acidic protein (GFAP). Final pathology report was EMC. Immediate postoperative MRI showed no remnant enhancing lesion suggesting complete removal of tumor. The patient recovered well without any significant neurologic deficit, except mild dysphagia and hypesthesia of left thigh. Adjuvant radiotherapy (54 Gy/27 fx) start-

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**Fig. 1.** Preoperative MRI of the patient. A: T1-weighted enhanced axial image. B: T2-weighted axial image. C: T1-weighted enhanced sagittal image. D: T2-weighted sagittal image. The tumor shows strong homogenous contrast enhancement on T1-weighted enhanced images and moderate to high signal on T2-weighted images.



**Fig. 2.** Microscopic images of tumor. The tumor was removed via telovelar approach. A: Cerebellum is exposed after dura incision. B: Tela choroidea is exposed after retraction of right cerebellar tonsil and vermis. C: The tumor attached to the choroid plexus and the fourth ventricle floor is removed *en bloc*.

ed at 1 month postoperatively, and MRI followed at 3 months after surgery showed no recurrence of tumor (Fig. 4). Patient remained free of any neurologic deficit.

## DISCUSSION

Intracranial chondrosarcoma is a very rare disease entity, with a portion of 0.16%–0.5% of all intracranial neoplasms [14,15]. It is categorized into three subtypes: classic (conventional), mesenchymal, and myxoid [16]. Of all, intracranial EMC is the rarest, with only 13 cases reported up to date (Table 1).

EMC shows heterogenous histological morphology. Common findings of the reported cases include lobulated basophil-

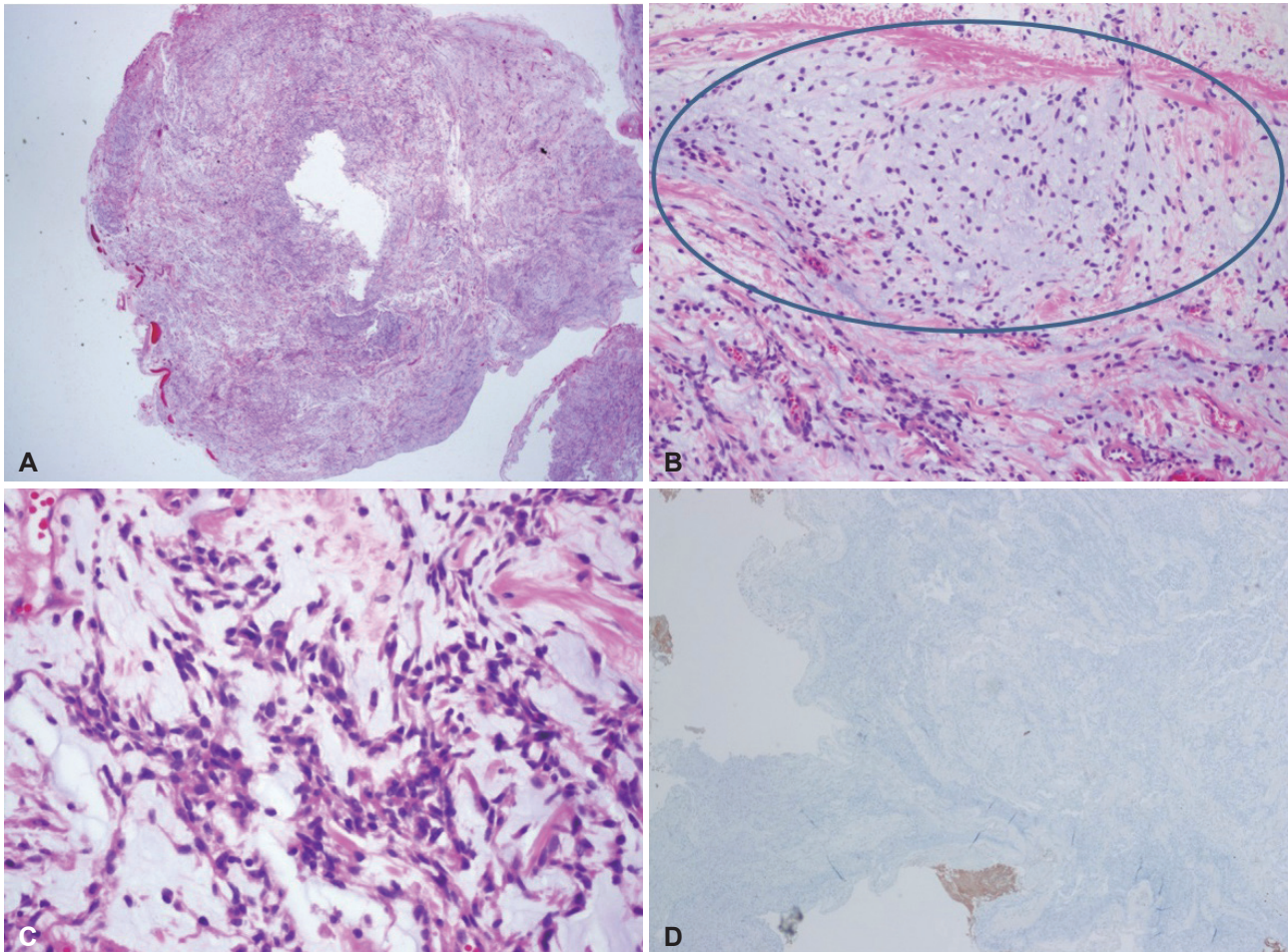
ic myxoid stroma with short spindle cells or small round cells. Cells consist of small, hyperchromatic nuclei with scant, eosinophilic cytoplasm. Mitoses counts are usually rare, and most of the reported cases showed no intra-tumoral bleeding or necrosis, suggestive of the relatively indolent nature of the tumor. Intraoperative findings of the reported cases vary; in most of the reports the tumor is described as a gray or brownish, well circumscribed, soft round mass without calcification.

IHC results are crucial in differentiating EMCs from other EMC-mimicking intracranial tumors. S100 staining shows diffuse, strong positivity in most of EMCs while only focal moderate staining in 40% of chordoid meningiomas. Pankeratin staining can be used to differentiate between chordoid gli-

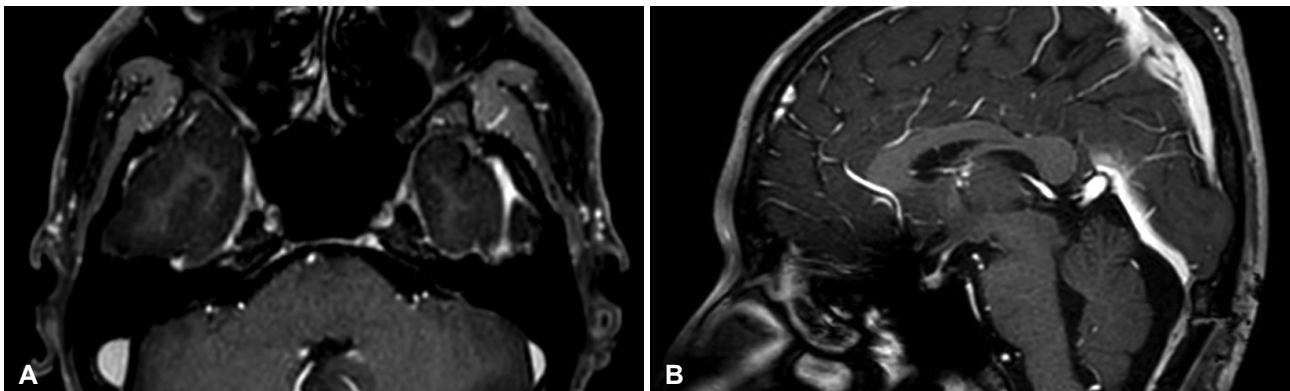


mas and chordomas from EMCs. Epithelial membrane antigen staining shows positive in most cases of chordoid gliomas, chordomas, and chordoid meningiomas while only 25% of EMCs show positivity. GFAP staining is used to differentiate EMCs from gliomas like pilocytic astrocytoma [17]. Of 13 case

reports, 10 studies had at least one IHC result reported. The results are described in Table 2. Neuronal markers such as GFAP, neuron-specific enolase, synaptophysin all showed negative, while vimentin was positive in all tested patients, and most of the patients showed negative in cytokeratin and EMA staining.



**Fig. 3.** Pathologic findings. A: Low power view (H&E stain,  $\times 12.5$ ) shows a somewhat well demarcated mass. B: In the mass, myxoid stroma (oval circle) is noted (H&E stain,  $\times 200$ ). C: High power view (H&E stain,  $\times 400$ ) shows haphazardly arranged spindle cells with myxoid stroma. D: The GFAP immunohistochemistry shows negative reaction (GFAP stain,  $\times 400$ ). These findings are compatible with extraskeletal myxoid chondrosarcoma. H&E, hematoxylin and eosin; GFAP, glial fibrillary acidic protein.



**Fig. 4.** Postoperative MRI at 3 months after surgery. T1-weighted enhanced axial (A) and sagittal (B) images show no residual tumor.

**Table 1.** Clinical characteristics of previously reported cases of intracranial myxoid chondrosarcomas

Study	Sex/age	Location	Size (cm)	Extent of resection	Adjuvant treatment	Prognosis	Etc
Scott et al. [1]	M/39	Fourth ventricle	N/A	Subtotal removal (50%)	N/A	V-P shunt after 5 days → deceased 13 days postop	Rock-hard consistency, calcification, decalcification needed
Smith et al. [2]	M/12	Left cerebellum	3.5×1.0×0.5	Total removal	None	No recurrence 13 mo	Foramen magnum dura, bone not involved
Salcman et al. [3]	F/28	Left parafalcine	7×5×4	Total removal → reop	125-I radioactive seeds brachytherapy	Recur 8 mt → reop → no recur 12 mo	N/A
Sato et al. [4]	F/43	Pineal region	N/A	Subtotal removal	Radiotherapy (6,000 cGy) +chemotherapy	Deceased 37 mo after diagnosis	Leptomeningeal seeding
Sala et al. [5]	F/55	Right cerebellum	N/A	Total removal	None	Recur 10, 16, 31, 43 mo (reop) → deceased 7 yrs	Right petrous bone origin
González-Lois et al. [7]	F/17	Right fronto-temporal convexity	Less than 3	Total removal → reop	Radiotherapy (6,000 cGy)	Recur 16 mo → reop → recurrence 4 mo	N/A
Chaskis et al. [6]	M/69	Right frontal	1.5	Total removal	None	Deceased 1 mo	Subcortical, parenchymal
Im et al. [8]	M/43	Left parietal	1.2×1.0×1.0	Total removal	Radiotherapy (5,940 cGy)	No recur 36 mo	Subcortical, parenchymal
Sorimachi et al. [10]	F/37	Pineal region	N/A	Subtotal removal → reop	None	Progression 14 mo → reop → no recur 7 mo	Tumor bleeding, calcification in 2nd path, S100 (-) → (+)
O'Brien et al. [9]	F/26	Left cerebellopontine angle	2.5	Biopsy → subtotal	Proton therapy	No recur 12 mo	20 wk pregnant
Park et al. [12]	F/21	Left thalamus and lateral ventricle	3.2×6.3×4.8	Total removal	Radiotherapy (6,080 cGy)	No recur 6 mo	Parenchymal
Dulou et al. [11]	F/70	Left parasagittal	N/A	Neoadj RTx → total removal	Chemotherapy (ifosfamide)	Recur 3 mo → CTx → deceased 10 mo	Breast cancer patient
Qin et al. [13]	F/41	Left cerebellum	3×3×3	Subtotal removal	Radiotherapy (4,060 cGy) + chemotherapy (TMZ)	No recur 20 mo	Poor dissection margin, peritumoral bleeding, skull destruction
Present case	M/36	Fourth ventricle	1.6	Total removal	Radiotherapy (5,400 cGy/27 fx)	No recur 3 mo	Medulla dorsal surface, no bone involvement

**Table 2.** Immunohistochemistry results of previously reported cases of intracranial myxoid chondrosarcomas

Study	GFAP	Cytokeratin	EMA	S-100	Vimentin	NSE	Synaptophysin	Chromogranin A
Smith et al. [2]	(-)							
Salcman et al. [3]	(-)	(-)	(-)	(-)	(++)			
Sato et al. [4]		(-)		(++)	(++)			
González-Lois et al. [7]			(-)	(+), focal	(+)	(-)		
Im et al. [8]	(-)	(-)	(-)	(+), weak	(+)			
Sorimachi et al. [10]	(-)	(-)	(-)	(-)	(+)		(-)	(-)
O'Brien et al. [9]	(-)	(-)	(-)	(-)		(-)	(-)	(-)
Park et al. [12]	(-)		(+), focal strong	(-)	(+)			
Dulou et al. [11]		(+), AE1/AE3	(+), strong	(+), weak				
Qin et al. [13]	(-)	(-)	(-)	(+)				

Papers with tested markers less than two were removed from the table. GFAP, glial fibrillary acidic protein; EMA, epithelial membrane antigen; NSE, neuron-specific enolase

These results are largely congruent with previous studies of extracranial EMCs, providing validity to their diagnosis [18].

Of 13 cases previously reported, two cases were questionable of their validity of diagnosis. The first case report of 1976 [1] reported the tumor had a 'rock-hard' consistency and 'had to be attacked with... rongeurs and scissors.' Pre-op X-ray image showed prominent calcification of the tumor. Tumor specimen had to be decalcified before microscopic observation, which showed presence of osteoid tissue. No other case reported prominent calcification or presence of osteoid tissue. The tumor was more likely a mixed sarcoma with prominent osteoid formation as suggested in another case report [2]. Another case from Poland presented a known triple negative breast cancer patient diagnosed with parenchymal brain tumor of left frontal lobe [11]. Although the authors confirmed the histological diagnosis as myxoid chondrosarcoma, the report did not present any suitable IHC results to claim so. According to the report, the specimen showed strong staining in EMA and cytokeratin; no results regarding vimentin or GFAP were presented. EMA and cytokeratin are known to show positivity mostly in epithelial origin tumor and these findings do not match with other previously reported cases of EMCs. Chordoid meningioma can be a considerable diagnosis, considering its EMA positivity. But the tumor seems intraaxial in given MRI image, and the pathology report also claims infiltration of tumor into brain parenchyma. Considering the patient's medical history, the lesion could be a metastatic adenocarcinoma with myxoid stromal change [19] or a metastatic mucinous breast lesion mimicking myxoid stroma [20].

Because of the rarity of the disease, there is no solid theory or evidence regarding how a chondrosarcoma can primarily form inside a cranium. Intracranial chondrosarcomas are supposed to originate from embryonic rests of the chondrocranium or from metaplasia of meningeal fibroblasts and typically arise from the base of the skull [21]. Previous case reports present-

ed choroid plexus, remaining multipotent mesenchymal cells of skull base or dura mater as possible origins of the tumor. To our knowledge, this case is the second intraventricular EMC reported [12] and first EMC to be histologically confirmed with IHC results that formed inside fourth ventricle.

Optimal treatment of EMCs is still debated. In most of the cases the tumor was separated well from surrounding tissue. In 9 out of 14 cases, including present case, the tumor was totally removed by surgery. However, it is unclear if the extent of removal is associated with lower recurrence or better prognosis. Three cases reported recurrence of tumor after total removal. Adjuvant therapy also varied widely. A recent phase II trial of pazopanib in advanced EMCs showed anti-tumor activity, but it is even more difficult to treat intracranial EMCs because central nervous system permeability needs to be considered [22]. Five cases have undergone adjuvant radiotherapy, of which two with concurrent chemotherapy. Further studies need to be done regarding necessity and efficacy of adjuvant treatment.

In conclusion, we present a rare case of intracranial EMC originated from the choroid plexus inside fourth ventricle. IHC staining results are crucial in differential diagnosis of intracranial EMCs from other intracranial tumors mimicking its pathologic morphology. Optimal treatment of the disease is still debated; more cases and further studies are needed regarding the necessity of radical excision, adjuvant chemotherapy and radiotherapy.

### Ethics Statement



The Institutional Review Board of Severance Hospital exempted informed consent due to its retrospective nature and minimal risk for harm to the patient, and this report was conducted according to the guidelines of the Declaration of Helsinki for biomedical research.

### Availability of Data and Material

All data generated or analyzed during the study are included in this published article (and its supplementary information files).



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**Conflicts of Interest**

The authors have no potential conflicts of interest to disclose.

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None

**REFERENCES**

1. Scott RM, Dickersin R, Wolpert SM, Twitchell T. Myxochondrosarcoma of the fourth ventricle. Case report. *J Neurosurg* 1976;44:386-9.
2. Smith TW, Davidson RI. Primary meningeal myxochondrosarcoma presenting as a cerebellar mass: case report. *Neurosurgery* 1981;8:577-81.
3. Salcman M, Scholtz H, Kristt D, Numaguchi Y. Extraskelletal myxoid chondrosarcoma of the falx. *Neurosurgery* 1992;31:344-8.
4. Sato K, Kubota T, Yoshida K, Murata H. Intracranial extraskelletal myxoid chondrosarcoma with special reference to lamellar inclusions in the rough endoplasmic reticulum. *Acta Neuropathol* 1993;86:525-8.
5. Sala F, Talacchi A, Beltramello A, Iuzzolino P, Bricolo A. Intracranial myxoid chondrosarcoma with early intradural growth. *J Neurosurg Sci* 1998;42:159-63.
6. Chaskis C, Michotte A, Goossens A, Stadnik T, Koerts G, D'Haens J. Primary intracerebral myxoid chondrosarcoma. Case illustration. *J Neurosurg* 2002;97:228.
7. González-Lois C, Cuevas C, Abdullah O, Ricoy JR. Intracranial extraskelletal myxoid chondrosarcoma: case report and review of the literature. *Acta Neurochir (Wien)* 2002;144:735-40.
8. Im SH, Kim DG, Park IA, Chi JG. Primary intracranial myxoid chondrosarcoma: report of a case and review of the literature. *J Korean Med Sci* 2003;18:301-7.
9. O'Brien J, Thornton J, Cawley D, et al. Extraskelletal myxoid chondrosarcoma of the cerebellopontine angle presenting during pregnancy. *Br J Neurosurg* 2008;22:429-32.
10. Sorimachi T, Sasaki O, Nakazato S, Koike T, Shibuya H. Myxoid chondrosarcoma in the pineal region. *J Neurosurg* 2008;109:904-7.
11. Dulou R, Chargari C, Dagain A, et al. Primary intracranial extraskelletal myxoid chondrosarcoma. *Neurol Neurochir Pol* 2012;46:76-81.
12. Park JH, Kim MJ, Kim CJ, Kim JH. Intracranial extraskelletal myxoid chondrosarcoma: case report and literature review. *J Korean Neurosurg Soc* 2012;52:246-9.
13. Qin Y, Zhang HB, Ke CS, et al. Primary extraskelletal myxoid chondrosarcoma in cerebellum: a case report with literature review. *Medicine (Baltimore)* 2017;96:e8684.
14. Velz J, Agaimy A, Frontzek K, et al. Molecular and clinicopathologic heterogeneity of intracranial tumors mimicking extraskelletal myxoid chondrosarcoma. *J Neuropathol Exp Neurol* 2018;77:727-35.
15. Jroundi L, Kacemi L, Bounhir B, Chami I, Boujida N, Bacadi D. Intracerebral chondrosarcoma in a 12 year old child. *J Radiol* 2005;86:173-5.
16. Korten AG, ter Berg HJ, Spincemaille GH, van der Laan RT, Van de Wel AM. Intracranial chondrosarcoma: review of the literature and report of 15 cases. *J Neurol Neurosurg Psychiatry* 1998;65:88-92.
17. Sangoi AR, Dulai MS, Beck AH, Brat DJ, Vogel H. Distinguishing choroid meningiomas from their histologic mimics: an immunohistochemical evaluation. *Am J Surg Pathol* 2009;33:669-81.
18. Oliveira AM, Sebo TJ, McGrory JE, Gaffey TA, Rock MG, Nascimento AG. Extraskelletal myxoid chondrosarcoma: a clinicopathologic, immunohistochemical, and ploidy analysis of 23 cases. *Mod Pathol* 2000;13:900-8.
19. Wernicke M, Piñeiro LC, Caramutti D, et al. Breast cancer stromal myxoid changes are associated with tumor invasion and metastasis: a central role for hyaluronan. *Mod Pathol* 2003;16:99-107.
20. Harrison BT, Dillon DA. An update of mucinous lesions of the breast. *Surg Pathol Clin* 2018;11:61-90.
21. Drilon AD, Popat S, Bhuchar G, et al. Extraskelletal myxoid chondrosarcoma: a retrospective review from 2 referral centers emphasizing long-term outcomes with surgery and chemotherapy. *Cancer* 2008;113:3364-71.
22. Stacchiotti S, Ferrari S, Redondo A, et al. Pazopanib for treatment of advanced extraskelletal myxoid chondrosarcoma: a multicentre, single-arm, phase 2 trial. *Lancet Oncol* 2019;20:1252-62.