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Primary Intracranial Myxoid Chondrosarcoma
: Report of a Case and Review of the Literature

The authors present a case of primary intracranial extraosseous myxoid chondrosarcoma without any attachment to the cranium or the meninges. The clinical and radiological findings of the primary intraparenchymal tumor are described with a review of the literature concerning cranial and intracranial myxoid chondrosarcoma.

Key Words : *Chondrosarcoma; Central Nervous System Neoplasms*

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INTRODUCTION

Primary cranial chondrosarcoma is not an uncommon neoplasm and usually arises at the synchondroses of the skull base, particularly the sphenoid bone and the clival basiocciput (1-3). Primary intracranial extraosseous chondrosarcoma is rare and most are attached to the dura, the presumed site of origin of these tumors (4-7). However, seven cases of primary intracranial chondrosarcomas unrelated to the cranium or the meninges have been reported and all of these tumors were histologically typed as mesenchymal variants (3, 5). Recently, the authors experienced a case of primary intraparenchymal myxoid chondrosarcoma of the brain without any attachment to the cranium or the meninges. We believe it worthwhile to document the clinical manifestations and radiological findings of this case, because to the best of our knowledge, this condition has not been previously reported. The authors discuss pathologic differential diagnosis between histologically similar tumors, such as chordoma, parachordoma, chordoid meningioma and chordoid glioma for the meticulous histologic differentiation of tumors, although cords of epithelioid cells reminiscent of typical chordomas are not the significant histologic finding in present case.

CASE REPORT

A 43-yr-old man was admitted to the neurosurgery department due to a history of occipital headache, nausea, and vomiting of two months' duration. He complained of general weakness, myalgia, tinnitus in the left ear, and an intermittent tingling sensation in the distribution of the bilateral mandibular division of the V cranial nerve. He had been managed with an insulin pump due to longstanding diabetes mellitus, and the generalized vague symptoms, mentioned previously, were considered to be complications of the diabetes mellitus. Neurological and physical examinations revealed no abnormalities. A pre-contrast computed tomography (CT) scan showed a 2 cm, non-calcified, slightly low density mass with severe peritumoral edema in the left parietal lobe. A post-contrast CT scan revealed strong homogeneous enhancement of the mass (Fig. 1), which was of low signal intensity on T1-weighted magnetic resonance (MR) imaging and high signal intensity on T2-weighted MR imaging. Post-contrast MR imaging revealed a homogeneously enhancing mass in the left parietal lobe (Fig. 2). A bone scan showed no abnormal uptake. A serum tumor marker study, performed under the impression of metastatic brain tumor, was negative for AFP, CEA, CA125, CA19-9, PAP, and PSA. Whole body ^{18}F-FDG-PET (positron emission tomography) showed a focal hypermetabolic lesion in the parietal area, however, there was no abnormality outside the brain. The patient underwent a left parietal osteoplastic craniotomy under the impression of atypical malignant glioma, lymphoma, or metastatic tumor. Skull bone and dural surface looked normal and a cruciate dural incision was made. There

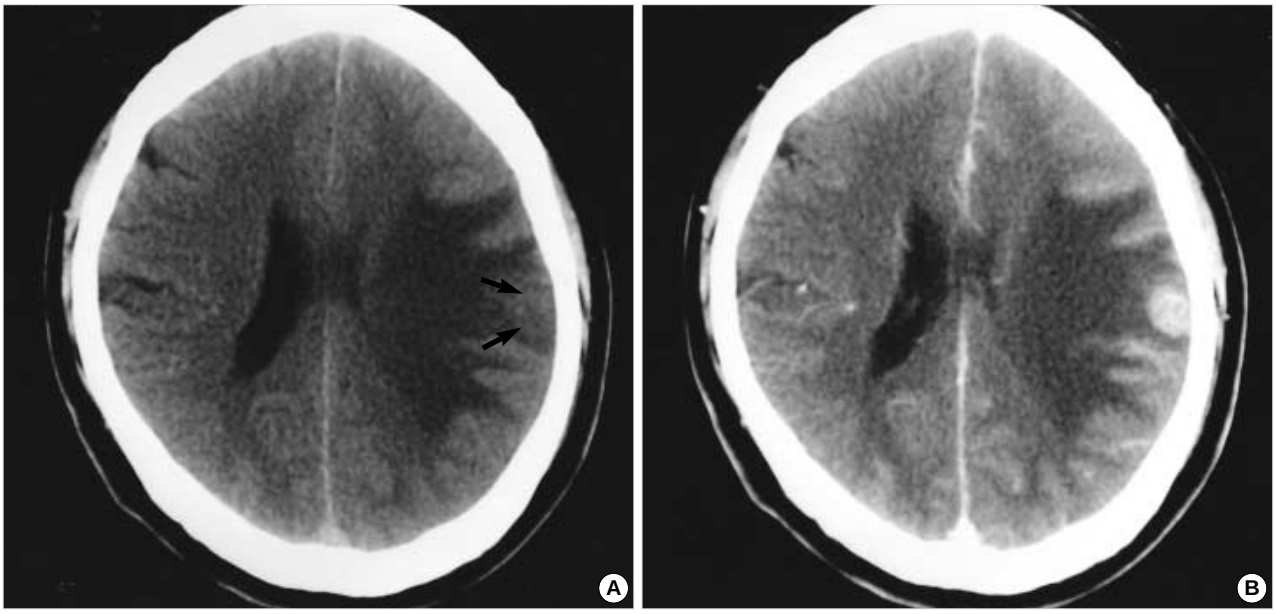

Fig. 1. (A) Pre-contrast computed tomography (CT) showing an ill-defined isodense mass (arrows), with severe surrounding edema in the left parietal cortex. (B) Strong homogeneous enhancement of the mass as seen in postcontrast CT.

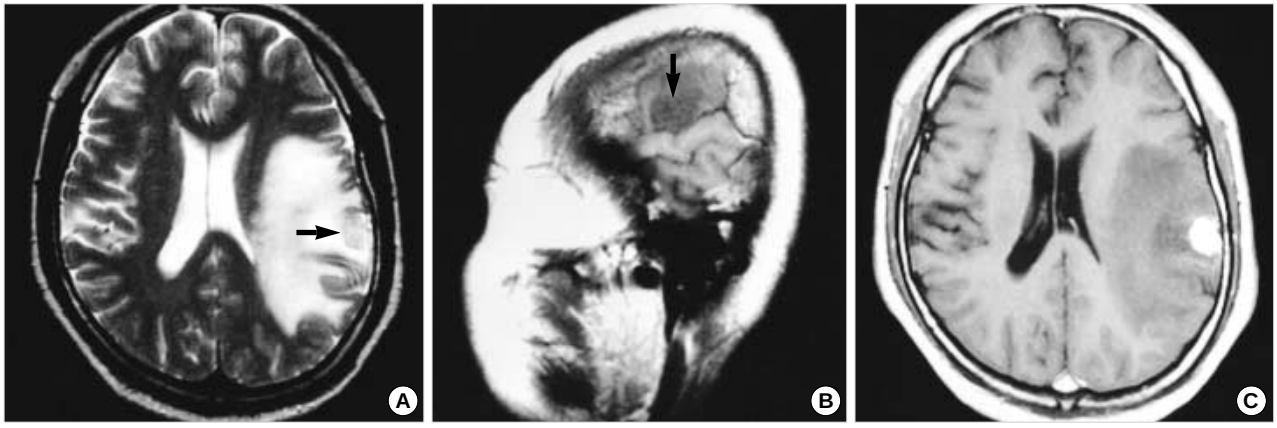

Fig. 2. (A) Axial T2-weighted magnetic resonance (MR) image showing slightly high signal intensity mass with severe surrounding edema in the left parietal cortex (arrow). (B) Sagittal T1-weighted MR image revealing an ill-defined low signal intensity mass (arrow). (C) Strong homogeneous enhancement of the mass as seen on the axial post-contrast T1-weighted MR image. The mass is located just beneath the dura, however, there was no connection to the dura.

was no adhesion or attachment between the dura and the cerebral cortex and the cortical surface also showed a normal architecture. An incision was made on the surface of the parietal lobe and a well encapsulated mass was found just beneath the cortex. The tumor was readily dissected from the surrounding gliotic plane and an en-bloc removal was performed. The immediate postoperative course was uneventful. The patient received postoperative radiotherapy of 5,940 cGy in 33 fractions. He remains in good medical condition and follow-up MR images taken three years after the operation showed no recurrence.

Pathological Findings

Macroscopically, the tumor had a nodular and lobulated appearance and measured $1.2 \times 1.0 \times 1.0$ cm (Fig. 3). It had a grayish surface and showed a yellowish gray gelatinous area on serial section. It was firm to slightly hard in consistency.

Microscopically, the periphery of the tumor was surrounded partly by a thin fibrous tissue and partly by a somewhat compressed brain parenchyma. On low power cross-sectional view, the tumor had paucicellular areas interspersed with areas containing moderate numbers of cellular foci. The tumor showed an associated basophilic myxoid matrix, separated by thin

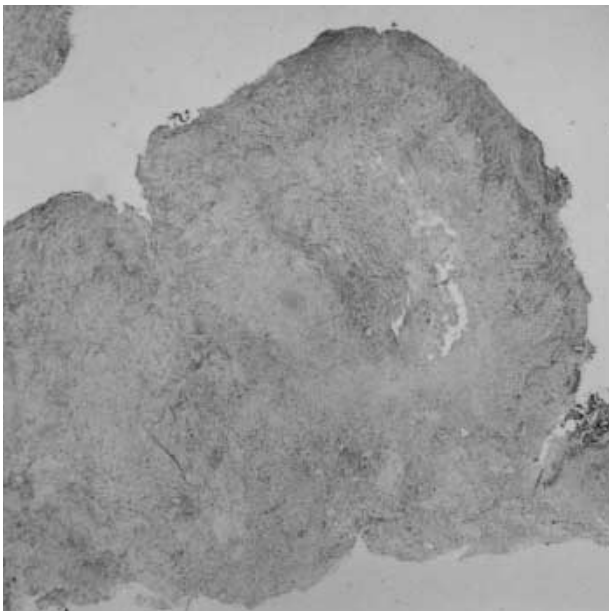

Fig. 3. Photomicrograph showing a nodular and lobulated appearance of tumor (H&E, ×10).

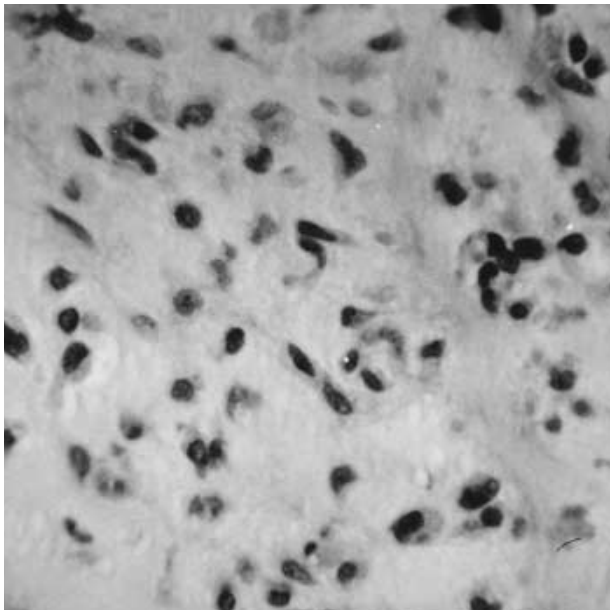

Fig. 4. High power photomicrograph of the tumor shows epithelioid to spindle shaped cells dispersed in a myxochondroid matrix (H&E, ×400).

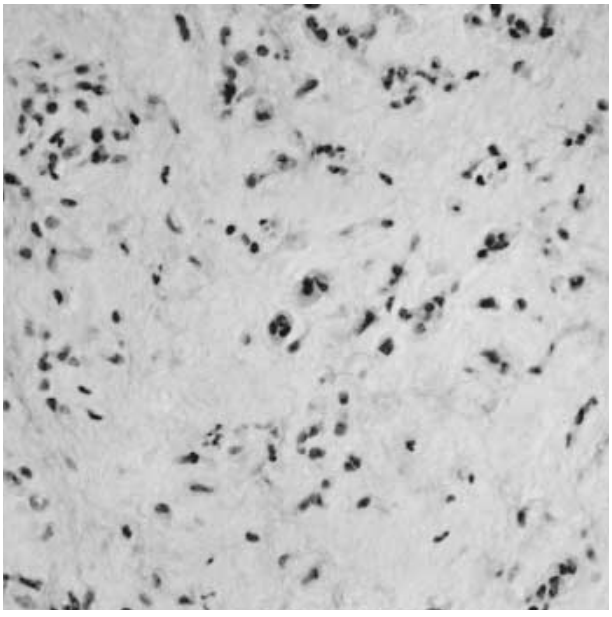

Fig. 5. Photomicrograph of the tumor cells, which are arranged in strands and cords within a large amount of stroma. Round or slightly elongated cells are separated by abundant myxoid stroma (H&E, ×200).

connective tissue bands, and was composed of round or slightly elongated cells separated by abundant myxoid stroma. The individual cells possessed small hyperchromatic, slightly irregular nuclei and a narrow rim of deeply eosinophilic cytoplasm, and were arranged in short anastomosing cords and strands in myxoid matrix (Fig. 4, 5). The histology of this tumor resembled that of an extraskeletal myxoid chondrosarcoma of other soft tissues. Microscopically, neither hemorrhage nor necrosis was observed. Mitoses were extremely rare. Portions of the tumor contained numerous thin-walled vessels.

The following antibodies were used for immunohistochemical analyses; a polyclonal antibody to S100 (1:400; Dako A/S, Glostrup, Denmark) and monoclonal antisera to glial fibrillary acidic protein (GFAP) (Dako, 1:500), vimentin (clone V9; 1:100; Dako A/S, Glostrup, Denmark), epithelial membrane antigen (EMA) (clone E29; 1:50; Dako A/S, Glostrup, Denmark), cytokeratin 19 (clone RCK 108; 1:50; Dako A/S, Glostrup, Denmark), and cytokeratin, high molecular weight (clone 34βE12; 1:50; Dako A/S, Glostrup, Denmark). Immunohistochemical studies were performed using the avidin-biotin-peroxidase complex method. Diaminobenzidine was used as a substrate. On immunohistochemical studies, the neoplastic cells showed a weak positive staining for S100, positive staining for vimentin, and a lack of staining for EMA, cytokeratin 19, GFAP, and high molecular weight cytokeratin, which confirmed the diagnosis of myxoid chondrosarcoma (Fig. 6).

DISCUSSION

Primary cranial chondrosarcomas normally arise from the skull base and are usually located extradurally (1-3). Primary intracranial extraosseous chondrosarcomas have been less commonly reported than cranial chondrosarcomas and their locations include the cerebral convexity, falx, fourth ventricle,

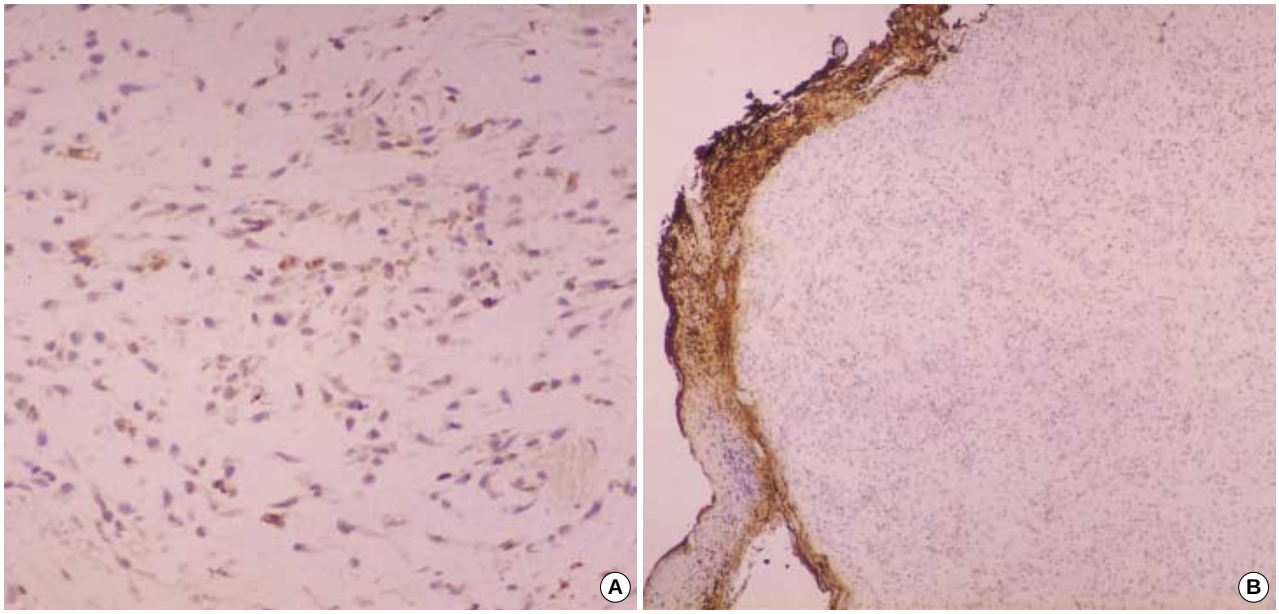

Fig. 6. On immunohistochemical studies, the myxoid chondrosarcoma shows a weak positive staining for S100 (A, ×200) and a lack of staining for GFAP (B, ×40).

cerebellum, and thalamus (3, 6-10). Theoretically, a chondrosarcoma should originate from the mesenchymal tissues, like cartilage, therefore, those arising from the skull base are quite natural. Intracranial chondrosarcomas are also thought to arise from the mesenchymal elements of the central nervous system, such as, the primitive multipotential mesenchymal cells or their mature descendents (fibroblasts, meningeal cells, and pial cells) located within the leptomeninges, the pia-arachnoid surrounding blood vessels or in the vessel walls, the stroma of the choroid plexus and aberrant embryonal cartilagenous rests (4, 7, 9-16). In the case of primary intraparenchymal chondrosarcoma, misplaced embryonal cartilagenous rests or primitive multipotential mesenchymal cells in leptomeningeal sheaths around vessels or the vessel walls have been suggested to be origins without definitive evidence (3, 5, 7, 8, 10, 17-21). The tumor in present case was located just beneath the cortex so that the leptomeningeal tissue or a vessel in the depths of the sulcus might be a possible origin. This hypothesis was suggested by some authors (13, 22) and our case might be an example.

Histologically, three subtypes of chondrosarcomas have been described; classic chondrosarcoma, mesenchymal chondrosarcoma, and myxoid chondrosarcoma (5, 17). Most of the primary intracranial extraosseous chondrosarcomas show a dural involvement. However, those within the brain parenchyme without any attachment to the cranium or the meninges are very rare with only seven cases reported. These include a thalamic, three cerebellar, two frontal, and one parietal tumors (3, 5, 8, 11, 12, 17). All of these primary intraparenchymal chondrosarcomas were of a mesenchymal histological subtype. A case of radiation-induced classic chondrosarcoma of the cerebellum occurred 16 yr after radiation therapy for a cerebellar astrocytoma (23). However, primary intraparenchymal myxoid chondrosarcoma without any dural involvement has not been previously reported.

The classic cranial and intracranial chondrosarcomas usually arise at the skull base and most frequently affect adults (3, 7, 18). The classic subtype has a better prognosis than the mesenchymal subtype (5, 7, 18). Intracranial extraosseous mesenchymal chondrosarcoma usually occurs in the frontoparietal region and is highly vascular (5, 7). It is the most aggressive subtype with a tendency for recurrence and metastasis (3, 5, 17). The 5-yr survival rate is about 40%, and only occasional long-term survivals have been reported (7). Cranial or intracranial myxoid chondrosarcoma is a rare variant and only 10 cranial cases and four intracranial cases have been reported (2, 3, 7, 9, 10, 13, 14, 19-21) (Table 1, 2).

Calcification was more common in cranial myxoid chondrosarcoma. The masses were found to be of low density or isodense on CT scan. MR imaging showed the tumors to be of low signal intensity on T1-weighted images and of high signal intensity on T2-weighted images. Tumors showed modest to strong enhancements on CT and/or MRI. Severe peritumoral brain edema was seen only in the present case. Three patients who had undergone a gross total removal with or without postoperative radiation therapy were in good medical condition during the follow-up period of 13 months to three years. Two patients who had undergone a gross total removal experienced tumor recurrences. Five patients who underwent a partial resection with or without postoperative radiation therapy were alive during the follow-up period of three months to eight years (mean 5.5 yr).

Table 1. Clinical features of 10 patients with cranial myxoid chondrosarcoma

Author/yr	Age (yr)/ Sex	Location	Origin	Presentation	Duration of symptom	Skull x-rays	Cerebral angiography	CT	MRI	Op	Radiotherapy	Outcome	F/U
Mott/ 1899	28/M	parasellar	sella turcica	-	-	-	-	ND	ND	ND	ND	died serveral years after the onset of symptoms	
Naufa/ 1973	27/F	petrous apex, right	foramen lacerum	headache, multiple CN deficits, BS sign	24 mos	hyperostosis, destruction of petrous apex	ND	ND	ND	PR	ND	died of pneumonia POD 12 days	
Gacek/ 1975	31/F	petrous apex, left	foramen lacerum	headache, multiple CN deficits	24 mos	erosion of petrous apex	avascular mass	ND	ND	PR	6,125 cGy proton beam	alive, no recurence radiation necrosis	8 yr
Hassounah et al./1985	33/F	posterior fossa, right	cranium, T&O	ICP symptom, cbll sign	20 mos	calcification	avascular mass	low dense mass, calcification	ND	GTR	5,400 cGy proton beam	alive, no recurence	3 yr
Bourgouin et al./1992	Three men & Two women	cerebellopontine, left	embryonal resets in the skull base	multiple CN deficits, bilateral pyramidal syndrome	2 mos	-	-	Isodense on Postcontrast-CT	hyperintense T2, hypointense T1,	PR	-	alive	3 mos to 7 yr (mean, 3 yr)
		cerebellopontine, right	embryonal resets in the skull base	multiple CN deficits, bilateral pyramidal syndrome	7 mos	-	-	Isodense on Postcontrast-CT	hyperintense T2, hypointense T1,	PR	-	alive	
	17-46 (mean, 30)	parasellar, supra-sellar, cerebellopontine, right	embryonal resets in the skull base	diplopia, left pyramidal syndrome	36 mos	-	-	hyperdense, calcification, mild enhance	N/A	PR	-	alive	
		petroclinoid, caverous sinus, right	embryonal resets in the skull base	diplopia, right VI nerve palsy	6 mos	-	-	hyperdense, calcification, mild enhance	hyperintense T2, hypointense T1,	PR	-	alive	
		petroclinoid, interpeduncular, suprasellar cisterns	embryonal resets in the skull base	multiple CN deficits, bilateral pyramidal syndrome	12 mos	-	-	hyperdense, calcification, mild enhance	hyperintense T2, hypointense T1,	PR	-	alive	
Sala et al./ 1998	55/F	petro-occipital junction, right (intradural extension)	petrous bone	vertigo, vomiting, cbll sign,	1 month	-	-	Calcification, osteolysis	hyperintense T2, hypointense T1, strong enhance	GTR	ND	died, postop 7 yr, reoperation at 10, 16, 31, and 43 months after initial op	

−: information is not available, ND: not done, T&O: temporo-occipital, yr: year, CN:cranial nerve, BS: brain stem, ICP: intracranial pressure, cbll: cerebellar, mos: months, CT: computed tomography, MRI: magnetic resonance imaging, T2: T2-weighted image, T1: T1-weighted image, enhance:enhancement, Op: operation, PR: partial resection, GTR: gross total resection, POD: postopeation day, F/U: follow-up.

Table 2. Clinical features of 5 patients with intracranial myxoid chondrosarcoma

Author/yr	Age (yr)/ Sex	Location	Origin	Presentation	Duration of symptom	Skull x-rays	Cerebral angiography	CT	MRI	Op	Radiotherapy	Outcome	F/U
Scott et al./ 1976	39/M	4th ventricle	stroma of the choroid plexus	ICP symptom, cbll sign	9 mos	calcification	avascular mass, hydrocephalus	ND	ND	PR	ND	died of sepsis POD 13 days	
Smith and Davidson/ 1981	12/M	cerebellar hemisphere, left (dural attachment)	meninges	ICP symptom, cbll sign	4 days	ND	avascular mass	hemorrhage, mild enhance, hydrocephalus	ND	GTR	ND	alive, no recurrence	13 mos
Salcman et al./1992	28/F	falx, left	sheath of blood vessels	headache, hemiparesis, dysphasia	2 mos	ND	ND	isodense mass, minimal enhance	hyperintense T2, hypointense T1, modest enhance	GTR	ND	alive, recurred at 10 mos 2nd Op &15,000 cGy ^{125}I-brachytherapy died of local recurrence with meningeal dissemination, POD 3 yr	22 mos
Sato et al./ 1993	43/F	pineal region	mesenchymal cells in the tentorium	blurred vision, gait disturbance	2 mos	-	-	multilobulated, cystic mass, moderate enhance	-	PR	6,000 cGy chemotherapy		
Present case	43/M	parietal cortex, left	?	ICP symptom	2 mos	normal	ND	Isodense mass, severe edema, strong enhance	hyperintense T2, hypointense T1, strong enhance, severe edema	GTR	5,940 cGy photon beam	alive, no recurrence	3 yr

– : information is not available, ND: not done, yr: year, ICP: intracranial pressure, mos: months, CT: computed tomography, MRI: magnetic resonance imaging, T2: T2-weighted image, T1: T1-weighted image, enhance: enhancement, Op: operation, PR: partial resection, GTR: gross total resection, POD: postopeation day, F/U: follow-up, 2nd: second.

Histologically, chordoma consists of epithelial cells with abundant, foamy cytoplasm, resembling the cells in adenocarcinoma (24). Chondroid chordomas have morphologic features similar to those of typical chordomas except the additional features of cartilagenous foci resembling those of chondroma or conventional chondrosarcoma (25). Parachordoma resembles chordoma histologically with nests of uniform-appearing, vacuolated epithelioid cells deposited in a myxochondroid matrix, however, with a wider range of appearance (26, 27). Chordoid meningioma presents as encapsulated mass. Histologically, chordoid meningiomas were composed of meningothelial cells, mimicking the features of chordoma with nests and cords of epithelioid and spindle cells with abundant myxoid matrix, and often associated with peritumoral lymphoplasmacellular infiltration (28). Chordoid glioma occurs preferentially in the third ventricle with a discrete margin (29). Histologically, the tumor also reminiscents of chordoma with cords and lobules of oval-to-polygonal epithelioid cells in a mucoid matrix (29).

Immunohistochemically, chordoma and parachordoma coexpress S-100 protein, cytokeratin and EMA, and the two neoplasms differ in their detailed cytokeratin immunophenotype, whereas myxoid chondrosarcoma consistently lacked cytokeratin (26). Chordoid meningiomas were immunohistochemically consistently negative for S-100 protein, cytokeratin and EMA (30). The cells of chordoid glioma showed diffuse and intense immunoreactivity for GFAP and vimentin, whereas immunoreactivity for EMA and cytokeratin was nonreactive to focally reactive (29, 31, 32). Immunohistochemical finding of present case, showing slight and focal reactivity for S-100 protein, whereas negative immunoreactivity for cytokeratin, GFAP and EMA, is not compatible with neither chordoma and related tumors, chordoid meningioma nor chordoid glioma but is compatible with myxoid

chondrosarcoma.

Primary intracranial myxoid chondrosarcoma is so uncommon that no definitive statement can be made about the optimal treatment and prognosis. However, most patients showed a relatively benign clinical course during the follow-up period. Radical excision might play an important role in the management. Postoperative radiotherapy should be considered to prevent recurrence and progression of the tumor.

REFERENCES

1. Bahr AL, Gayler BW. *Cranial chondrosarcomas. Report of four cases and review of literature. Radiology 1977; 124: 151-6.*
2. Gacek RR. *Diagnosis and management of primary tumors of the petrous apex. Ann Otol Rhinol Laryngol 1975; 84: 1-20.*
3. Hassounah M, Al-Mefty O, Akhtar M, Jinkins JR, Fox JL. *Primary cranial and intracranial chondrosarcoma. A survey. Acta Neurochir (Wien) 1985; 78: 123-32.*
4. Alpers BJ. *Cerebral osteochondroma of dural origin. Ann Surg 1935; 101: 27-37.*
5. Bingaman KD, Alleyne CH, Olson JJ. *Intracranial extraskeletal mesenchymal chondrosarcoma: case report. Neurosurgery 2000; 46: 207-12.*
6. Gerszten PC, Pollack IF, Hamilton RL. *Primary parafalcine chondrosarcoma in a child. Acta Neuropathol 1998; 95: 111-4.*
7. Salcman M, Scholtz H, Kristt D, Numaguchi Y. *Extraskeletal myxoid chondrosarcoma of the falx. Neurosurgery 1992; 31: 344-8.*
8. Heros RC, Martinez AJ, Ahn HS. *Intracranial mesenchymal chondrosarcoma. Surg Neurol 1980; 14: 311-7.*
9. Scott RM, Dickersin R, Wolpert SM, Twitchell T. *Myxochondrosarcoma of the fourth ventricle. Case report. J Neurosurg 1976; 44: 386-9.*
10. Smith TW, Davidson RI. *Primary meningeal myxochondrosarcoma presenting as a cerebellar mass: case report. Neurosurgery 1981; 8: 577-81.*
11. Parker JR, Zarabi MC, Parker JC Jr. *Intracerebral mesenchymal chondrosarcoma. Ann Clin Lab Sci 1989; 19: 401-7.*
12. Raskind R, Grant S. *Primary mesenchymal chondrosarcoma of the cerebrum: report of a case. J Neurosurg 1966; 24: 676-8.*
13. Naufal PM. *Primary sarcomas of the temporal bone. Arch Otolaryngol 1973; 98: 44-50.*
14. Sato K, Kubota T, Yoshida K, Murata H. *Intracranial extraskeletal myxoid chondrosarcoma with special reference to lamellar inclusions in the rough endoplasmic reticulum. Acta Neuropathol 1993; 86: 525-8.*
15. 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.*
16. Scheithauer BW, Rubinstein LJ. *Meningeal mesenchymal chondrosarcoma: Report of 8 cases with review of the literature. Cancer 1978; 42: 2744-52.*
17. Harsh GR IV, Wilson CB. *Central nervous system mesenchymal chondrosarcoma: Case report. J Neurosurg 1984; 61: 375-81.*
18. Rubinstein LJ. *Sarcomas of the nervous system. In : Minckler J (ed) Pathology of the nervous system, vol 2. McGraw-Hill, New York, 1971: 2144-64.*
19. Bourgouin PM, Tampieri D, Robitaille Y, Robert F, Bergeron D, del Carpio R, Melancon D, Ethier R. *Low-grade myxoid chondrosarcoma of the base of the skull: CT, MR, and histopathology. J Comput Assist Tomogr 1992; 16: 268-73.*
20. Mott FW. *Chondrosarcoma springing from the sella turcica. Arch Neurol Psychiat 1899; 1: 432-3.*
21. Sala F, Talacchi A, Beltramello A, Iuzzolino P, Bricolo A. *Intracranial myxoid chondrosarcoma with early intradural growth. J Neurosurg 1998; 42: 159-63.*
22. Lynch PG, Uriburu E. *An intracranial cartilage-containing meningeal tumor. Case report. J Neurosurg 1973; 39: 261-4.*
23. Bernstein M, Perrin RG, Platts ME. *Radiation-induced cerebellar chondrosarcoma. Case report. J Neurosurg 1984; 61: 174-7.*
24. Povysil C, Matejovsky Z. *A comparative ultrastructural study of chondrosarcoma, chordoid sarcoma, chordoma and chordoma periphericum. Pathol Res Pract 1985; 179: 546-59.*
25. Rossiello R, Ferrara G, Varricchio A, Baldi A, Motta S, Motta G. *Chondroid chordoma of the lateral skull base. ORL J Otorhinolaryngol Relat Spec 2001; 63: 114-8.*
26. Folpe AL, Agoff SN, Willis J, Weiss SW. *Parachordoma is immunohistochemically and cytogenetically distinct from axial chordoma and extraskeletal myxoid chondrosarcoma. Am J Surg Pathol 1999; 23: 1059-67.*
27. Fisher C. *Parachordoma exists--but what is it?. Adv Anat Pathol 2000; 7: 141-8.*
28. Couce ME, Aker FV, Scheithauer BW. *Chordoid meningioma: a clinicopathologic study of 42 cases. Am J Surg Pathol 2000; 24: 899-905.*
29. Brat DJ, Scheithauer BW, Staugaitis SM, Cortez SC, Brecher K, Burger PC. *Third ventricular chordoid glioma: a distinct clinicopathologic entity. J Neuropathol Exp Neurol 1998; 57: 283-90.*
30. Mori S, Oka K, Hakozaki H, Soga Y, Hayano M, Oka T, Nakazato Y, Mori N. *Chordoid meningioma. A case report. Pathol Res Pract 2001; 197: 515-8.*
31. Ricoy JR, Lobato RD, Baez B, Cabello A, Martinez MA, Rodriguez G. *Suprasellar chordoid glioma. Acta Neuropathol 2000; 99: 699-703.*
32. Cenacchi G, Roncaroli F, Cerasoli S, Ficarra G, Merli GA, Giangaspero F. *Chordoid glioma of the third ventricle: an ultrastructural study of three cases with a histogenetic hypothesis. Am J Surg Pathol 2001; 25: 401-5.*