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.

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 meningoima 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 18F-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

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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 × 1.0 × 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
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 extraskeletal chondrosarcomas have been less commonly reported than cranial chondrosarcomas and their locations include the cerebral convexity, falx, fourth ventricle,
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 extrasosseous 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 extrasosseous 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 | Site | Presentations | Duration of symptoms | Skull x-rays | Cerebral angiography | CT | MRI | Op | Radiotherapy | Outcome |
|-----------|--------------|----------|------|---------------|----------------------|-------------|-----------------------|----|-----|----|-------------|---------|
| Mott/1999 | 28/M         | parasellar | sella turcica | headache, multiple CN deficits, BS sign | 24 mos | hydropsis, destruction of petrous apex | avascular mass | ND | ND | ND | ND | died several years after the onset of symptoms |
|  | 27/F         | petrous apex, right | foramen lacerum | headache, multiple CN deficits | 24 mos | hyperintense T2, hypointense T1 | PR | ND | ND | ND | died of pneumonia POD 12 days |
| Gacek/1975 | 31/F         | petrous apex, left | foramen lacerum | headache, multiple CN deficits | 24 mos | avascular mass | low dense mass, calcification | ND | GTR | 5,400 cGy proton beam | alive, no recurrence radiation nécrosis |
| Hassounah et al./1985 | 33/F       | posterior fossa, right | cranium, T&O | ICP symptom, cbll sign | 20 mos | calcification | avascular mass | ND | PR | - | alive |
| Bourguin et al./1992 | Three men & Two women | cerebello-pontine, left | embryonal rests in the skull base | multiple CN 2 deficits, bilateral pyramidal syndrome | 2 mos | - | hyperintense T2, hypointense T1 | PR | - | - | alive |
|  | 17-46 (mean, 30) | cerebello-pontine, right | embryonal rests in the skull base | multiple CN 7 deficits, bilateral pyramidal syndrome | 7 mos | - | hyperintense T2, hypointense T1 | PR | - | - | alive |
|  |  | parasellar, supra-sellar, cerebello-pontine, right | embryonal rests in the skull base | diplopia, left pyramidal syndrome | 36 mos | - | hyper-dense, calcification, mild enhance hyper-dense, calcification, mild enhance hyper-dense, calcification, mild enhance hyper-dense, calcification, mild enhance | N/A | PR | - | alive |
|  |  | petroclinoïd, caverous sinus, right | embryonal rests in the skull base | diplopia, right VI nerve palsy | 6 mos | - | 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 | - | hyperintense T2, hypointense T1, strong enhance | GTR | ND | - | died, postop 7 yr, reoperation at 10, 16, 31, and 43 months after initial op |

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- : 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: postoperative day, F/U: follow-up.
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 lymphoplasmacelluar 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 chordosarcoma 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.

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