Primary Intraspinal Mesenchymal Chondrosarcoma: A Case Report and Literature Review

Kuo-Feng Huang, MD; Wen-Ching Tzaan, MD; Chin-Yew Lin[1], MD

Mesenchymal chondrosarcomas are rare malignant tumors of the bone and soft tissue. Extraskeletal mesenchymal chondrosarcomas, especially those that arise in the central nervous system, are even rarer. Most of those described were intracranially located, with only a very few cases having been reported in an intraspinal region. Therapeutic experience with primary spinal mesenchymal chondrosarcomas is also extremely limited. We report on a case of a 21-year-old man with back pain and bilateral progressive weakness and numbness of the lower extremities. A T1-weighted magnetic resonance image revealed a hypointense tumor located at the T8 level. The tumor was completely excised through a posterior approach. Microscopic examination and immunohistochemical studies confirmed the diagnosis of mesenchymal chondrosarcoma. Spinal irradiation and chemotherapy were also administered for prevention of local recurrence and metastasis. The patient has been symptom-free for 1 year after surgery. Herein, we review the 22 cases of primary intraspinal mesenchymal chondrosarcomas in the literature and discuss their clinical presentations, pathology, imaging studies, treatments, and outcomes. *(Chang Gung Med J 2003;26:370-6)*

Key words: mesenchymal chondrosarcoma, primary intraspinal tumor.

In 1959, Lichenstein and Bernstein first reported 2 cases of primitive chondrosarcoma of the bone, which had distinctive histopathological features, and subsequently designated them "mesenchymal chondrosarcoma".[1] Dowling described the first case of a mesenchymal chondrosarcoma confirmed to be of nonosseous origin on the basis of autopsy findings.[2] Subsequently, multiple sites of extraosseous primary occurrence were reported by Guccion et al.[3] It is a rare primary malignant neoplasm of the bone and soft tissue with a propensity towards distant metastases.[4-6] This very rare tumor has to be distinguished from a chondrosarcoma both clinically and histologically. Clinical experience with intraspinal mesenchymal chondrosarcomas is limited. Only a few cases of primary intraspinal mesenchymal chondrosarcoma have previously been reported in the medical literature. We report on a 21-year-old patient with a primary intraspinal mesenchymal chondrosarcoma located at the T8 level which was treated with total excision and postoperative radiotherapy and chemotherapy. A review of the literature on primary intraspinal mesenchymal chondrosarcomas is also presented. To our knowledge, this is the largest and most up-to-date review of a series of detailed clinical analyses of primary intraspinal mesenchymal chondrosarcomas.

CASE REPORT

This 21-year-old man suffered from insidiously

From the Department of Neurosurgery, [1]Department of Pathology, Chang Gung Memorial Hospital, Taipei.
Received: Jun. 24, 2002; Accepted: Oct. 28, 2002
Address for reprints: Dr. Kuo-Feng Huang, Department of Neurosurgery, Chang Gung Memorial Hospital. 222, Maijin Rd., Anle Chiu, Keelung, Taiwan 204, R.O.C. Tel.: 886-2-24313131 ext. 2670; Fax: 886-2-24332655; E-mail: tina1234@ms5.hinet.net

progressive dull back pain for about 6 months. One month prior to admission, his back pain became aggravated and was accompanied by progressively ascending bilateral numbness and weakness of the lower extremities. A general physical examination was normal. Neurological examinations, including mental status, cranial nerves, cerebellar testing, and motor and sensory tests of the upper extremities were also normal. However, there were marked decreased muscle power (3/5) of both lower extremities with increased deep tendon reflexes of the knees and ankles. Pinprick sensation was decreased below the level of T8 bilaterally. Bowel and bladder functions were preserved. Radiographic studies of the thoracolumbar spine showed a suspicious defect in the posterior portion of the T8 vertebral body. Magnetic resonance (MR) images of the thoracic spine revealed a tumor at T8 with a marked erosion defect at the posterior portion of the T8 vertebral body (Fig. 1A, B). The tumor occupied the right anterolateral region of the spinal canal of T8 and had pushed the spinal cord to the opposite side. A clinical and radiological impression of a T8 spinal meningioma was made preoperatively.

T7-T9 laminectomy was performed. A large, firm, reddish, hypervascular tumor was found in the epidural space predominantly on the right side. It did not arise from the dura, but had displaced the dura sac as depicted in the MR image. The tumor was completely removed. Grossly, the tumor tissues appeared grayish-white and pink with a soft to firm consistency. Focal areas contained granules of calcification. On microscopic examination, the tumor revealed 2 distinctive morphologic regions: hypercellular, undifferentiated small round or spindle-shaped cells unevenly alternating with islands of differentiated chondroid tissues. The undifferentiated cellular components appeared in patterns of diffuse or solid sheets with areas of hemangiopericytomatous lesions noted (Fig. 2A, B). The chondroid tissue showed well-differentiated cartilage. Mitotic figures were occasionally noted in the former regions. The transformation between these 2 regions was abrupt. Further immunohistochemical study revealed that the undifferentiated small round or spindle-shaped cells stained positively for neuron-specific enolase (NSE) and negatively for S-100. Alternatively, the well-differentiated cartilaginous components were positive for S-100 but negative for

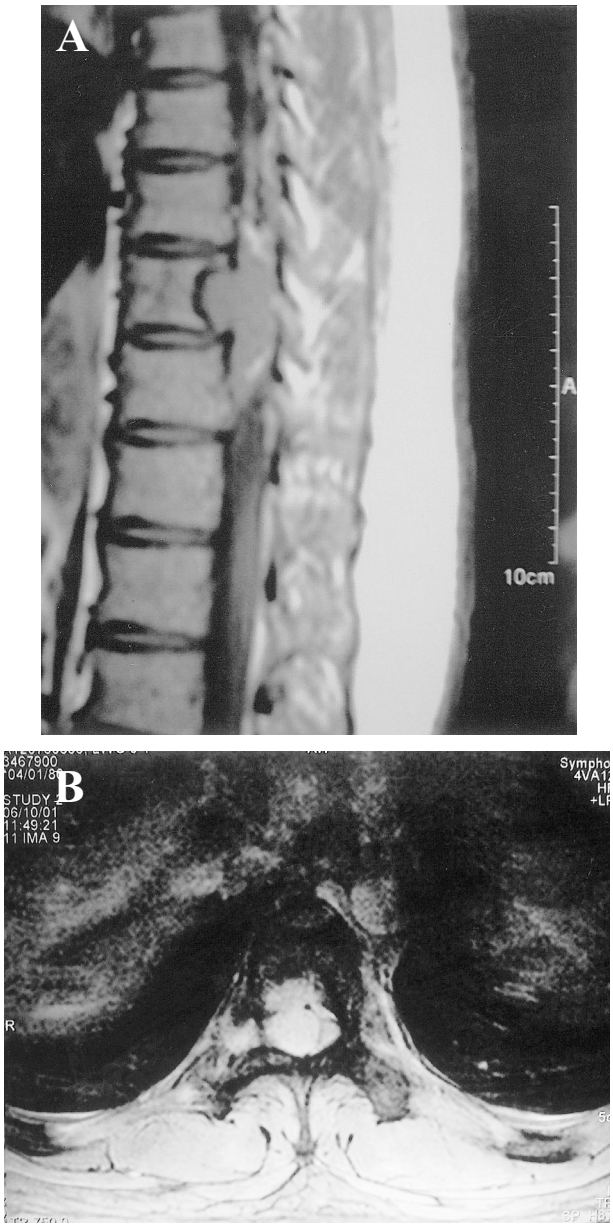

Fig. 1 MR images revealing a tumor at T8 with a marked erosion defect in the posterior portion of the T8 vertebral body. The tumor occupied the right anterolateral region of the spinal canal of T8 and had pushed the spinal cord to the opposite side. (A) T1-weighted sagittal view; (B) T2-weighted, horizontal view.

NSE. Immunohistochemical staining for epithelial membrane antigen (EMA) and that for glial fibrillary acidic protein (GFAP) were negative for both cellular components. These characteristic features and

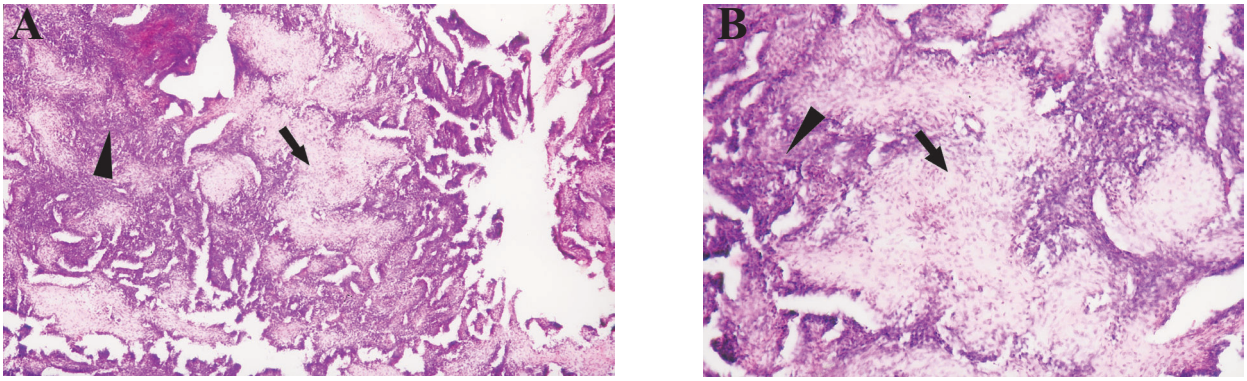

Fig. 2 (A) Low-power-field photomicrograph revealing areas of hemangiopericytoma-like spaces (arrowhead) surrounded by hypercellular undifferentiated mesenchymal cells which are densely stained. Relatively pale staining chondroid components are also shown (arrow) (H&E ×50). (B) Photomicrograph illustrating characteristic biphasic patterns of tumor cells. The central portion shows islands of pale stained chondroid components (arrow). The peripheral areas of the chondroid tissue demonstrate hypercellular small, round, undifferentiated mesenchymal cells (arrowhead) with some of them surrounding hemangiopericytoma-like vascular spaces. (H&E ×100)

immunohistochemical results confirmed the diagnosis of mesenchymal chondrosarcoma.

The postoperative recovery was smooth and rapid with full recovery of strength and sensation in both lower extremities. He returned to his school and recovered well. On the basis of the diagnosis, radiation therapies as well as chemotherapy were prescribed. He accepted radiotherapy of 5000 cGy in 25 fractions and 6 weeks of subsequent chemotherapy (Vincristine, Adriamycin, Doxorubicin, Cyclophosphamide). Follow-up MR images 6 months postoperatively showed no evidence of local recurrence. This patient had been symptom-free for 8 months at the time of this report.

DISCUSSION

Mesenchymal chondrosarcomas are rare tumors that are 2 to 3 times more common in bone than in soft tissue.[5] Primary central nervous system mesenchymal chondrosarcomas are even rarer. Most of those were reported intracranially, but only very rare cases have been reported in intraspinal locations.[2-18]

According to previous reports, extraosseous mesenchymal chondrosarcomas are preponderantly found in young adults.[2-6] They are fully malignant tumors that pursue a rapid clinical course and metastasize in a high percentage of cases.[2-6] The major metastatic sites are the lungs.[2-6] Several cases had a protracted clinical course and late metastases, but there seem to be no evident prognostic relations to the patient's age or to the degree of cellular differentiation.[2-6]

The radiological appearances of mesenchymal chondrosarcomas are those of osteolytic neoplasms with permeative patterns, poor periosteal reactions, and ill-defined margins.[6,7] An irregular sclerotic rim is sometimes encountered.[6,7] There are often stippled or mottled calcifications within the tumors mimicking conventional chondrosarcomas.[5] MR images are better than CT scans because of the multiplanar and non-invasive myelographic imaging, and they allow evaluation of nerve root and spinal canal involvement. However, none of these imaging modalities is capable of differentiating mesenchymal chondrosarcomas from other malignant tumors.

Histological examination is essential for a definitive diagnosis. An important consideration in establishing a diagnosis of a mesenchymal chondrosarcoma is to determine if the lesion has a dimorphic pattern, characterized by areas of undifferentiated primitive mesenchymal cells alternating with chondroid tissue at various stages of differentiation.[1] Characteristically, the small cells are arranged in diffuse patterns and may include large, irregular, branching staghorn-shaped vascular spaces reminiscent of the appearance of a hemangiopericytoma.[1,8] Mitoses may be present within them, in contrast to

regions of chondroid tissue from which they are always absent.[8] Well-differentiated chondrosarcomas, calcifications, and even osteoid formation were reported in the cartilaginous islands.[8] The transformation zones between these 2 components are usually abrupt.[8] Immunohistochemical studies may be used to confirm a diagnosis of mesenchymal chondrosarcoma. The chondroid components are consistently positive for S-100 protein in all cases, including our case.[8] Undifferentiated mesenchymal cells tend to be immunoreactive for vimentin but are usually negative for S-100 protein.[8] However, there is no expression of EMA in either cartilaginous or undifferentiated components.[8] Variable staining for cytokeratin and GFAP has also been reported for undifferentiated tumor cells.[8]

The clinical features of our case and the 22 cases of primary spinal mesenchymal chondrosarcoma reported in the previous literature are summarized in Table 1.[7-18] The age of the patients at presentation ranged from 1 to 52 (mean, 19.4) years. Adolescents seemed to comprise the prevalent age group. Of these patients, 17 were female, and 6 were male. No familial or racial predisposition was noted. The clinical presentations of these cases fit the pattern of progressive expanding masses. The durations of symptoms before diagnosis were usually several months. There were 3 tumors located in the cervical spine, 12 tumors in the thorax, 6 lumbar tumors, and 2 tumors in the sacral spine. Primary mesenchymal chondrosarcomas can be found in any part of the spine, but they mostly occur in the thoracic segment. Almost all of the tumors were described as epidurally located except for 1 located intradurally with attachment to the pia matter. Among them, dural attachments were definitely claimed in 11 of 23 tumors. All patients received surgical excision. Gross total resection (GTR) of the tumor was claimed in 14 of 23 cases. In the other 9 cases, the completeness of resection was unspecified. Obstacles to complete removal of the tumor were the vascularity and, less frequently, diffuse invasion by the tumor. Adjuvant therapy (radiotherapy and/or chemotherapy) was used in 14 cases. Radiation doses applied

Table 1. Data on Previously Reported Cases of Primary Intraspinal Mesenchymal Chondrosarcomas

Case	Author	Year	Age	Gender	Level	Dura attachment	Treatment*	Post-operative course	Survival time
1	Scheithauer-1	1978	15	F	T9-10	+	R	Well	Alive after 2 yr
2	Scheithauer-2	1978	18	F	T9	+	GTR	Recurrence at 6 yr	Alive after 9 yr
3	Scheithauer-3	1978	7	F	T10	+	R	Well	Alive after 3 yr
4	Scheithauer-4	1978	5	M	L2-4	+	R	Well	Alive after 2 yr
5	Scheithauer-5	1978	17	M	T6	+	R	Metastases at 3 mon	Died after 3 mon
6	Harsh GR	1984	28	F	T10-11	+	GTR+RT+CT	Local recurrence at 6 yr	Alive
7	Chan HS-1	1984	13.5	F	T9-10	-	R	Metastases to lung and brain	Died after 4 weeks
8	Chan HS-2	1984	10.5	F	T1-4	+	GTR+RT+CT	Well	Alive after 18 mon
9	Reif J	1987	3	M	L1-5	-	GTRx3+RT+CT	Recurrence and metastasis	Died after 19 mon
10	Lee ST	1989	18	F	T5-6	+	GTR+RT	Well	Alive after 3 yr
11	Di Lorenzo	1989	40	F	L5-S1	-	GTR+RT+CT	Well	Alive after 5 yr
12	Nguyen	1993	20	F	S1	-	R	Well	Alive after 14 mon
13	Ranjan	1994	52	M	C3-6	Intradural	GTR	Well	Alive after 6 mon
14	Rushing-1	1996	14	F	T12-L2	-	GTR+RT+CT	Well	Alive after 5 yr
15	Rushing-2	1996	19	M	T5-10	+	GTR+RT	Well	Alive after 14 yr
16	Rushing-3	1996	21	F	L5	-	GTR	Well	Alive after 1 yr
17	Rushing-4	1996	32	F	C5-6	-	GTR+RT+CT	Well	Alive after 3 yr 2 mon
18	Rushing-5	1996	48	F	T10-12	-	GTR+RT, re-Opx2	Metastases to lung and brain	Died at 7 yr
19	Tasdemiroglu-1	1996	1	F	L1-2	+	R+RT+CT	Well	Alive after 20 mon
20	Tasdemiroglu-2	1996	12	F	L5	+	GTR+RT+CT	Well	Alive after 10 mon
21	Kruse	1997	9	F	C2.3	-	R+RT+CT	Recurrence and metastasis	Died at 5 yr
22	Biagni	2000	23	F	Sacrum	-	R+RT+CT	Well	Alive
23	Huang KF	2002	21	M	T8	-	GTR+RT+CT	Well	Alive after 8 mon

Abbreviations: R: Resection; GTR: gross total resection; RT: radiotherapy; CT: chemotherapy.

ranged from 4400 to 6000 cGy. Chemotherapy was applied in 11 of 23 patients; the medications of chemotherapy included Ifosfamide, Doxorubicin, Cisplatin, VP-16, Carboplatinum, Epirubicin, Cyclophosphamide, Adriamycin, Methotrexate, and Actinomycin D.

The duration of follow-up for these cases ranged from 4 weeks to 14 years with an average of 28 months. Four recurrences were reported. Five cases experienced systemic metastasis. The major metastatic sites were the lungs and brains. Totally, 15 of 23 patients were well and free of malignancy in the postoperative course. Five patients died of the disease. The duration of survival ranged from 4 weeks to 14 years, with the average of 33 months.

Generally, the prognosis with a mesenchymal chondrosarcoma is poor because of hematogenous and lymphatic metastases.[2-6] Nakashima et al. demonstrated 5- and 10-year survival rates of 54.6% and 27.3%, respectively.[5] But some authors have suggested that intraspinal mesenchymal chondrosarcomas with dura attachment have a more-favorable prognosis in comparison with those at other locations.[7,9,10,12] This may be because spinal cord compression by small tumors leads to early diagnosis and early surgical intervention. The limited follow-up period and small number of these cases preclude any definite conclusions. Curettage alone or incomplete excision leads to a high rate of recurrence or metastasis. Scheithauer and Rubinstein were the first to recognize the limited significance of 5-year disease-free survival in patients with meningeal mesenchymal chondrosarcoma.[9] Salvador reported a patient who had a local recurrence at 9.6 years after the initial resection.[6]

No chemotherapeutic agents have been proven to be of benefit for mesenchymal chondrosarcomas as isolated treatment. Several authors have suggested that chemotherapy, with or without radiotherapy, may aid in local control.[7,8,10,13,16-18] The benefits of chemotherapy and radiation therapy are not evident even though some improvement was seen in some cases.[7,8,10,13,16-18]

In summary, we report a case with a primary intraspinal mesenchymal chondrosarcoma who presented with the symptoms of acute spinal cord compression. MRI was the best imaging modality for the assessment of the neoplasm and for the surgical decision-making process. Histological study is mandatory for a final pathological diagnosis. To the present, radical surgical excision combined with chemotherapy or radiotherapy appears to be the treatment of choice.

REFERENCES

1. Lichtenstein L, Bernstein D. Unusual benign and malignant chondroid tumors of the bone. A survey of some mesenchymal cartilage tumors and a malignant chondroblastic tumor including a few multicentric ones, as well as many atypical benign chondroblastomas and chondromyxoid fibromas. Cancer 1959;12:1142-57.
2. Dowling EA. Mesenchymal chondrosarcoma. J Bone Joint Surg (Am) 1964;46:747-54.
3. Guccion JG, Font RL, Enzinger FM. Extraskeletal mesenchymal chondrosarcoma. Arch Pathol 1973;95:336-40.
4. Huvos AG, Rosen G, Dabska M, Marcove RC. Mesenchymal chondrosarcoma. A clinicopathologic analysis of 35 patients with emphasis on treatment. Cancer 1983;51:1230.
5. Nakashima Y, Unni KK, Shives TC. Mesenchymal chondrosarcoma of bone and soft tissue. A review of 111 cases. Cancer 1986;57:2444-53.
6. Salvador AH, Beabout JW, Dahlin DC. Mesenchymal chondrosarcoma observations in 30 new cases. Cancer 1971;28:605-15.
7. Chan HS, Turner-Gomes SO, Chuang SH, Fitz CR, Daneman A, Martin DJ, Becker LE. A rare cause of spinal cord compression in childhood from intraspinal mesenchymal chondrosarcoma. A report of two cases and review of the literature. Neuroradiology 1984;26:323-7.
8. Rushing EJ, Armonda RA, Ansari Q, Mena H. Mesenchymal chondrosarcoma: a clinicopathologic and flow cytometric study of 13 cases presenting in the central nervous system. Cancer 1996;77:1884-91.
9. Scheithauer BW, Rubinstein LJ. Meningeal mesenchymal chondrosarcoma: report of 8 cases with review of the literature. Cancer 1978;42:2744-52.
10. Harsh GR IV, Wilson GB. CNS mesenchymal chondrosarcoma (case report). J Neurosurgery 1984;61:375-81.
11. Reif J, Graf N. Intraspinal mesenchymal chondrosarcoma in a three-year-old boy. Neurosurg Rev 1987;10:311-4.
12. Lee ST, Lui TN, Tsai MD. Primary intraspinal dura mesenchymal chondrosarcoma. Surg Neurol 1989;31:54-7.
13. Di Lorenzo N, Palatinsky E, Artico M, Palma L. Dural mesenchymal chondrosarcoma of the lumbar spine. Case report. Surg Neurol 1989;31:470-2.
14. Nguyen BD, Daffner RH, Dash N, Rothfus WE, Nathan G, Toca AR Jr. Case report 790. Mesenchymal chondrosarcoma of the sacrum. Skeletal Radiol 1993;22:362-6.
15. Ranjan A, Chacko G, Joseph T, Chandi SM. Intraspinal mesenchymal chondrosarcoma - case report. J Neurosurgery 1994;80:928-30.

16. Tasdemiroglu E, Bagatur E, Ayan I, Darendeliler E, Patchell RA. Primary spinal column sarcomas. Acta Neurochir 1996;138:1261-6.
17. Kruse R, Simon RG, Stanton R, Grissom LE, Conard K, Mesenchymal chondrosarcoma of the cervical spine in a child. Am J Orthop (Chatham, NJ) 1997;26:279-82.
18. Biagini R, Orsini U, Demitri S, Ruggieri P, Ferrari S, Bertoni F. Mesenchymal chondrosarcoma of the sacrum: a case report and review of the literature. Tumori 2000; 86:75-8.

原發性脊椎內間質軟骨肉瘤：病例報告及文獻回顧

黃國烽 昝文清 林進耀[1]

間質軟骨肉瘤是一種相當少見的骨骼與軟組織的惡性種瘤。在骨骼架構以外的間質軟骨肉瘤特別是發生在中樞神經系統是更少見。大部份在中樞神經的間質軟骨肉瘤也以在顱內居多，間質軟骨肉瘤發生在脊椎只有少數的病例報告。原發性脊椎內間質軟骨肉瘤治療的經驗是非常的有限。我們報告一例21歲的男性有背痛與進行性的兩下肢無力與麻木。T1核磁共振影像呈現出在T8的部位有低強度的腫瘤。這個腫瘤是由後方手術並完全切除。顯微鏡檢查與免疫組織生化研究確定其診斷是間質軟骨肉瘤。脊椎放射線治療與化學治療也同時給予以預防局部的復發與轉移。這個病患在手術之後一年的追蹤中完全沒有症狀。在此，我們也回顧了目前文獻報告過的22例原發性脊椎內間質軟骨肉瘤，並且討論其臨床表現、病理、影像檢查、治療與預後。(長庚醫誌 2003;26:370-6)

關鍵字：間質軟骨肉瘤，原發性脊椎內腫瘤。

長庚紀念醫院 基隆院區 神經外科，[1]病理科
受文日期：民國91年6月24日；接受刊載：民國91年10月28日。
索取抽印本處：黃國烽醫師，長庚紀念醫院 神經外二科。基隆市麥金路222號。Tel.: (02)24313131轉2670; Fax: (02)24332655; E-mail: tina1234@ms5.hinet.net