

## Intracranial Osteosarcoma After Radiosurgery —Case Report—

Naoko SANNO, Shinkichi HAYASHI, Toshiro SHIMURA, Shotaro MAEDA\*,  
and Akira TERAMOTO

Departments of Neurosurgery and \*Pathology, Nippon Medical School, Tokyo

### Abstract

A 56-year-old woman presented with an intracranial osteosarcoma at the site of previous radiosurgery, manifesting as sudden onset of headache and left hemiparesis with aphasia. She had a previous history of stereotactic radiosurgery for an intracranial tumor under a diagnosis of falk meningioma. Computed tomography showed intratumoral and peritumoral hemorrhage at the right parietofrontal region. Gross total resection of the tumor with hematoma was performed. The histological diagnosis was osteosarcoma. Sarcomatous change is a rare complication of radiotherapy. This case illustrates that osteosarcoma may develop years after radiosurgery for benign brain neoplasm.

Key words: osteosarcoma, radiosurgery-induced neoplasm, brain neoplasm

### Introduction

Osteosarcoma is a highly malignant tumor of mesenchymal cell origin, and is the most common primary cancer in the bones. Intracranial osteosarcoma is rare as a primary tumor and usually occurs as metastases. Only a few cases of primary intracranial osteosarcoma have been described.<sup>2-5,8,18,20,24,25)</sup> Here we report a case of intracranial osteosarcoma which developed at the site of radiosurgery for a benign neoplasm.

### Case Report

A 53-year-old woman was referred to our clinic because of headache and head heaviness in 1997. Computed tomography (CT) and magnetic resonance (MR) imaging revealed an intracranial mass, 20 mm in diameter. MR imaging with contrast medium showed a homogeneously enhanced, well-demarcated mass attached to the falk (Fig. 1). The patient had previously suffered from breast cancer which was in remission at that time. The possibility of metastatic lesion was excluded carefully. CT of the thorax and abdomen failed to discover any other tumor. Tumor markers including alpha-fetoprotein,

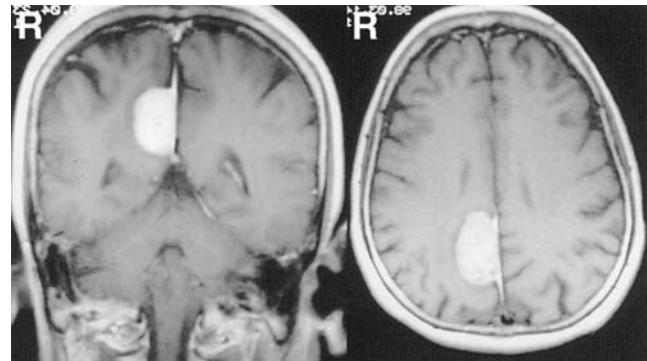
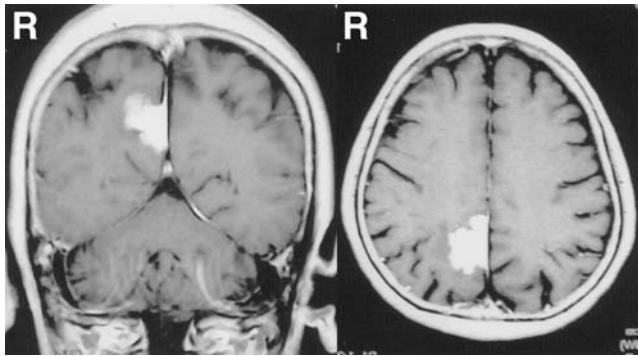


Fig. 1 T<sub>1</sub>-weighted magnetic resonance images showing a mass lesion in the right frontoparietal parasagittal region, and with contrast medium showing a homogeneously enhanced lesion attached to the falk with so-called dural tail sign.

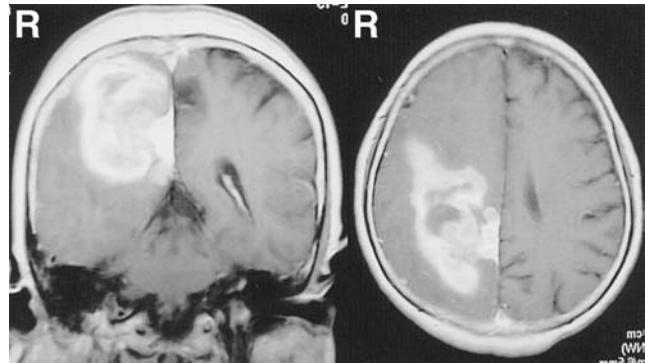
carcinoembryonic antigen, and CA19-9 were negative. Scintigraphy of the whole body revealed no abnormal uptake. The clinical and radiological diagnosis of the tumor was falk meningioma. The patient refused the recommended operation. She underwent three courses of radiosurgery for the

Received March 12, 2003; Accepted August 1, 2003

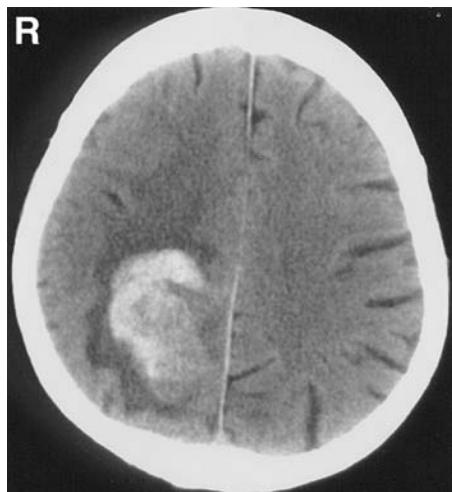
Author's present address: N. Sanno, M.D., Department of Neurosurgery, Nippon Medical School Tamanagayama Hospital, Tama, Tokyo, Japan.



**Fig. 2** T<sub>1</sub>-weighted magnetic resonance images with contrast medium 4 years after radiosurgery (60 Gy) showing shrinkage of the lesion.



**Fig. 4** T<sub>1</sub>-weighted magnetic resonance images with contrast medium showing hemorrhage with edema from the lesion.



**Fig. 3** Brain computed tomography scan revealing intra- and peritumoral hemorrhage in the right frontoparietal region.

intracranial tumor using a 201-source <sup>60</sup>Co gamma knife system at another hospital during 6 months in 1998. The maximum and marginal radiation doses were 60 and 30 Gy, respectively. After the procedure, she came to our clinic every 6 months for follow-up CT or MR imaging. The latest MR imaging in September 2001 showed shrinkage of the tumor (Fig. 2). She remained without symptoms for 4 years.

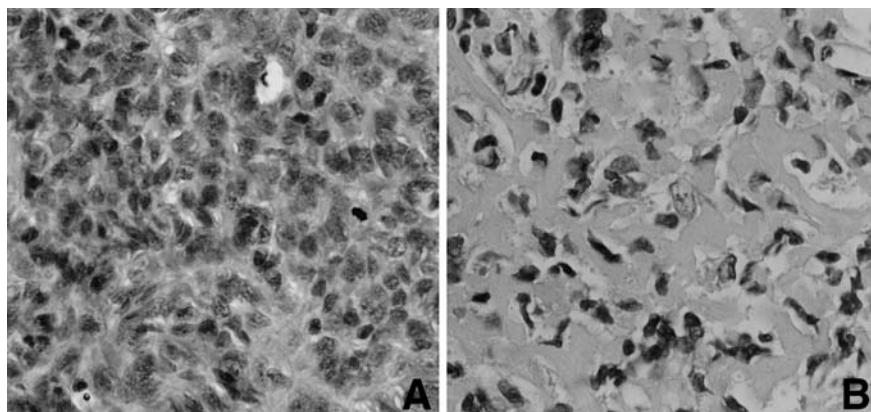
The patient presented to our emergency room because of sudden onset of headache, left hemiparesis, and aphasia in May 2002. Brain CT revealed intra- and peritumoral hemorrhage (Fig. 3). MR imaging revealed a brain tumor in the right parietal lobe (Fig. 4). Angiography showed no vessel abnormality such as arteriovenous malformation or

cerebral aneurysm. CT of the thorax and abdomen discovered no other tumor. Scintigraphy of the whole body revealed no abnormalities.

Craniotomy exposed the fibrous and firm tumor attached to the falx. The skull was not involved. The tumor with the attached falx and hematoma were grossly totally removed. Postoperatively, her right hemiparesis improved gradually with eventual full recovery except for mild motor aphasia and agraphia. Complete systemic evaluation showed no evidence of other disease. Brain MR imaging and technetium-99m bone scintigraphy showed only postoperative changes.

Four weeks after surgery, adjuvant combination chemotherapy was initiated, consisting of high-dose methotrexate, doxorubicin, and cisplatin. Twelve months after diagnosis, MR imaging of the brain displayed nonspecific changes in the white matter. Follow-up bone scintigraphy, and chest and abdominal CT showed no abnormalities.

Histological examination showed the tumor consisted of small round cells with neoplastic osteoid or bone lamellae (Fig. 5). Vascularized medullary-like structures were observed in some areas whereas intratumoral hemorrhage was not observed. Mitotic figures were frequently observed. There was no evidence of meningioma or metastatic tumor in any of the resected tissue. Immunohistochemical staining was negative for neuron-specific enolase, S-100 protein, and glial fibrillary acidic protein, and slightly positive for epithelial membrane antigen and vimentin. The Ki-67 labeling index measured using MIB-1 monoclonal antibody was 8.9%. The histological diagnosis was malignant osteosarcoma.



**Fig. 5** Photomicrographs showing (A) the tumor consisted of anaplastic small round cells with frequent mitotic figures, and (B) neoplastic osteoid cells with marked nuclear anaplasia and bone lamellae. HE stain, original magnification  $\times 200$ .

## Discussion

The delayed risk of both benign and malignant neoplasms in tissues exposed to conventional radiation therapy is well known and has an incidence of about 0.5/1000 after 10 years.<sup>1,23)</sup> Sarcomatous change is a rare complication of radiation.<sup>1,12,21,22)</sup> A sarcoma, usually high grade, will develop in 1 in 1000 patients treated with conventional radiotherapy who survive for 5 years.<sup>1)</sup> The latency period ranges from 3 to 25 years. The criteria for postradiation sarcoma include development of the sarcoma within the radiation field and period of latency of at least 3 years between radiation and malignant tumor development.<sup>4)</sup>

The present case of intracranial osteosarcoma at the site of radiosurgery for benign neoplasm does meet the criteria for radiation-induced tumors.<sup>7)</sup> These criteria require that the secondary tumor arises in the irradiated field; the latency period is at least several years; histological and/or imaging evidence is available of the initial tumor; histological confirmation is obtained of the secondary neoplasm; and the secondary tumor must differ histologically from the original irradiated tumor. No previous histological results were available in the present case to confirm that the osteosarcoma differed from the primary lesion. We believe that the primary lesion was benign tumor because no change in size occurred for at least 4 years. The histology of the resected tumor showed highly malignant osteosarcoma. We speculate that the radiosurgery may have induced malignant degeneration. The present patient had a history of previous breast cancer. Whether this patient was more prone to the development of malignant neoplasm remains unknown.

Stereotactic radiosurgery implies high-precision focusing of beams of radiation toward a focal and sharply circumscribed intracranial target volume to achieve tissue destruction or arrest of tumor

growth.<sup>14)</sup> This method has been used in the treatment of a variety of intracranial lesions, including arteriovenous malformations, metastatic tumors, gliomas, pituitary adenomas, acoustic neurinomas, and meningiomas.<sup>6,11,13,16,17)</sup> Experience in using radiosurgery for benign intracranial lesions is increasing. Irradiation-induced malignancy after exposure to radiosurgery is to be anticipated, but has so far been reported in only a few patients.<sup>2,10,19,27)</sup> The radiobiological effects of radiosurgery on intracranial tumors typically cause central degeneration or necrosis of the tumor and peripheral proliferative vascular changes in postmortem and surgical specimens.

Modern treatment for osteosarcoma includes neoadjuvant chemotherapy, surgery, and postoperative chemotherapy. Most patients with primary brain osteosarcoma received adjuvant chemotherapy using high-dose methotrexate, adriamycin, and cisplatin.<sup>9,15,26)</sup> In the present case, we decided against radiotherapy because the present patient had received three courses of radiosurgery. Recently, stereotactic radiosurgery has been increasingly applied for various intracranial lesions. However, the options should be considered carefully for easily accessible benign lesions.

## References

- 1) Aanesen JP, Olofsson J: Irradiation-induced tumours of the head and neck. *Acta Otolaryngol (Stockh)* 360: 178-181, 1979
- 2) Bance M, Guha A: Radiation-induced malignant tumors after stereotactic radiosurgery. *Otol Neurotol* 22: 124-125, 2001
- 3) Bane BL, Evans HL, Ro JY: Extraskeletal osteogenic sarcoma: A clinicopathologic review of 26 cases. *Cancer* 66: 2762-2770, 1990
- 4) Bar-Sela G, Tzuk-Shina T, Zaaron M, Vlodarsky Y, Tsalik M, Kuten A: Primary osteogenic sarcoma arising from the dura mater: case report. *Am J Clin Neurol Med Chir (Tokyo)* 44, January, 2004

- Oncol 24: 418–420, 2001
- 5) Bauman GS, Wara WM, Ciriello SF, Davis RL, Zoger S, Edwards MS: Primary intracerebral osteosarcoma: a case report. *J Neurooncol* 32: 209–213, 1997
  - 6) Brada M: Radiosurgery for brain tumours. *Eur J Cancer* 27: 1545–1548, 1991
  - 7) Cahan WG, Woodard HQ, Higinbotham NL, Stewart FW, Coley BL: Sarcoma arising in irradiated bone: report of eleven cases. *Cancer* 82: 8–34, 1998
  - 8) Cannon TC, Bane BL, Kistler D: Primary intracerebellar osteosarcoma arising within an epidermoid cyst. *Arch Pathol Lab Med* 122: 737–739, 1998
  - 9) Eilber F, Giuliano A, Eckardt J, Patterson K, Moseley S, Goodnight J: Adjuvant chemotherapy for osteosarcoma: a randomized prospective trial. *J Clin Oncol* 5: 21–26, 1987
  - 10) Gnanalingham KK, Chakraborty A, Galloway M, Revesz T, Powell M: Osteosarcoma and fibrosarcoma caused by postoperative radiotherapy for a pituitary adenoma. Case report. *J Neurosurg* 96: 960–963, 2002
  - 11) Goodman ML: Gamma knife radiosurgery: current status and review. *South Med J* 83: 551–554, 1990
  - 12) Kaido T, Hoshida T, Uranishi R, Akita N, Kotani A, Nishi N, Sakaki T: Radiosurgery-induced brain tumor. Case report. *J Neurosurg* 95: 710–713, 2001
  - 13) Kihlström L, Karlsson B, Lindquist C: Gamma knife surgery for cerebral metastases. *Acta Neurochir Suppl (Wien)* 52: 87–89, 1991
  - 14) Leksell L: The stereotactic method and radiosurgery of the brain. *Acta Chir Scand* 102: 316–319, 1951
  - 15) Link MP, Goorin AM, Horowitz M, Meyer WH, Belasco J, Baker A, Ayala A, Shuster J: Adjuvant chemotherapy of high grade osteosarcoma of the extremity. *Clin Orthop* 270: 8–14, 1991
  - 16) Lunsford LD, Kondziolka D, Flickinger JC: Stereotactic radiosurgery for arteriovenous malformations of the brain. *J Neurosurg* 75: 512–524, 1991
  - 17) Pollock BE, Lunsford LD, Kondziolka D: Outcome analysis of acoustic neuroma management: a comparison of microsurgery and stereotactic radiosurgery. *Neurosurgery* 36: 215–229, 1995
  - 18) Reznik M, Lenelle J: Primary intracranial osteosarcoma. *Cancer* 68: 793–797, 1991
  - 19) Shamisa A, Bance M, Nag S, Tator C, Wong S, Noren G, Guha A: Glioblastoma multiforme occurring in a patient treated with gamma knife surgery. Case report and review of the literature. *J Neurosurg* 94: 816–821, 2001
  - 20) Sipos EP, Tamargo RJ, Epstein JI, North RB: Primary intracerebral small cell osteosarcoma in an adolescent girl: report of a case. *J Neurooncol* 32: 169–174, 1997
  - 21) Smith MM, Thompson JE, Castillo M: Radiation-induced cerebral osteogenic sarcoma. *AJR Am J Roentgenol* 167: 1067, 1996
  - 22) Tanaka S, Nishio S, Morioka T, Fukui M, Kitamura K, Hikita K: Radiation induced osteosarcoma of the sphenoid bone. *Neurosurgery* 25: 640–643, 1989
  - 23) Waga S, Handa H: Radiation-induced meningioma: with review of literature. *Surg Neurol* 5: 215–219, 1976
  - 24) Walker MT, Toye LR, Coons SW, Porter RW, Wallace RC: Intradural primary chondroblastic osteosarcoma: case report. *AJNR Am J Neuroradiol* 22: 1960–1962, 2001
  - 25) Wang AM, Fitzgerald TJ, Lichtman AH, Power TC, Zamani AA, Haykal HA, Rumbaugh CL: Neuroradiologic features of primary falx osteosarcoma. *AJNR Am J Neuroradiol* 7: 729–732, 1986
  - 26) Weiner MA, Harris MB, Lewis M, Jones R, Sherry H, Feurer EJ, Johnson J, Lahman E: Neoadjuvant high dose methotrexate, cisplatin and doxorubicin for the management of cancer patients with non-metastatic osteosarcoma. *Cancer Treat Rep* 70: 1431–1432, 1986
  - 27) Yu JS, Yong WH, Wilson D, Black KL: Glioblastoma induction after radiosurgery for meningioma. *Lancet* 356: 1576–1577, 2000

---

Address reprint requests to: N. Sanno, M.D., Department of Neurosurgery, Nippon Medical School Tamanagayama Hospital, 1-7-1 Nagayama, Tama, Tokyo 206-8512, Japan.