

# Malignant Giant Cell Tumor of the Skull

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Giant cell tumor(GCT) is a rare primary bone tumor that seldom involves the skull. Malignant change in the GCT series also develops on rare occasions, but when it does, it most commonly occurs several years after radiation therapy. Furthermore, the malignant change from benign GCT without radiation therapy is extremely rare. The authors present a case of primary malignant GCT that received no previous radiation therapy and that arose from multiple areas of the skull, predominantly in the parieto-occipital region.

**KEY WORDS :** Giant cell tumors · Skull.

## Introduction

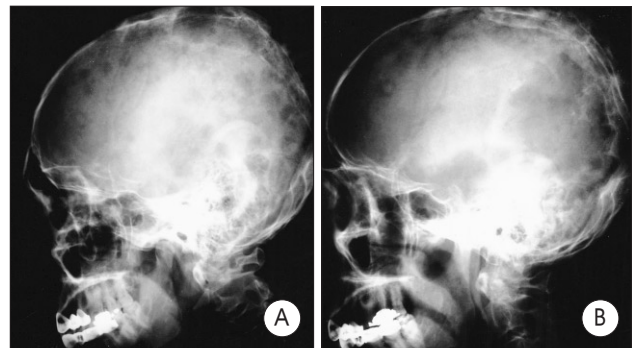
Giant cell tumor(GCT) is a rare tumor that comprises only 5% of all primary tumors of bones. Of these, the majority of cases occur in the epiphysis of long bones<sup>10,17</sup>. It predominantly affects women between the third and fourth decades. It rarely occurs in the skull, where it preferentially develops in the sphenoid and temporal bones. It is a usually benign but potentially aggressive lesion with local recurrence and metastases<sup>3</sup>. Giant cell tumors are usually a single lesion, but multicentric GCTs occur in approximately 1% of all patients<sup>7</sup>. Malignant GCTs, whether representing primary malignancy or secondary change from an originally benign tumor, are extremely rare. Malignant change usually occurs several years after radiation therapy<sup>17</sup>.

Authors present a case report about a patient with multicentric malignant GCT located in the parieto-occipital bones. The patient underwent operations three times because of tumor recurrences at the original site. After the second operation, radiation therapy was done. However, the tumor extended to the bilateral brain parenchyma, and the patient died twenty-one months after the first operation.

## Case Report

A 63-year-old male was admitted after showing signs of decreased visual acuity and field, hearing impairment

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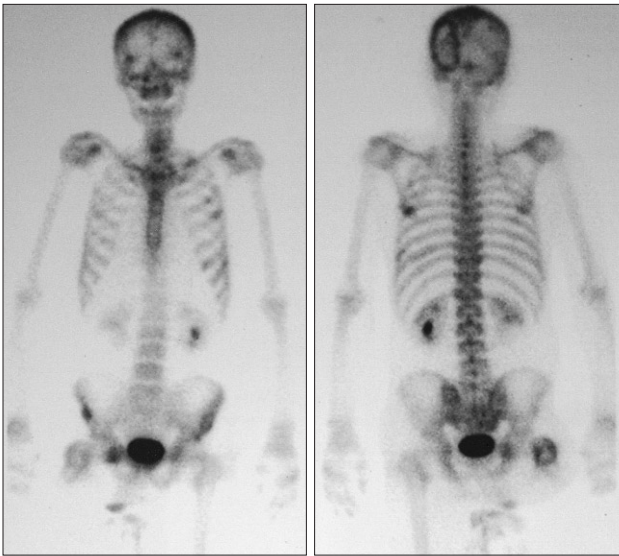
**Fig. 1.** A : Five years ago, skull X-ray showing multiple osteolytic lesions and a 4 cm sized osteolytic lesion on vertex, B : At admission, the osteolytic lesion on the left parieto-occipital area is aggravated.

of left side, soft palpable mass, and tenderness of scalp for two months.

Five years ago, he had received a bone biopsy on his vertex due to the presence of multiple osteolytic lesions in the skull, pelvis, greater trochanter of right femur, pedicle of twelfth thoracic vertebra and right clavicle. The histopathologic diagnosis was a multicentric GCT.

In admission, the physical examination demonstrated a soft palpable mass (3 × 3 × 3cm) and tenderness on the left parieto-occipital scalp. The neurologic examination showed right homonymous hemianopsia and hearing impairment on the left side. Routine laboratory studies did not detect any abnormal findings. Radiographic findings revealed multiple osteolytic lesions of the skull, including the huge osteolytic lesion in the left parieto-occipital region (Fig. 1A, B).

A radionuclide bone scan showed the area of decreased uptake in the lesions corresponding to the abnormal areas shown in radiographic study and increased uptake of surrounding area in the left parieto-occipital bone. Increased uptake in radionuclide bone scan was observed in the right

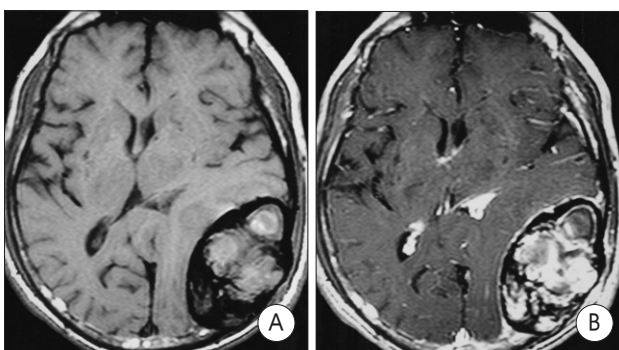


**Fig. 2.** A radionuclide bone scan showing the area of decreased uptake and increased uptake of surrounding area in the left parieto-occipital bone.

pelvis, the left anterior superior iliac spine, the right proximal femur, the right sacro-iliac joint, and the third and fourth ribs. The left parieto-occipital bone lesion was extended, compared to a previous bone scan (Fig. 2).

The magnetic resonance imaging of the brain demonstrated a well demarcated and heterogeneously enhancing mass lesion located in the left parieto-occipital area. The mass lesion seems to originate from the skull showing heterogenous signal intensity in the centers, and low signal intensity on the periphery on T1 weighted image (Fig. 3A, B).

The patient underwent a resection of the tumor and surrounding osteolytic skull lesion. The tumor was measured 8×9×6cm with central necrosis and lobulated by bony septum. The tumor extended to the level of left transverse sinus inferiorly and sagittal sinus superiorly. There was massive



**Fig. 3.** A : The T1-weighted axial magnetic resonance image shows an extraaxial huge mass in the left parieto-occipital area, B : The Gadolinium-enhanced T1-weighted axial image shows the heterogenous enhancement of the lesion.

bleeding during the operation because of the hypervascular nature of the tumor. Five pints of packed RBC was transfused. The tumor was removed gross-totally. The underlying dura and brain were not apparently invaded.

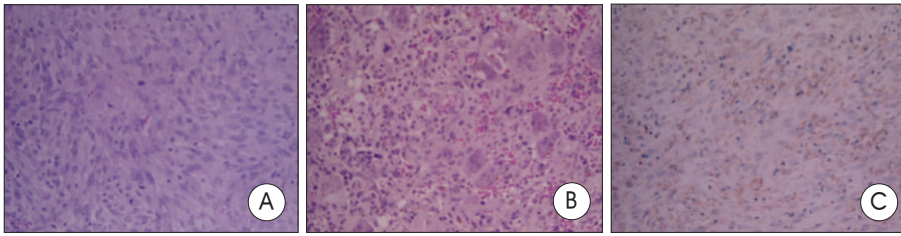
The histopathologic findings revealed a characteristic storiform pattern consisted of spindle-or ovoid-shaped cells showing atypia and mitosis, and of many multi-nucleated giant cells (Fig. 4A, B). Immunohistochemical stain for vimentin was positive (Fig. 4C). These findings converge to the malignant transformation of a GCT, all of which lead to a diagnosis of malignant fibrous histiocytoma.

Two months after the first operation, he was admitted again because of dysarthria, gait disturbance, dysphagia, and a palpable mass on the left temporo-parieto-occipital area. Magnetic resonance imaging demonstrated a recurrence of the tumor larger than the initial size with heterogenous signal intensity in the centers, and low signal intensity on the periphery. Venous angiography shows obstruction of the left transverse sinus. Gross total removal of the tumor was done again. Because of the rapid tumor recurrence after the first operation, radiation therapy was performed after the second operation with a total dose of 5040cGy for five weeks. Twenty-one months after the first operation, the tumor extended to the bilateral brain parenchyma, and then the patient died.

## Discussion

A tumor originating from the skull is uncommon consisting of about 2.5% of all primary bone tumors<sup>6,11</sup>. Giant cell tumor of the bone is also uncommon, which accounts for 5% of primary bone tumors<sup>21</sup>. Giant cell tumor usually occurs in the epiphysis of long bones, involving, in order of frequency, the lower end of the femur, the upper end of the tibia, and the lower end of the radius. A small portion of GCT also occurs in the sacrum, the patella, the vertebra and the skull<sup>4,12,16,17</sup>. Giant cell tumor rarely develops in the skull. The sphenoid and temporal bones are most commonly affected by GCTs, while other cranial bones are affected infrequently<sup>3,13,17,18</sup>. Leonard, et al.<sup>13</sup> reviewed 2,404 cases of bone tumors, and reported that only 24 (1%) of 2,404 cases occurred in the cranium excluding the jaw bones. Motomochi, et al.<sup>15</sup> analyzed 22 cases of GCT of the cerebral cranium, other than the sphenoid bone. The most frequent site was the temporal bone, with 15 cases. Three were in the occipital bone, two in the frontal bone, one in the parietal bone, and one in the frontoparietal area. Giant cell tumors in the skull are usually a typical solitary lesion. But several large

## Malignant Giant Cell Tumor



**Fig. 4.** A : The tumor shows spindle or ovoid-shaped tumor cells that are arranged in a storiform pattern, mitosis, and nuclear atypia (H&E,  $\times 200$ ), B : Another part of tumor shows numeric multinucleated giant cells (H&E,  $\times 200$ ), C : The immuno-histochemical stain for vimentin was positive and the others are negative ( $\times 200$ ).

series of GCTs report multicentric tumors. Less than 50 cases of multicentric GCTs have been reported in the literature. The possible pathogenesis of multicentric GCT includes direct extension, metastasis, and multiple independent foci of disease<sup>19</sup>. In metastasis with GCTs, the frequency ranges from 1 to 6% in larger series. The most common location is in the lungs, but other sites such as the regional lymph nodes, the mediastinum, and the pelvis are reported as well. The mortality rate of the metastatic disease is approximately 25%<sup>4</sup>.

In this report, osteolytic lesions are located in the patient's skull, the right clavicle, the right greater trochanter of a femur, the left pedicle of 12th thoracic vertebra, and the pelvis, all of which occurs in multicentric form. In the skull, the lesion was located predominantly in the parieto-occipital area, which is extremely uncommon considering the lesion's preferred location. A chest X-ray showed no metastatic lesion.

There is a predominance in females, and the age of occurrence is usually in the third and fourth decades<sup>18</sup>. However, our patient was male in the 7th decade.

On x-ray imaging, the GCT usually shows the nonspecific appearance of an expansile, destructive soft-tissue mass, with no typical radiologic features<sup>3,18</sup>. It is a radiolucent expanding lesion. Computed tomography and magnetic resonance imaging are not specific for GCT, but both techniques are useful for evaluating the spread of the tumor. Angiography shows increased vascularization in 64% of cases, decreased vascularization in 25%, and no vascularization in 10%. Bone scanning shows a variable degree of hyperactivity at the site of the tumor<sup>16</sup>.

The treatment of choice is a complete surgical excision<sup>8,10,14</sup>. However, GCTs are locally aggressive and frequently recur. Therefore, the radiation therapy could be recommended. But the role of radiation therapy is controversial because sarcomatous degeneration is more frequent after irradiation. Radiation treatment is, as a rule, restricted to inoperable or not radically operated cases<sup>10,12,15</sup>.

The role of chemotherapy is unclear in malignant GCT<sup>2</sup>. Grossly, a resected GCT is typically gray, brown, or shows a mottling of these colors. Microscopically, the tumor is composed of a vascular network of spindle-shaped or oval stromal cells and multi-nucleated giant cells<sup>12</sup>. In the authors' case, the patient's tumor was not completely resected because of the extension

of the tumor to the nearby sagittal and transverse sinus. The authors performed gross total resection of the tumor. The resected tumor is yellowish, showed central necrosis and separated by bony tissue. Microscopical findings revealed the presence of ovoid-shaped tumor cells with an arrangement of a storiform pattern, mitosis, and nuclear atypia with multinucleated giant cells.

Malignancy develops in approximately 5 to 10% of GCT cases<sup>13,16</sup>. The Malignant change can be subdivided into primary and secondary, according to Hutter, et al<sup>9</sup>. and Dahlin, et al<sup>5</sup>. A primary malignancy is a lesion in which there are areas of synchronous high-grade sarcomatous growth next to areas of benign GCT. A secondary malignancy is a metachronous, high-grade sarcomatous growth superimposed on a previous, biopsy-verified, benign GCT that has been treated by either surgery or radiotherapy<sup>2,21</sup>. The two types of secondary malignancy, postsurgical and radiotherapy-induced, are believed to have different etiologies but they cannot be distinguished from each other on the basis of radiographic and histologic presentation. The etiology of malignant transformation of benign GCTs remains unknown.

The histological diagnosis of malignant GCT is established only when the stromal cells are truly sarcomatous, as indicated by pleomorphism, atypia, and high mitotic activity. In addition, the areas of typical benign GCT should be present in the tumor at the time of diagnosis, or in previous tissue taken from the same lesion<sup>21</sup>. The histological features of the reported sarcomas include fibrosarcoma, osteosarcoma, malignant fibrous histiocytoma, and undifferentiated sarcoma. Fibrosarcoma is the most commonly reported histological type of sarcoma originating from GCTs, while the others are less frequent<sup>2,14,16,21</sup>.

Primary malignancies in GCTs are very rare and are considered to represent dedifferentiation in GCTs. In the series from the Mayo Clinic in 1996, of the 35 malignancies in GCTs, 30 cases were secondary. Of the secondary malignancies, 24 cases were post-irradiation sarcomas, and six occurred after



surgical treatment only<sup>20</sup>). Bertoni, et al.<sup>1)</sup> reviewed five cases of primary malignancy and 12 cases of secondary malignancy between 1961 and 2001. Out of 17 cases, six occurred after radiation therapy and other six arose spontaneously.

This case is about primary malignancy because multicentric benign GCT was transformed into a malignant GCT without surgical and radiation therapy. The result of a previous bone biopsy was benign lesion.

Malignancy in GCT of skull is exceedingly rare. In the authors' case, the patient's tumor was developed in the parieto-occipital bone, a location that is not a preferred area of GCTs in skull.

Although the cumulative risk for the development of malignant tumors after irradiation ranges from 5 to 12%, secondary malignancies from benign GCTs without previous radiation therapy are extremely rare. In reviewing the English language medical literature, there have been more than 100 cases of malignant GCTs. These include only 18 cases transforming into sarcomas from originally benign GCTs, with no associated prior radiation therapy<sup>14</sup>). For patients who received previous radiotherapy, the interval between radiotherapy and diagnosis of the malignancy was 1.7-15 years<sup>2)</sup>. For patients with post-surgical secondary malignant GCTs, the average interval between benign GCT diagnosis and sarcoma diagnosis was 18 years, much longer than the average interval observed in patients who received previous radiotherapy<sup>2)</sup>.

The prognosis for secondary malignant GCT is poor. The survival rate is approximately 33%<sup>21)</sup>. In contrast, primary malignant GCT appears to have a slightly better prognosis. In the Mayo Clinic experience the survival rate was 42%<sup>21)</sup>. Hutter, et al.<sup>9)</sup> reported that the mortality rate in malignant GCTs was 52% and 70% in the lesion designated as being fully malignant or anaplastic, with eight months average survival time. In the author's case, the patient died twenty-one months after the first operation.

## Conclusion

Authors report an extremely rare case of multicentric GCT occurring in the parieto-occipital bone and spontaneously evolving into malignant tumors without radiation and surgical treatment. Our presentation suggests that repeated surgery for tumor recurrence, especially for the primary malignant GCTs, can relatively extend a survival time.

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