Radiation-induced Osteosarcoma of the Calvaria
—Case Report—

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Abstract

The authors report a case of radiation-induced calvarial osteosarcoma. A 58-year-old female received subtotal removal of the pituitary adenoma and 5000 rads postoperative irradiation. Seven years later, an osteoblastic osteosarcoma occurred in the frontotemporal region. She received total tumor removal and chemotherapy. However, computed tomography subsequently revealed multiple small lesions at the margin of the bone flap. A chest x-ray film demonstrated lung metastasis. Local recurrence and lung metastasis require careful attention in radiation-induced osteosarcoma patients.

Key words: acromegaly, computed tomography, magnetic resonance imaging, osteosarcoma, radiation-induced tumor

Introduction

Radiation-induced osteosarcomas of the calvaria are rare, among the reported radiation-induced brain tumors. Such complications of radiation therapy may occur when the therapy is used to treat secondary malignant neoplasms.

Here, we report a case of osteosarcoma of the calvaria following radiation therapy for pituitary adenoma.

Case Report

A 58-year-old female was first admitted in June, 1983, with a 6-month history of diabetes mellitus and hypertension, and symptoms of acromegaly. Computed tomographic (CT) scanning indicated pituitary adenoma with extrasellar extension. Laboratory tests confirmed growth-hormone producing adenoma. The tumor was subtotally removed through a right craniotomy. Postoperative irradiation using a linear accelerator delivered 5000 rads to the square lateral opposing field over 5 cm distance. She was then discharged and followed as an out-patient.

She complained of an enlarging mass in the right temporal region, and was readmitted on January 23, 1990. A lateral skull x-ray film indicated marked sclerosis of the frontotemporal bone. A tangential skull x-ray film showed the typical "sun-ray appearance." A chest x-ray film demonstrated lung metastasis. Local recurrence and lung metastasis require careful attention in radiation-induced osteosarcoma patients.

Fig. 1 Plain skull x-ray films on readmission. left: Lateral x-ray film showing marked sclerosis of the frontotemporal bone. right: Tangential x-ray film showing the typical "sun-ray appearance."

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triamine-pentaacetic acid (Gd-DTPA) demonstrated an irregularly enhanced tumor in the right temporal region, invading the brain parenchyma (Fig. 2 right). Right craniectomy on March 9, 1990 demonstrated the tumor growing from the margin of the former free bone flap, and invading the temporal muscle, dura matter, and frontal lobe considerably. Gross total removal and cranioplasty were performed. Histological examination confirmed the diagnosis of osteoblastic osteosarcoma (Fig. 3).

Postoperatively, she received methotrexate (500 mg/day) and vincristine (1.5 mg/day) intravenously at 3-week intervals for 2 months (total dose; methotrexate 1500 mg, vincristine 4.5 mg). However, subsequent CT scans indicated multiple high-density small lesions at the site of the craniectomy. Cisplatin (100 mg) through the external carotid artery was given on June 25, 1990.

Partial tumor removal and dural plasty were again performed on September 7, 1990. Multiple tumor nodules were still present at the margin of the craniectomy bone flap. The tumor had also invaded the superior margin of the zygomatic arch. Postoperatively, cisplatin (90 mg) and adriamycin (60 mg) were administered intravenously. On September 4, 1990, a chest x-ray film had indicated possible metastasis (Fig. 4). Chemotherapy is presently continuing.

**Discussion**

In 1948, Cahan et al. described the following criteria for postradiation sarcomas: 1) microscopic or roentgenographic evidence of a non-malignant initial bone condition; 2) sarcoma originating in an area within the previous radiotherapeutic beam; 3) a relatively long, asymptomatic latent period following irradiation before the clinical appearance of a bone sarcoma; and 4) histological confirmation of sarcomas.

Our patient satisfied all these criteria. Only eight cases, including ours, of calvarial osteosarcoma have been reported (Table 1). Five patients were less than 40 years old. The latent period varied from 3.5 to 21 years (mean 9.1 years). The radiation dosage varied from 2052 to 11,000 rads (mean 6122 rads). The pathogenesis of radiation-induced calvarial osteosarcoma is unknown. Radiation dosages exceeding 3000 rads may induce sarcoma, although no significant relationship with orthovoltage, megavoltage equipment, age at irradiation, or fraction size has been established.

Goldberg et al. studied 104 acromegalic patients and found four cases of malignant intracranial
Table 1  Reported cases of radiation-induced calvarial osteosarcoma

<table>
<thead>
<tr>
<th>Author (Year)</th>
<th>Age at onset, Sex</th>
<th>Primary lesion treated with irradiation</th>
<th>Dosage</th>
<th>Latency (years)</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skolnik et al. (1956)</td>
<td>20, M</td>
<td>keloid</td>
<td>6050 rads</td>
<td>3.5</td>
<td>died (10 mos postop)</td>
</tr>
<tr>
<td></td>
<td>0.5, F</td>
<td>retinoblastoma</td>
<td>9600 mg/hr*</td>
<td>10</td>
<td>died (2 mos postop)</td>
</tr>
<tr>
<td>Meredith et al. (1960)</td>
<td>51, F</td>
<td>pituitary adenoma</td>
<td>2052 rads</td>
<td>6</td>
<td>died (15 hrs postop)</td>
</tr>
<tr>
<td>Sparagana et al. (1972)</td>
<td>29, M</td>
<td>pituitary adenoma</td>
<td>7750 rads</td>
<td>21</td>
<td>died (5 mos postop)</td>
</tr>
<tr>
<td>Casentini et al. (1985)</td>
<td>5, F</td>
<td>cerebellar astrocytoma</td>
<td>5450 rads</td>
<td>4.5</td>
<td>unknown</td>
</tr>
<tr>
<td>Tanaka et al. (1989)</td>
<td>42, M</td>
<td>craniofaryngioma</td>
<td>11000 rads</td>
<td>15</td>
<td>died (2 weeks postop)</td>
</tr>
<tr>
<td>Kellie et al. (1989)</td>
<td>4, F</td>
<td>cerebellar astrocytoma</td>
<td>5550 rads</td>
<td>6</td>
<td>survival (3 yrs postop)</td>
</tr>
<tr>
<td>Present case</td>
<td>58, F</td>
<td>pituitary adenoma</td>
<td>5000 rads</td>
<td>7</td>
<td>survival (13 mos postop)</td>
</tr>
</tbody>
</table>

*Radium therapy.

Recently, bromocriptine treatment for pituitary adenoma has been reported.17,24,28 This treatment is preferable to radiation for postoperative residual pituitary adenoma.

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