Fibrosarcoma After High Energy Radiation Therapy for Pituitary Adenoma

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Fibrosarcoma After High Energy Radiation Therapy for Pituitary Adenoma

William H. Martin,1 Wayne S. Cail,2 J. Leon Morris,2 and William C. Constable2

Pituitary sarcoma is a rare late complication of radiotherapy for pituitary tumors. Although early case reports involved multiple courses of relatively low-energy radiation therapy, pituitary sarcoma has been seen with single courses of high-energy x-ray or heavy particle radiotherapy. This report describes a fibrosarcoma of the pituitary occurring 5 years after 4,500 rad (45 Gy) of X-irradiation delivered in 20 treatments over 3 weeks by an 8 MeV linear accelerator.

Case Report

An 18-year-old woman was admitted to the University of Virginia Hospital. For several years prior to admission, she had noted a progressive decrease in vision. She had had only two or three scanty menstrual periods since menarche and had been amenorrheic for the previous year. On physical examination, the patient was found to have bilateral optic atrophy, a right temporal hemianopsia, and total blindness in the left eye. The rest of the physical and neurological examination was unremarkable except for obesity.

Skull films demonstrated enlargement of the left side of the pituitary fossa (figs. 1A and 1B). Cerebral arteriography revealed slight displacement of the left internal carotid and anterior cerebral arteries consistent with suprasellar extension of a pituitary mass.

Endocrine evaluation included a normal T-4 and T-3 resin uptake, a normal plasma cortisol level, and normal urinary steroid excretion. However, hypogonadism was present with undetectable urinary gonadotropin excretion.

A bifrontal craniotomy was performed and a large gray mass was found between the optic nerves. Subtotal intracapsular removal was carried out and pathologic examination of the specimen confirmed the diagnosis of chromophobe adenoma.

The patient did well postoperatively except for transient diabetes insipidus. She began radiation therapy 7 weeks after admission. A total of 4,500 rad (45 Gy) was delivered in 20 treatments over 3 weeks using a three-field technique with an 8 MeV linear accelerator.

The patient was empirically placed on thyroid and steroid replacement therapy and followed closely. She was electively admitted 4 years later for reevaluation. Serum prolactin levels were markedly elevated, ranging from 375 to 539 ng/ml (normal, < 20). The basal serum growth hormone and that after insulin-induced hypoglycemia were both undetectable. Other endocrine function appeared unchanged. The pituitary fossa had diminished and calcifications had developed above the sella turcica.

The development of pain in the left eye prompted readmission 10 months later. In addition to the previous visual field defects, she had ptosis and complete ophthalmoplegia on the left side. Skull films showed displacement of the dural clips upward out of the pituitary fossa. The small calcifications were also displaced upward above the sella turcica (fig. 1C). CT showed a large enhancing mass eroding the left side of the sella turcica (figs. 1D and 1E). The mass contained small calcifications and extended into the suprasellar cistern deforming the upper brainstem. Cerebral angiography again showed displacement of the suprachiasmatic internal carotid and the proximal anterior cerebral arteries. In addition, neovascularity was present in the left side of the pituitary fossa (fig. 1F).

Dynamic endocrine testing showed the patient to be deficient in growth hormone, gonadotrophin, thyrotropin, and corticotropin. However, the serum prolactin levels remained elevated at 168–222 ng/ml. She was thus believed to have a recurrent, expanding pituitary adenoma and was continued on thyroid and steroid replacement. Because the tumor was believed to be unresectable, bromocriptine (2.5 mg three times a day) was started in an attempt to retard tumor growth [1–3].

The patient was readmitted 3 months later with nausea, vomiting, and lethargy. Skull films showed marked destruction of the dorsum sellae. CT and angiography demonstrated marked interval enlargement of the tumor.

Because of her deteriorating condition, palliative surgery was undertaken. A large tumor was found extending out of the sella and subtotal removal was performed. Pathologic examination of the surgical specimen showed a histology that was markedly different from the original tumor and now represented a fibrosarcoma. The postoperative course was complicated and she died 20 days after surgery.

Discussion

Radiation-induced neoplasm is an infrequent complication of radiation therapy. Terry et al. [4] were the first to document the occurrence of fibrosarcoma of the pituitary in

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patients who had previously received radiation therapy for pituitary adenoma. Since the report of those three patients, 11 additional patients have now been reported with postirradiation pituitary fibrosarcoma [5–11]. Other sarcomas occurring in this context have also been reported: osteosarcoma [12], malignant fibrous histiocytoma [13], and undifferentiated sarcoma [14, 15].

The radiation treatments used in these cases are summarized in Table 1. Seven patients were acromegalic; 11 patients had chromophobe adenomas. The time span between the initial radiation therapy and diagnosis of sarcoma ranged from 4 to 27 years (median, 10).

Goldberg et al. [14] raised the possibility that multiple courses of radiation therapy might increase the risk of developing sarcoma. However, most cases reported subsequent to his report have undergone only a single course of therapy.

Waltz and Brownell [8] put forth the hope that use of higher energy or heavy-particle radiotherapy might eliminate the appearance of postirradiation sarcomas. Although the majority of reported cases received orthovoltage radiation, the most recent ones have involved the higher energy radiation of cobalt-60, betatron, and linear accelerator therapy and the heavy particles of cyclotron radiotherapy.

Waltz and Brownell [8] also called attention to the fact that prior to about 1950, the dose of radiation to pituitary adenomas varied between 1,500 and 2,500 rad (15–25 Gy). No case of sarcoma has been reported resulting from treatment during that time. Postirradiation sarcomas have all been associated with doses exceeding 3,000 rad (30
POSTIRRADIATION FIBROSARCOMA

TABLE 1: Review of Patients with Postirradiation Sarcoma

<table>
<thead>
<tr>
<th>Original Adenoma/Patient [Reference]</th>
<th>Ultimate Pituitary Malignancy</th>
<th>Radiation Source</th>
<th>No. Courses</th>
<th>Total Dose (rad)</th>
<th>Interval Between Initial Radiation and Sarcoma (yrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chromophobe:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 [4]*</td>
<td>Fibrosarcoma</td>
<td>X-ray</td>
<td>5</td>
<td>13,150</td>
<td>8</td>
</tr>
<tr>
<td>2 [4]*</td>
<td>Fibrosarcoma</td>
<td>X-ray</td>
<td>3</td>
<td>13,150</td>
<td>5</td>
</tr>
<tr>
<td>3 [4]*</td>
<td>Fibrosarcoma</td>
<td>X-ray</td>
<td>4</td>
<td>12,000</td>
<td>6</td>
</tr>
<tr>
<td>4 [8]*</td>
<td>Fibrosarcoma</td>
<td>X-ray (250 kVp)</td>
<td>1</td>
<td>3,500</td>
<td>8</td>
</tr>
<tr>
<td>5 [8]*</td>
<td>Fibrosarcoma</td>
<td>X-ray (250 kVp)</td>
<td>1</td>
<td>4,000</td>
<td>5</td>
</tr>
<tr>
<td>6 [15]</td>
<td>Sarcoma</td>
<td>X-ray (250 kVp)</td>
<td>&quot;Multiple&quot;</td>
<td>?</td>
<td>27</td>
</tr>
<tr>
<td>7 [13]*</td>
<td>Malignant fibrous histiocyтома</td>
<td>X-ray</td>
<td>2</td>
<td>5,000</td>
<td>10</td>
</tr>
<tr>
<td>8 [12]*</td>
<td>Osteogenic sarcoma</td>
<td>Betatron</td>
<td>1</td>
<td>5,100</td>
<td>10</td>
</tr>
<tr>
<td>9 [9]</td>
<td>Fibrosarcoma</td>
<td>Cobalt-60</td>
<td>1</td>
<td>5,000</td>
<td>13</td>
</tr>
<tr>
<td>10 [10]*</td>
<td>Fibrosarcoma</td>
<td>Cobalt-60</td>
<td>1</td>
<td>4,092</td>
<td>10</td>
</tr>
<tr>
<td>11 [present case]*</td>
<td>Fibrosarcoma</td>
<td>Linear acceler­ator (8 MeV)</td>
<td>1</td>
<td>4,500</td>
<td>5</td>
</tr>
<tr>
<td>Eosinophilic:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14 [14]</td>
<td>Fibrosarcoma</td>
<td>X-ray</td>
<td>2</td>
<td>3,940</td>
<td>10</td>
</tr>
<tr>
<td>15 [14]</td>
<td>Undifferentiated sarcoma</td>
<td>X-ray (200 and 1000 kVp)</td>
<td>3</td>
<td>6,000</td>
<td>10</td>
</tr>
<tr>
<td>16 [7]</td>
<td>Fibrosarcoma</td>
<td>X-ray (1000 kVp)</td>
<td>2</td>
<td>8,000</td>
<td>7</td>
</tr>
<tr>
<td>17 [8]†</td>
<td>Fibrosarcoma</td>
<td>X-ray</td>
<td>1</td>
<td>?</td>
<td>15</td>
</tr>
<tr>
<td>18 [11]</td>
<td>Fibrosarcoma</td>
<td>Cyclotron (Pro­ton)</td>
<td>1</td>
<td>14,800</td>
<td>8</td>
</tr>
</tbody>
</table>

* Biopsy proven chromophobe adenoma.
† JA Russell, personal communication.

This late complication might be avoided by using radiation doses below this level. However, the best results of radiotherapy for chromophobe adenoma, either as the primary treatment or after surgery, have been obtained with doses of 3,000–5,000 rad (30–50 Gy) [15]. Conventional supervoltage irradiation of the same magnitude has also been required for effective treatment of acromegaly [16]. Heavy-particle therapy capable of giving good control without surgery has used doses of 3,500–10,000 rad (35–100 Gy) or higher [17].

It thus seems that all current forms of radiation used in the treatment of pituitary adenoma are capable of inducing fibrosarcoma. Since irradiation is an effective therapy for pituitary adenoma and the occurrence of fibrosarcoma is only a rare complication, it will continue to be used. It is therefore important for physicians to be aware of this complication. The sudden “recurrence” of a rapidly growing, locally destructive sellar mass in a patient who was effectively treated for pituitary adenoma with radiotherapy years earlier should suggest the diagnosis of fibrosarcoma. Early diagnosis may make surgery feasible as the only hope for palliation.

ACKNOWLEDGMENT

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REFERENCES

5. Newton TH, Burhenne HJ, Palubinskas AJ. Primary carcinoma of the pituitary. AJR 1962;87:110–120


