Radiation-Induced Spinal Cord Anaplastic Astrocytoma Subsequent to Radiotherapy for Testicular Seminoma
—Case Report—

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Abstract

A 54-year-old man presented with weakness and numbness of the left lower extremity in August 2009. He visited a local doctor and then was referred to our hospital in November 2009. Neurological examinations revealed mild weakness of the left lower extremity (manual muscle test grade 4/5, mainly quadriceps), reduced sensation in the whole left lower extremity, hyperreflexia of the lower extremities including hyperactive ankle jerks with 5 to 6 beats of unsustained clonus bilaterally, and spastic gait disturbance that forced him to use a cane. There was no remarkable bowel and bladder incontinence. His medical history revealed that he had undergone radiotherapy in 1973 under a diagnosis of testicular seminoma. A total dose of 30.6 Gy had been delivered and the T10–T12 vertebral bodies were included in this treatment.

Magnetic resonance (MR) imaging showed an intramedullary diffuse mass situated between the T9 and T12 vertebral bodies, corresponding to the previous radiation portal (Fig. 1). The patient underwent laminectomy at T9–T12 and subtotal removal of the lesion, leaving a small portion at the T9 level where the border between the tumor and normal tissue was unclear. Postoperative MR imaging demonstrated almost 90% removal of the tumor (Fig. 2). Histological examination revealed the cells had morphological resemblance to astrocytes and were immunocytochemically positive for glial fibrillary acidic protein. In addition, the lesion showed high cellularity, hyperchromatic nuclei, high nuclear cytoplasmic ratio, marked cellular atypia and pleomorphism, multinucleated

Introduction

Radiotherapy has a great value in the treatment of malignant tumors, but also has major side effects such as radionecrosis or oncogenesis. The involvement of radiation in the induction of central nervous system tumors has been documented repeatedly.14) Such tumors are most frequently meningiomas,23) sarcomas,16,19) and more recently gliomas, especially malignant types.9) Only eight cases of radiation-induced spinal cord glioma have been reported since the first case in 1980 (Table 1).2,4,7,13,15,18,21,24) Survival is very limited in these cases, regardless of various combinations of surgical resection, radiotherapy, and chemotherapy. Only 2 cases of spinal cord neoplasms have been reported following radiotherapy for testicular seminoma (peripheral nerve sheath tumor and angiosarcoma).1,11) Here we describe a case of anaplastic astrocytoma that occurred after radiotherapy for testicular seminoma.

Case Report

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## Table 1 Summary of all cases of radiation-induced spinal cord astrocytoma

<table>
<thead>
<tr>
<th>Authors (Year)</th>
<th>Age at radiation (yrs)</th>
<th>Sex</th>
<th>Primary disease</th>
<th>Radiation dose (Gy)</th>
<th>Latency (yrs)</th>
<th>Survival time (wks)</th>
<th>Treatment</th>
<th>Tumor type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clifton et al. (1980)</td>
<td>21</td>
<td>M</td>
<td>Hodgkin's lymphoma</td>
<td>50</td>
<td>6</td>
<td>10</td>
<td>biopsy</td>
<td>cervicothoracic glioblastoma</td>
</tr>
<tr>
<td>Steinbok (1980)</td>
<td>20–23</td>
<td>F</td>
<td>Pulmonary tuberculosis</td>
<td>unknown</td>
<td>25</td>
<td>unknown</td>
<td>biopsy/radiotherapy</td>
<td>cervicothoracic low grade astrocytoma</td>
</tr>
<tr>
<td>Marus et al. (1986)</td>
<td>19</td>
<td>F</td>
<td>Thyroid cancer</td>
<td>45–55</td>
<td>23</td>
<td>86</td>
<td>resection (2 times)</td>
<td>upper thoracic anaplastic astrocytoma</td>
</tr>
<tr>
<td>Bazan et al. (1990)</td>
<td>19</td>
<td>M</td>
<td>Hodgkin's lymphoma</td>
<td>40</td>
<td>7</td>
<td>unknown</td>
<td>biopsy/chemotherapy</td>
<td>cervical grade II–III astrocytoma</td>
</tr>
<tr>
<td>Grabb et al. (1996)</td>
<td>3</td>
<td>F</td>
<td>Medulloblastoma</td>
<td>30</td>
<td>17</td>
<td>16</td>
<td>resection</td>
<td>cervical anaplastic astrocytoma</td>
</tr>
<tr>
<td>Riffaud et al. (2006)</td>
<td>30</td>
<td>M</td>
<td>Hodgkin's lymphoma</td>
<td>40</td>
<td>9</td>
<td>45</td>
<td>biopsy/chemotherapy/radiotherapy</td>
<td>cervicothoracic malignant astrocytoma</td>
</tr>
<tr>
<td>Yeung et al. (2006)</td>
<td>28</td>
<td>F</td>
<td>Nasopharyngeal carcinoma</td>
<td>86</td>
<td>7</td>
<td>35</td>
<td>biopsy/chemotherapy</td>
<td>cervical glioblastoma</td>
</tr>
<tr>
<td>Ng et al. (2007)</td>
<td>23</td>
<td>M</td>
<td>Hodgkin's lymphoma</td>
<td>30.6</td>
<td>3</td>
<td>several</td>
<td>biopsy/chemotherapy/radiotherapy</td>
<td>thoracic glioblastoma</td>
</tr>
<tr>
<td>Present case</td>
<td>18</td>
<td>M</td>
<td>Testicular seminoma</td>
<td>30.6</td>
<td>37</td>
<td>36</td>
<td>resection/chemotherapy</td>
<td>thoracic anaplastic astrocytoma</td>
</tr>
</tbody>
</table>

**Fig. 1** A: Preoperative sagittal T1-weighted magnetic resonance (MR) image showing a hyperintense intramedullary lesion at the T9–T12 levels. B: Preoperative sagittal T2-weighted MR image with gadolinium demonstrating an enhanced right intramedullary mass lesion. C: Preoperative axial T1-weighted MR image with gadolinium at the T10 level showing a hyperintense right intramedullary lesion. D: Preoperative axial T1-weighted MR image with gadolinium at the T10 level demonstrating an enhanced right intramedullary mass lesion.

**Fig. 2** A: Postoperative sagittal T1-weighted magnetic resonance (MR) image showing a decrease in the hyperintense right intramedullary lesion. B: Postoperative sagittal T1-weighted MR image with gadolinium at the T10 level showing about 90% removal of the enhanced right intramedullary mass lesion. C: Postoperative axial T2-weighted MR image at the T10 level showing the around 90% removal of the hyperintense right intramedullary lesion. D: Postoperative axial T1-weighted MR image with gadolinium at the T10 level demonstrating around 90% removal of the enhanced right intramedullary mass lesion.

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Fig. 3 Photomicrographs of the surgical specimen showing histological features consistent with anaplastic astrocytoma. A: Neoplastic astrocytes with high cellularity, hyperchromatic nuclei, high nuclear cytoplasmic ratio, and multinucleated cells. Hematoxylin and eosin stain, original magnification $\times 200$. B: Increased number of mitotic figures and abnormal multipolar mitoses. Hematoxylin and eosin stain, original magnification $\times 400$. C: Positive staining for glial fibrillary acidic protein (GFAP) within the tumor cell cytoplasm. GFAP immunostain, original magnification $\times 400$. D: Ki-67 index is up to 33%. Ki-67 stain, original magnification $\times 400$.

Fig. 4 A: Sagittal $T_2$-weighted magnetic resonance (MR) image on readmission showing a hyperintense intramedullary lesion with syrinx at the T3–T12 levels. B: Sagittal $T_2$-weighted MR image with gadolinium on readmission demonstrating an enhanced mass lesion at the T5–T12 levels. C: Axial head $T_2$-weighted MR image on readmission showing no remarkable hydrocephalus. D: Axial head $T_2$-weighted MR image with gadolinium on readmission demonstrating no remarkable enhanced mass lesion.

Fig. 5 A: Sagittal $T_2$-weighted magnetic resonance (MR) image in July 2010 showing a hyperintense intramedullary lesion with syrinx expanding to the medulla oblongata. B: Sagittal $T_2$-weighted MR image with gadolinium in July 2010 demonstrating an enhanced mass lesion expanding to the medulla oblongata. C: Axial head computed tomography scan in July 2010 demonstrating hydrocephalus.

Radiation-Induced Spinal Anaplastic Astrocytoma

Four criteria have been proposed for determining if a tumor is radiation-induced neoplasm: the second tumor must arise in the irradiated field; a latent period of several years must have elapsed between radiation exposure and development of a second neoplasm; the tumor diagnosis must be confirmed histopathologically; and the second tumor must be histopathologically distinct from the original tumor.15,18) The present case fulfilled all these criteria for a radiation-induced neoplasm, so we conclude that the spinal cord anaplastic astrocytoma in this patient was induced by radiotherapy. In the present case, the second tumor arose after a latency period of 37 years, the longest latency period for a radiation-induced astrocytoma compared to another case after 25 years (Table 1), indicating that radiation-induced spinal cord astrocytoma may occur even several decades after the radiotherapy. In our case, the tumor arose following radiotherapy for testicular seminoma, in which the lower thoracic vertebral bodies are usually included in the radiation field. In four of eight

Discussion

Four criteria have been proposed for determining if a tumor is radiation-induced neoplasm: the second tumor must arise in the irradiated field; a latent period of several years must have elapsed between radiation exposure and development of a second neoplasm; the tumor diagnosis must be confirmed histopathologically; and the second tumor must be histopathologically distinct from the original tumor.15,18) The present case fulfilled all these criteria for a radiation-induced neoplasm, so we conclude that the spinal cord anaplastic astrocytoma in this patient was induced by radiotherapy. In the present case, the second tumor arose after a latency period of 37 years, the longest latency period for a radiation-induced astrocytoma compared to another case after 25 years (Table 1), indicating that radiation-induced spinal cord astrocytoma may occur even several decades after the radiotherapy. In our case, the tumor arose following radiotherapy for testicular seminoma, in which the lower thoracic vertebral bodies are usually included in the radiation field. In four of eight
reported cases of radiation-induced spinal cord astrocytoma, the tumors arose following treatment for Hodgkin’s lymphoma, in which the vertebral bodies were usually included in the radiation field. The cervical vertebral bodies were also affected in the radiotherapy for thyroid carcinoma, nasopharyngeal carcinoma, medulloblastoma, and pulmonary tuberculosis. Therefore, we need to pay special attention to the clinical history of these diseases in assessing a case of spinal cord astrocytoma.

Radiation-induced spinal malignant astrocytoma (anaplastic astrocytoma and glioblastoma multiforme) is extremely rare. These tumors are notoriously difficult to treat because total removal of tumor without causing new neurological deficits may be impossible. Moreover, they are relatively resistant to the radiotherapy and chemotherapy, and the effects of immunotherapy and neuron therapy are still unclear. The average survival period in our case and the five reported cases was about 38 weeks, although several therapeutic modalities including radiotherapy and chemotherapy were attempted. On the other hand, the survival times with spinal anaplastic astrocytoma and glioblastoma are around 80 weeks and 75 weeks, respectively. These results indicate that the prognosis of radiation-induced spinal high grade astrocytoma is worse than that of spontaneous spinal high grade astrocytoma. Therefore, we need to carefully check for a past history of radiotherapy preoperatively if spinal high grade astrocytoma is suspected. An initial strategy of past history of radiotherapy preoperatively if spinal high grade astrocytoma is suspected. Therefore, we need to carefully check for a past history of radiotherapy preoperatively if spinal high grade astrocytoma is suspected. An initial strategy of biopsy may be more appropriate than attempted resection for a patient with suspected radiation-induced spinal astrocytoma.

Cordectomy is advocated as a reasonable alternative treatment for spinal malignant astrocytoma presenting with complete deficit below the lesion, for the treatment of pain, spasticity, and posttraumatic syringomyelia. The effects of cordectomy for spinal malignant astrocytoma with remaining function below the lesion are unknown. To perform cordectomy in such cases, the patients need to accept complete deficits below the lesion and decreased quality of life after cordectomy. However, judging from the results that 90% removal of tumor and chemotherapy had little influence on the quality of life and the length of survival in this case, and the poor outcome reported, cordectomy may be the optimum treatment for radiation-induced spinal cord anaplastic astrocytoma.

References


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