Postradiation lower motor neuron syndrome presenting as monomelic amyotrophy

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Abstract
Monomelic amyotrophy developed 16 months, nine and 12 years after irradiation of the lumbo-sacral spinal cord for seminoma in one patient and for Hodgkin's disease in two others. In two patients, involvement was clinically limited to one leg, with a subacute course followed by plateau in the first case and with progressive worsening in the second one. In the third patient, the course was progressive with involvement of the other lower limb occurring five years later. From clinical and electrophysiological data, it seems probable that the disease process was a result of a selective injury to the lower motor neuron in the lower spinal cord.

Patients may rarely develop a lower motor neuron syndrome (LMNS) after radiotherapy encompassing the lumbo-sacral spinal cord, roots and plexuses. The clinical picture is in most cases a paraparesis with amyotrophy and areflexia, without sensory loss or sphincter disturbances.

We report three unusual cases of LMNS following radiotherapy presenting as a monomelic amyotrophy. In one case, involvement of the other limb occurred five years later, while in the other two patients amyotrophy remained monomelic during follow up seven and eight years respectively.

Case reports
The clinical features and outcome of the three patients are summarised in the table. In all cases, the radiation field involved the lumbo-sacral spinal cord, roots and plexuses. Initial neurological examination showed atrophy and weakness with fasciculations and areflexia limited to one lower limb. Light touch, pin-prick, temperature, joint position, vibration sense and two-point discrimination threshold were entirely normal. Strength was intact in the other lower limb and in the upper limbs. Plantar responses were flexor. There were no sphincter disturbances. Electrophysiological examination showed advanced denervation in the atrophic lower limb, more marked distally, with large amplitude motor unit potentials. Myokymic discharges were not found. Motor and sensory conduction velocities, distal latencies, sensory nerve potential amplitude, and SEPS obtained in both lower limbs with stimulation of the posterior tibial nerve were normal in all cases. Neurogenic changes were present in the contralateral lower limb in patients 2 and 3. General examination, laboratory investigations, radiographs of the chest and of the spine revealed no abnormalities. CSF examination in patient 2 showed a protein content of 105 mg/100 ml with a normal cell count. MRI of the lumbar and sacral spinal cord, performed in patients 1 and 2, was normal.

Discussion
The prolonged and self-limited course of the neurological disease without pain, sensory or autonomic dysfunction in these three cases and its occurrence while the patients were in remission all argue against a recurrence of the neoplastic process, with leptomeningeal metastases or tumour infiltration of nerve roots or plexuses. This was supported by normal MRI appearance and negative CSF cytological examination. From clinical and electrophysiological data, it seems clear that the disease process was a result of a selective injury to the lower motor neuron.

Selective lower motor neuron dysfunction in patients treated with radiotherapy has already been reported but a monomelic amyotrophy is exceptional. Indeed, most reported patients have subacutely developed bilateral lower motor neuron weakness confined to the lower limbs, with amyotrophy, cramps and fasciculations, without sensory or sphincter distur-

Table  Clinical characteristics, radiation doses and outcome of the three patients with monomelic amyotrophy

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (year)</th>
<th>Sex</th>
<th>Initial illness</th>
<th>Radiation therapy (Cobalt 60)</th>
<th>Presenting neurological signs</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Mantle field</td>
<td>Lumbo-aortic nodes</td>
<td>Latent period</td>
</tr>
<tr>
<td>1</td>
<td>32</td>
<td>Male</td>
<td>Hodgkin's disease</td>
<td>4000</td>
<td>4000</td>
<td>9 year</td>
</tr>
<tr>
<td>2</td>
<td>30</td>
<td>Male</td>
<td>Seminoma</td>
<td>3000</td>
<td>3000</td>
<td>12 year</td>
</tr>
<tr>
<td>3</td>
<td>26</td>
<td>Female</td>
<td>Hodgkin's disease</td>
<td>4000</td>
<td>4000</td>
<td>16 months</td>
</tr>
</tbody>
</table>
bances, resulting in a flaccid and symmetrical paraparesis. A few patients presented with tetraparesis. This disorder has been mostly reported after irradiation for malignant testicular tumours, Hodgkin’s disease or other lymphomas and occasionally after irradiation for medulloblastoma, pheochromocytoma and oesophagus carcinoma. In one third of cases, radiation doses were higher than 4000 rads and in another third higher than 5000 rads. Delay between radiation therapy and onset of neurological symptoms ranged from three months to 13 years. All cases of paraparesis have followed irradiation encompassing the lower end of the spinal cord, either in isolation (about 50% of cases) or as part of a more diffuse irradiation. In the four patients presenting with tetraparesis, radiation fields encompassed the mantle and para-aortic areas. Cytological studies of the CSF were always normal. Magnetic resonance imaging of the thoracolumbar spinal cord has been reported in only one case and was normal, as in our patients.

The prognosis of LMNS following radiotherapy and the risk of further contralateral involvement in cases of monomelic amyotrophy are difficult to evaluate. In cases presenting as paraparesis, a stabilisation was usually noted after a subacute and self limited clinical course ranging from a few months to one or two years. Nevertheless, spontaneous improvement, sometimes with complete recovery, or conversely gradual worsening without remission has also been reported. Corticosteroids were used in some patients with paraparesis and appeared to have no effect. In patients with monomelic amyotrophy, the presence of contralateral neurogenic changes at electrophysiological examination seems to have no predicting value of further contralateral involvement. Two of our patients had contralateral neurogenic changes at initial electrophysiological examination: in one (case 2), the amyotrophy remained clinically monomelic during an eight year follow up; whereas in the other (case 3), clinical involvement of the contralateral lower limb occurred five years later (table).

Regarding the nervous system involvement, the normal clinical and electrophysiological sensory examination and the absence of myokymic discharges in our three cases all argue against a radiation-induced plexopathy. The disease process was most likely a result of a selective injury to the lower motor neuron either in the anterior horn of the spinal cord or in the lumbar and sacral motor roots. The presence of large amplitude and long duration potentials point to an anterior horn cell lesion.

Neuropathological examination in three cases of LMNS following radiotherapy presenting as paraparesis showed prominent neuronal degeneration restricted to the anterior horns of the spinal cord and mild demyelination of the posterior columns and the anterior roots.

This injury to the anterior horn of the spinal cord may be due to a direct effect of radiation therapy upon nervous tissue or to a selective anterior horn cell degeneration as a manifestation of ischaemic cell damage. The selective damage to lumbar-sacral anterior horn cells in patients who received whole neuraxis irradiation or the unilateral involvement in two of our cases, either regional selective cell vulnerability or radiation fields overlaps are possible explanations. Lower motor neuron syndrome has been reported rarely in patients with lymphoma who had not received radiotherapy. In these cases, opportunistic viral infection has been proposed as a possible pathogenetic mechanism.

In conclusion, a clinical picture of monomelic amyotrophy may occur rarely after irradiation of the lower spinal cord, presumably due to a selective injury to the anterior horn cells of the lumbo-sacral spinal cord. Further involvement of the contralateral limb is unpredictable and may be delayed for several years.