Chemotherapy as the initial treatment of spinal cord compression due to disseminated neuroblastoma


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During a 12-month trial period, all children attending the Hospitals for Sick Children, London, England, for management of spinal cord compression due to disseminated neuroblastoma were given chemotherapy as initial treatment rather than radiotherapy or laminectomy. Response to treatment was evaluated by a neurosurgeon as well as by oncologists. Four children were treated in this way and all made a full recovery of spinal cord function.

Keywords: neuroblastoma - chemotherapy - spinal cord tumor

Neuroblastoma is one of the most invasive malignancies of childhood, and can involve the central nervous system. Intracranial invasion is unusual but “dumbbell” epidural extension of extraspinal tumors, leading to spinal cord compression, is often seen. Conventionally, children with neuroblastoma and spinal cord compression have been treated with radiotherapy and/or laminectomy; however, serious long-term complications such as poor bone growth and scoliosis have been recorded in over 50% of survivors. In addition, initial radiotherapy and/or surgery inevitably delays the start of combination chemotherapy, prolonging the time before control of the metastatic disease can begin.

Newly diagnosed neuroblastoma is almost always chemosensitive. Hayes, et al., have successfully used chemotherapy as the primary treatment in children with epidural neuroblastoma or Ewing’s tumor. To try to confirm these findings, it was decided to give chemotherapy as first-line treatment of any child with advanced neuroblastoma and evidence of spinal cord compression.

Summary of Cases

Patients and Methods

All children presenting to the Oncology Unit at this hospital in the 12 months beginning in August, 1985, were eligible for the study. The diagnosis of neuroblastoma was established according to the criteria of the European Neuroblastoma Study Group before starting therapy. Sites of spread were evaluated by bone-marrow aspiration (with conventional cytology and monoclonal antibody immunostaining) and trephine biopsies, together with anteroposterior chest x-ray studies, abdominal ultrasonography, computerized tomography (CT), and isotope bone scanning. Imaging of the spinal cord and column was by myelography and/or CT scanning, usually with intrathecal metrizamide, on an individual basis. Based on the information gained, a stage was assigned using the criteria of Evans, et al.

All children were assessed by both a neurosurgeon and a pediatric oncologist. Those with evidence of spinal cord compression received dexamethasone (1 mg/kg/day) in four divided doses followed by the first course of the four-drug “OPEC” regimen (Oncovin, cis-platinum, VM-26, and cyclophosphamide). Full neurological assessment, including evaluation of urinary output and stool frequency, was repeated three times daily during chemotherapy and twice daily until clear neurological improvement had been observed. Thereafter the patient’s neurological status was assessed weekly, and, for the purposes of this study, a full examination was conducted 3 months after diagnosis.

Treatment Results

During the 12 months of our study, 18 children with Stage III or IV neuroblastoma were brought to this hospital. Four (18%) had clinical evidence of spinal cord or cauda equina compression (Table 1). There were two girls and two boys with an age range of 2 to 20 months, and all had Stage IV tumors. Imaging (CT and myelography) confirmed spinal column encroachment by the tumor; this was presumably via extensions

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Chemotherapy for myelopathy from neuroblastoma

### TABLE 1

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (mos)</th>
<th>Cranial Nerves</th>
<th>Upper Limbs</th>
<th>Lower Limbs</th>
<th>Anus</th>
<th>Bladder</th>
<th>Time to Full Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>normal</td>
<td>normal</td>
<td>24-hr history of flaccidity of both lower limbs; no spontaneous movement of either limb; weak withdrawal on painful stimuli</td>
<td>normal</td>
<td>urine retention</td>
<td>1 wk</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>normal</td>
<td>normal</td>
<td>decreased tone in both lower limbs; poor movements, severe on rt side (uncertain duration)</td>
<td>patulous (uncertain duration)</td>
<td>normal</td>
<td>20 days</td>
</tr>
<tr>
<td>3</td>
<td>8</td>
<td>rt Horner's syndrome (4 mos)</td>
<td>severely reduced movements on rt</td>
<td>1-mo history of loss of ability to sit &amp; roll; severely reduced movement in lower limbs; moderately reduced tone; very brisk reflexes with marked ankle clonus</td>
<td>normal</td>
<td>normal</td>
<td>21 days</td>
</tr>
<tr>
<td>4</td>
<td>20</td>
<td>rt Horner's syndrome (uncertain duration)</td>
<td>24-hr history of loss of movement of rt arm; markedly increased tone</td>
<td>24-hr history of lower-limb weakness; lost ability to stand; plantar reflexes changed from flexor to extensor</td>
<td>normal</td>
<td>normal</td>
<td>21 days</td>
</tr>
</tbody>
</table>

through intervertebral foraminae in each case except Case 1 where a right-sided 4 × 5-cm paraspinal mass was clinically evident. In the three oldest children, deviation of the spinal cord was demonstrated. In the eldest child, a myelogram with lumbar puncture showed displacement of the theca in the lumbar area. To visualize the cord above C-4, contrast material had to be introduced. Computerized tomography with intrathecal administration of contrast material clearly showed compression of the spinal cord.

Assessment of the four children at 3 months after chemotherapy showed full spinal neurological recovery, including normal sphincter function. This finding coincided with the radiological improvement. The only persisting defect was Horner’s syndrome in two children. In both cases this abnormality was independent of cord compression.

Two children (Cases 1 and 3) developed abdominal recurrence of neuroblastoma 12 months and 16 months after diagnosis; however, neither showed any neurological deterioration at the time of the relapse. The two other patients have remained disease-free for 28 and 22 months since diagnosis and are neurologically normal.

### Discussion

Over the last 10 years, following the development and use of more effective chemotherapy, the cure rate of patients with Stage IV neuroblastoma has increased. The improvement has been modest in children over 1 year of age at diagnosis (15% to 20% long-term survival) but has been substantial for younger patients. Parallel improvements in response rates and the median progression-free interval have been observed, with excellent quality of life during remission for patients who eventually relapse and die of the disease. Other obvious advantages of chemotherapy over surgery and/or radiotherapy as the initial treatment for spinal cord or cauda equina compression are that control of other metastatic sites is more quickly achieved than if surgery or irradiation is used first, and the long-term adverse consequences of surgery and irradiation, such as scoliosis, growth disturbances, and the development of second tumors, are avoided. A major concern centers around whether chemotherapy works quickly enough to prevent permanent neurological damage. Our patients provide evidence that it does. Confirmatory evidence is available from the studies of Hayes, et al., in neuroblastoma and Ewing’s sacroma and of Gale, et al., in malignant germ-cell tumors.

Laminectomy may be necessary in cases of nonmetastatic neuroblastoma to provide a tissue diagnosis. However, based on the present observations in patients with Stage IV disease, the option exists to carry out a limited laminectomy (with no attempt to remove all gross tumor) so long as chemotherapy is started immediately afterward.

In summary, four children with spinal cord compression from metastatic neuroblastoma were treated with chemotherapy alone. All made complete neurological recoveries. The findings suggest that any child with acute cord or cauda equina compression thought to be caused by tumor should be urgently evaluated by both oncology and neurosurgical teams. Clinical, radiological, or hematological evidence of metastatic disease should lead to immediate attempts to make a diagnosis by bone marrow sampling or lymph node biopsy, without recourse to laminectomy. Once the diagnosis is available, administration of chemotherapy together with dexamethasone is the initial treatment of choice; laminectomy or radiotherapy should be considered only in the event of further neurological deterioration. With
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this approach, the late effects of surgery and radiotherapy, proportionately more important now that the median survival time of children with advanced neuroblastoma is at last improving, can be avoided.

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References


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