Clinical Oncology

Clinical Oncology (1999)11:405–406

Case Report

Metastatic Adult Medulloblastoma Showing Prolonged Response to Chemotherapy

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Introduction

Medulloblastoma is a malignant tumour arising in the cerebellum from primitive neuroepithelial cells. It is generally a childhood tumour, with a peak incidence at 5–9 years, but a second smaller peak is seen between 20 and 30 years. More than 80% of adult cases present before the age of 40. Overall it is a rare cause of a cranial space-occupying lesion in an adult, accounting for approximately 1% of all adult brain tumours [1].

Standard treatment consists of complete excision with postoperative craniospinal irradiation. Experience of the use of chemotherapy in adults is limited. Relapse is most commonly within the posterior fossa and systemic metastases are rare.

We present the case history of an adult with medulloblastoma, presenting at the age of 49, recurring with systemic but no local disease, and showing a prolonged response to chemotherapy.

Case Report

A 49-year-old man presented to his general practitioner in March 1993 with a vague history of unsteadiness of gait and progressive slurring of speech. Magnetic resonance imaging (MRI) in October 1993 showed a lesion in the posterior fossa. He underwent craniotomy and excision of a right cerebellar tumour in December 1993. The histopathology confirmed an intrinsic cerebellar primitive neuroectodermal tumour (PNET) with focal glial differentiation.

The patient was referred to the oncology department and, 1 month after surgery, commenced craniospinal irradiation: 35 Gy was administered to the entire neuroaxis (21 fractions of 1.67 Gy) and a 20 Gy boost (12 fractions of 1.67 Gy) to the posterior fossa, making the total dose to this area 55 Gy. The patient was well for 17 months. MRI at 12 months post-radiotherapy showed no evidence of local recurrence or spinal metastases.

He re-presented in October 1995 with multiple aches and pains in a girdle distribution, a raised ESR (78 mm/h) and raised alkaline phosphatase (301 iu/l). These levels improved with a trial of steroids and he was referred to a rheumatologist. At rheumatology view in March 1996 he was observed to have a leuco-erythroblastic blood film. An attempted bone marrow trephine encountered hard cortical bone. A bone biopsy and marrow aspiration confirmed the presence of metastatic PNET. Radiographic examination demonstrated mixed sclerotic and lytic metastases in the humeri, femora and pelvis.

The patient returned early to the oncology clinic. He was asymptomatic and no treatment was commenced. From July 1996 he required intermittent transfusions for recurrent anaemia. In September 1996 he underwent local radiotherapy to a painful metastasis in the left mandible (single fraction, 8 Gy), and by November 1996 transfusions were required 3-weekly. The patient had also developed clinically malignant right groin lymph nodes and more active treatment was felt to be appropriate. He received further radiotherapy (8 Gy in a single fraction) to the right groin and chemotherapy was commenced. Single-agent vincristine was used at a dose of 1 mg weekly in view of low blood counts (in particular, depressed platelets). In total 39 doses were given between November 1996 and September 1997. The blood indices improved, with platelets stabilizing at $>100 \times 10^9$/l, and only one blood transfusion being required in the 10-month period. In May 1997 a right acromioclavicular mass was noted and the vincristine was stopped. However, the patient rapidly developed recurrent leg and arm pain; the vincristine was restarted at the next review (4-week gap). In October 1997, once again there was increasing bony pain, especially in the pelvis. A bone scan confirmed metastases in the pelvis and lumbar spine, in addition to the previous sites. Chemotherapy was stopped and external beam radiotherapy (20 Gy in five fractions) administered to the right hemipelvis. Initially, he had good symptomatic benefit for the pelvic pain, but he rapidly developed generalized bony pain while off systemic chemotherapy. A new skin nodule was noted on the left shin. The improvement in the blood count since commencing chemotherapy allowed a combination regimen to be used. He was restarted on chemotherapy in November 1997 with a combination of carboplatin 175 mg/m^2 on days 1–3, intravenous etoposide 100 mg/m^2 on days 1–3, and vincristine 2 mg on day 2. He received six courses,

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becoming asymptomatic, with a reduction in the right acromioclavicular mass and resolution of the skin nodule. However, a dose reduction of 30% was required for courses five and six because of prolonged neutropenia.

The chemotherapy was discontinued in May 1998, the patient remaining well until October 1998 when there was a recurrence of generalized bone pain. A bone scan showed increased uptake throughout the skeleton. Palliative treatment with intravenous radioactive strontium-89 (150 MBq) gave good symptomatic relief, but there was a worsening of the blood indices, reducing the platelets to $< 40 \times 10^9$/l and the haemoglobin to 9.4 g/dl. This has been slow to recover and the patient is currently being reassessed for further chemotherapy, some 40 months after initially presenting with symptoms of metastatic disease.

Discussion

Adult medulloblastoma is an uncommon condition and system metastases are rare. Randomized trials to evaluate treatment are therefore difficult to perform, and published series are retrospective and diverse. Our patient presented at a late age, relapsed systemically, and has shown a prolonged response to chemotherapy.

A review of the current literature was undertaken using the University of Newcastle on-line Medline service. In the most recent published adult series [2–5], the age at presentation has been, in the majority of patients, under 30 years. However, occasional patients presenting in their 40s and 50s are seen in most series.

Series of adult medulloblastoma patients quote 5-year survival rates of 50%–80%, with 10-year survival falling to 25%–51% [2–5]. In the majority (>50%) of patients, local relapse in the posterior fossa is seen, either as a sole site or in association with other diseases. The next most common site for relapse is the spinal axis, then the supratentorial compartment. Systemic relapse rates of 7% [2], 9% [5], 10% [1] and 13% [3] are quoted. Most extra-central nervous system metastases are to the long bones and ribs, with lymph node secondaries being the next most common site [16].

Data on systemic chemotherapy at relapse are limited and there is no standard regimen. A wide range of drugs has been shown to be effective in medulloblastoma in children [1], with a median duration of response of 17 months. In adults, Moody et al. [3] successfully treated two patients with bone marrow relapse with VAC chemotherapy (vincristine 2 mg, adriamycin 40 mg/m^2, cyclophosphamide 600 mg/m^2). Repeated marrow aspirates were negative for malignant cells and these patients went on to receive high-dose melphalan (200 mg/m^2) with autologous bone marrow rescue. Both were well at < 2 years' follow-up. Cottu et al. [6] reported the case history of an 18-year-old who survived for 23 months after the diagnosis of systemic metastases, following treatment with mechlorethamine, vincristine, procarbazine and prednisone (MOPP), then high-dose chemotherapy (using carboplatin, etoposide and cyclophosphamide) with peripheral stem cell support.

In our patient, treatment with weekly vincristine was selected initially because of concerns over the picture of leuko-erythroblastic anaemia. He has always had rapid symptomatic relief while receiving radiotherapy or chemotherapy, and a rapid recurrence of musculoskeletal symptoms whenever chemotherapy is stopped. His disease remained chemosensitive for 18 months after commencing treatment, as evidence by the decrease in lymph node and skin nodule size.

It is now 40 months since the first symptoms from systemic relapse, and 34 months since a definitive diagnosis of bone marrow involvement. The systemic disease has behaved in an indolent fashion, being asymptomatic he received no treatment for the initial 8 months after diagnosis. He has remained generally well and has been able to work throughout the majority of the treatment.

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Received for publication February 1999
Accepted following revision August 1999