Case Report

Malignant Paraganglioma with Skeletal Metastases and Spinal Cord Compression: Response and Palliation with Chemotherapy

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Abstract. Paragangliomas (carotid body tumours, chemodectomas) may arise in any area of the body where sympathetic ganglia are present, including chemoreceptors, the adrenal medulla and retroperitoneal ganglia. Increasing numbers of patients are being reported with vertebral metastases and spinal cord compression for which either decompression laminectomy or external beam radiotherapy, or both, are required. Patients with vertebral metastases may develop progression of disease after radiation therapy.

There is little published information on the use of chemotherapy in this clinical situation. We report a case of metastatic paraganglioma complicated by spinal cord compression showing evidence of clinical benefit from chemotherapy after progressive disease and symptoms developed in a region previously treated by radiation therapy.

Keywords: Chemodectoma; Chemotherapy; Metastases; Paraganglioma; Radiotherapy; Spinal cord compression

INTRODUCTION

Paragangliomas are uncommon tumours with a low propensity to metastasize. Recurrences or metastases may occur long after initial diagnosis, occasionally up to 20 years [1]. Metastases to vertebrae, with or without extradural extension, are rare, with single cases constituting the reported literature [1–8].

External beam radiotherapy is effective in the treatment of bony metastases [8] as well as primary paragangliomas [9], with local control and excellent pain relief in a high proportion of cases. However, many patients studied did not have prolonged follow-up and progression may occur years after therapy. Decompression laminectomy may be complicated by bleeding from these

vascular tumours [7], and multiple level laminectomy may result in vertebral instability.

For patients with previously irradiated epidural disease who suffer pain or neurological symptoms despite surgery, or who are unable to undergo surgery, systemic chemotherapy may offer an alternative. We report a case of metastastic paraganglioma demonstrating tumour regression after chemotherapy in an area previously treated by external beam radiation.

CASE REPORT

In December 1980 a 23-year-old man developed symptoms of a flu-like illness. On physical examination an abdominal mass was found, confirmed by ultrasound and measuring $7 \times 9 \times 4$ cm, lying to the right of the mid-line at the level of the umbilicus. At laparotomy a large retroperitoneal mass, extending from the renal arteries to the bifurcation of the aorta, was removed. Histological evaluation revealed a non-chromaffin paraganglioma (Figs. 1, 2). The patient had had no history of hypertension or headaches, and assays for catecholamines were normal.

He was well until April 1986 when he developed back pain. A bone scan revealed increased uptake at the ninth thoracic vertebra, as well as the sacrum. Computed tomography (CT) of the pelvis revealed a
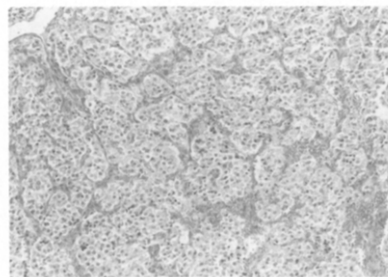

Fig. 1. Photomicrograph of original retroperitoneal tumour, illustrating uniform tumour cells arranged in nests ('Zellballen') separated by a prominent fibrovascular stroma (haematoxylin and eosin stain, original magnification ×400).
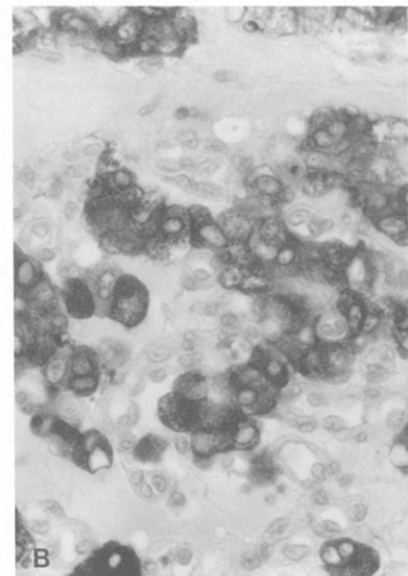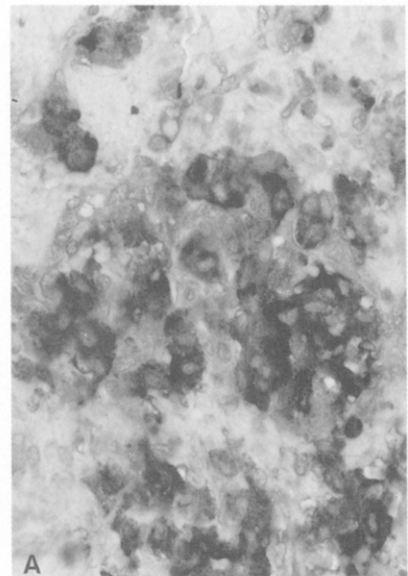

Fig. 2. Immunohistochemical stains demonstrating intense positive reactivity for neuron specific enolase (A) and chromogranin (B) (ABC-peroxidase stain, original magnification ×400).

large destructive lesion involving the sacrum, with an intrapelvic soft tissue component. A CT scan of T9 revealed destruction of the right side of this vertebral body with prominence of the adjacent paravertebral soft tissue. Open biopsy of the pelvic mass and a needle biopsy of T9 confirmed a diagnosis of paraganglioma. He subsequently received radiotherapy to the sacrum (total dose 5000 cGy in 25 fractions) and to the lower thoracic vertebrae (total dose 4000 cGy in 20 fractions).

He was again well until November 1988 whe he developed back and neck pain and a right C7 and C8 radiculopathy. Myelography revealed impingement by epidural extension of tumour of the C7 and C8 roots. He received radiotherapy (3000 cGy in 10 fractions) to the cervical vertebrae. Scanning with ^{131}I-MIBG did not reveal significant radioisotopic uptake.

In March 1989 he developed increasing pain at the level of T9, and Lhermitte's sign on forward neck flexion, as well as an episode of loss of leg control. On examination there was no evidence of spinal cord compression. A CT scan of the mid and lower thoracic vertebrae was performed (Fig. 3). Decompression laminectomy was suggested but the patient, concerned by the risk of back instability, declined. Chemotherapy (cyclophosphamide 750 mg/m^2 and vincristine 2 mg/m^2 given on day 1, and dacarbazine (DTIC) 600 mg on days 1 and 2 of a 28-day cycle) was commenced. After two courses the patient's pain (incompletely controlled on hydromorphone 6 mg every 4 hours) resolved, as did the Lhermitte's sign. A CT scan revealed a decrease in the paraspinal soft tissue mass (Fig. 4). Another CT scan obtained 2 months later revealed no further change.

As the patient suffered considerable nausea with this regimen, he was subsequently treated with carboplatin 300 mg/m^2 every 28 days. A CT scan obtained after two courses revealed further shrinkage of the soft tissue mass (Fig. 5), but no further shrinkage was achieved after two additional courses of carboplatin.

Thirteen months after completion of chemotherapy the patient developed further pain in the lower thoracic region and weakness on climbing stairs. CT scanning revealed progression of the soft tissue lesion and obliteration of the spinal canal at T9 and T10. Surgery was reconsidered but the risk of back instability was felt to be high. The patient commenced dexametha-
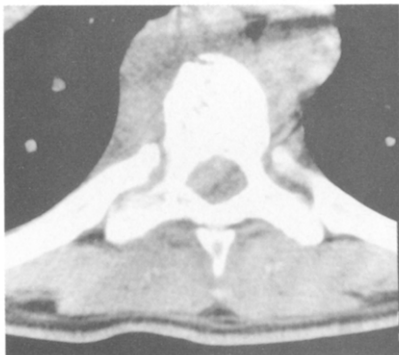

Fig. 3. CT scan through T9 vertebra revealing destructive lytic lesion of the body of the vertebra as well as paraspinal soft tumour extension. The epidural fat surrounding the spinal cord is displaced to the left and posteriorly.
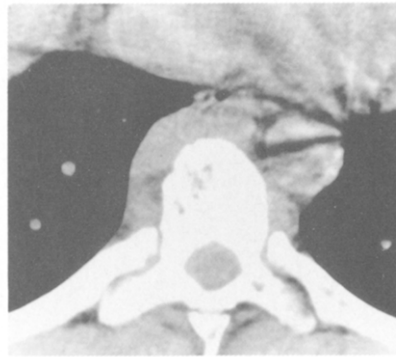

Fig. 4. CT scan of T9 vertebra after two courses of chemotherapy with cyclophosphamide, vincristine and dacarbazine. A noticeable decrease in the paraspinal mass is seen.

Fig. 5. CT scan through T9 vertebra after two further courses of chemotherapy with carboplatin. Still further shrinkage of the paraspinal mass is seen. The epidural fat surrounding the spinal cord is now well centred in the spinal canal, suggesting that the spinal cord is no longer displaced posteriorly.

sone and accepted treatment with cisplatin (25 mg/m^2 intervenously daily for 3 days) and etoposide (100 mg/m^2 intravenously daily for 3 days). Within 1 week the patient's leg weakness and back pain had resolved, but he experienced substantial fatigue, and further chemotherapy was declined.

The patient's pain recurred 4 weeks later, and decompression laminectomy was performed. Extensive bleeding resulted in abandonment of the planned anterior decompression. Although the canal appeared well decompressed by posterior laminectomy, the patient continued to lose function in his legs, and declined further intervention. He died 2 months later as a result of a pulmonary embolus; autopsy revealed two small deposits in the body of the pancreas as the only metastases outside the skeleton.

DISCUSSION

Little information is available on the chemotherapy of paraganglioma. Case reports of response to carboplatin (one partial [10] and one minor [11] response) have been published. Shepard et al. [12] reported a case achieving a complete response of pulmonary metastases and healing of lytic lesions with combination

cisplatin and etoposide, despite prior progressive disease with cyclophosphamide, doxorubicin and cisplatin, but with subsequent progression despite single agent etoposide. Vogl et al. [13] reported a partial response in a patient treated with doxorubicin and cisplatin and Mikhail et al. [5] reported a case of partial response to cyclophosphamide, doxorubicin, vincristine and dacarbazine (CYVADIC). In contrast, Poster et al. [14] and Massey and Wallner [8] treated patients with metastatic disease with various chemotherapy regimens, without evidence of response.

The present case demonstrates both measureable regression of evaluable disease and palliation of pain and other neurological symptoms at a previously irradiated site through the use of cytotoxic chemotherapy. Tumour shrinkage was documented for cyclophosphamide, vincristine and dacarbazine, with a suggestion of further improvement with the subsequent administration of carboplatin (dose reduced as a result of previous myelosuppression). When signs and symptoms of spinal cord compression recurred, a combination of etoposide and cisplatin was commenced, but the transient symptomatic improvement may well have been due to corticosteroid therapy.

Standard therapy for spinal cord compression includes external beam radiotherapy with or without surgical decompression [15]. However, the long natural history of this disease may result in a recurrence of symptoms at previously treated sites. This report suggests that chemotherapy, although a far from optimal therapy in this clinical situation, may induce response and symptomatic improvement at metastatic sites despite previous radiotherapy. Based on response rates obtained in phaeochromocytoma [16], cyclophosphamide, vincristine and dacarbazine should be considered for initial therapy, with other regimens, including single agent carboplatin, reserved for patients who develop intolerable toxicity or fail to respond to the initial regimen.

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Correspondence

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Assessment of Visual Function for Patients on Tamoxifen

SIR – A recent issue of the *Drug and Therapeutics Bulletin* [1] reviewed the process of follow-up in patients with a diagnosis of breast cancer. One of the justifications given for following patients in clinics was the monitoring of the effects of adjuvant therapy, including tamoxifen. The report mentioned the occurrence of rare ocular complications, including cataract and retinopathy, and suggests that visual acuity should be checked before treatment and probably annually while on tamoxifen.

I am not aware of many departments that do this routinely, and indeed, if visual function was to be properly assessed for every person on tamoxifen, this would create an enormous workload for the oncology follow-up clinics and for ophthal-mologists if these patients were referred for formal assessment.

The early reports of tamoxifen-associated retinopathy suggested that doses higher than those traditionally used in this country were to blame [2]. However, since then more recent reports, including a small prospective study published this year [3] suggest that long-term low dose tamoxifen can induce ocular toxicity, although this is not a consistent finding [4]. In the majority, but not all, of the reported cases the ocular changes are reversible.

I feel that this is one area of practice in which it would be very useful to have a consensus opinion on the need for visual assessment, to define what would be regarded as acceptable practice in this country. I wonder if others would wish to express their opinions through the correspondence columns of *Clinical Oncology*.

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