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Special Article

Effective Systemic Therapy for Spinal Epidural Metastases from Breast Carcinoma

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Abstract—*A complete resolution of spinal epidural metastases following systemic therapy, consisting of chemotherapy and/or hormonal therapy, is reported in four patients with breast carcinoma. Remissions were of substantially longer duration than previous remissions induced by radiotherapy. Single systemic therapy is an underestimated way of treatment for spinal epidural metastases. This way of treatment should be considered when radiotherapy has failed. Under certain circumstances it might even be considered as primary treatment. The protracted remissions following systemic therapy, even in the case of a complete myelographic block, warrant further clinical studies concerning this mode of treatment.*

INTRODUCTION

SPINAL epidural metastases are, second to cerebral metastases, the most common neurological complication in patients with carcinoma, and in women most commonly caused by metastatic breast carcinoma [1]. By compression of the spinal cord and roots the epidural metastases produce serious morbidity; only about a half of the patients are still ambulatory at the time of diagnosis. This high number of disabled patients is unfortunately not or only slightly altered by treatment [1, 2]. Nowadays, treatment generally consists of steroids and radiotherapy, and, under certain circumstances, of surgery [1–6]. Chemotherapy and hormonal therapy are considered to be of some value as additional treatment, but regarded as insufficient as a single treatment of spinal epidural metatases [3]. Substantial and protracted responses to chemotherapy and hormonal therapy alone have been described very rarely, predominantly in patients with epidural metastases from malignant lymphomas [7–10], and only occasionally in solid tumors [11, 12]. A documented beneficial effect of treatment with chemotherapy alone on epidural metastases from breast carcinoma has not been reported. The present report shows that a protracted remission of epidural metastases from breast carcinoma can be obtained by single treatment with systemic chemotherapy or hormonal therapy.

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PATIENTS AND METHODS AND RESULTS

All four patients involved in this report were known to have breast carcinoma when they presented with symptoms and signs of spinal epidural metastases. The patients' ages ranged from 40–72 years (mean 49 years). Epidural tumor was confirmed by myelography. In two patients, two separate epidural deposits were demonstrated. A complete myelographic block was noted in one patient. The epidural metastases were at the thoracic level (two times) and the lumbar level (four times). Two patients were treated with hormonal therapy for osseous metastases when the epidural metastases became symptomatic. In one of these patients tamoxifen was changed to aminogluthetimide 250 mg bid with hydrocortisone 20 mg bid leading to a complete clinical and myelographic remission lasting 7 months. After that period an epidural mass at another level became evident. In the other patient hormonal therapy was changed to chemotherapy consisting of cyclophosphamide (CTX) 100 mg PO for 14 days, methotrexate (MTX) 40 mg i.v., days

1 and 8 and 5-fluorouracil (5-FU) 600 mg i.v., days 1 and 8 (CMF). Nine cycles of CMF were given. The remission lasted 10 months. After that time, i.e. 2 months after cessation of chemotherapy, an epidural metastasis at another level became symptomatic. The other two patients had been treated with radiotherapy, respectively 2 and 6 months before they developed neurological symptoms and signs due to recurrence of epidural tumor at the same level. One of these patients, showing a complete myelographic block, was treated with chemotherapy consisting of CTX 500 mg/m^2, doxorubicin 50 mg/m^2 and 5-FU 500 mg/m^2 (CAF). A complete clinical and myelographic remission was achieved, still continuing after a follow-up of 12 months and after cessation of CAF. The other patient was treated with CMF (10 cycles) and tamoxifen. A complete remission was achieved (Figs. 1–3), which lasted 13 months, i.e. 2 months after cessation of chemotherapy. Recurrence of epidural tumor was demonstrated at the same level. She was now treated with a combination of low dose radiotherapy and CAF (12 cycles). Symptoms and signs gradually subsided and she is free of epidural tumor after 12 months follow-up.

In all patients the complete remission of epidural metastases was confirmed by myelography. In two patients additional dexamethasone was given during the first weeks of treatment. Surgical anterior decompression in these patients was not performed because of multiple epidural metastases and widespread metastatic involvement of adjacent vertebrae.

DISCUSSION

Radiotherapy in combination with glucocorticosteroids is the preferred mode of treatment of metastatic spinal cord compression [4, 5]. Surgery is advocated in (1) patients with spinal cord compression from an unknown primary tumor, when the correct diagnosis cannot be made by needle biopsy, and (2) when conservative treatment has failed or is not expected to be effective. Laminectomy can be useful in case of posterior cord compression. However, since the majority of the epidural metastases (85%) arise from the vertebral body, anterior decompression with vertebral body resection and stabilization will usually be the operation of choice [6, 13, 14]. Chemotherapy and hormonal therapy may be of some value as additional treatment, but are regarded insufficient as primary treatment of spinal epidural metastases [3].

A documented and objective favorable response of spinal epidural metastases following treatment with chemotherapy alone or in combination with corticosteroid has been reported in some patients with lymphoma [7–10]. We personally noted a favorable response to chemotherapy alone lasting 18 months in a patient with Hodgkin's lymphoma and severe metastatic spinal cord compression.

A successful and protracted effect of single treatment with chemotherapy on epidural metastases from solid tumors has been reported in children with neuroblastoma [11].

Hormonal treatment alone was reported to yield sustained improvement in three patients with a spinal epidural metastasis of a prostatic carcinoma [9, 12].

Neurological improvement of only a few weeks duration was observed after treatment with corticosteroids alone in a patient with an epidural metastasis from a thymoma, in a patient with a seminoma and a patient with Ewing's sarcoma [8].

It can be concluded that a well-documented substantial and protracted response to systemic chemotherapy and hormonal therapy alone has been reported only sporadically, predominantly in cases of lymphomas. Thus, in the management of spinal epidural metastases single treatment with systemic therapy is generally regarded inefficacious and therefore not applied [3]. It is stated that the epidural tumor mass will not respond to systemic therapy sufficiently and in time to arrest or diminish further tumor outgrowth and the subsequent neurological deficit. This would hold true especially for tumors which are relatively insensitive to chemotherapy, like carcinomas. The present study, however, demonstrates that objective and protracted remissions of spinal epidural metastases from breast carcinoma can be achieved by systemic therapy alone. Three patients were treated with chemotherapy, leading to remissions lasting 10, 13 and at least 12 months. The initial administration of corticosteroids in two patients may have contributed to the favourable response to chemotherapy, but in these cases dexamethasone was stopped within a few weeks. Besides, in the patient with the complete myelographic block, a complete remission was achieved without additional corticosteroids. Notably, the remissions induced by chemotherapy were of longer duration than those induced previously by radiotherapy. Recurrence of epidural tumoractivity occured in two patients, in both becoming symptomatic 2 months after the cessation of chemotherapy.

It is demonstrated that epidural metastatic tumor may also disappear following single treatment with hormonal therapy, although it did not prevent epidural tumor occurring at another level 7 months later.

It may be concluded tht chemotherapy and hormonal therapy can be of value as single treatment for spinal epidural metastases, not only from lymphomas but also from (breast) carcinomas. Thus, systemic therapy must be considered in cases of a local recurrence in which retreatment with radiation

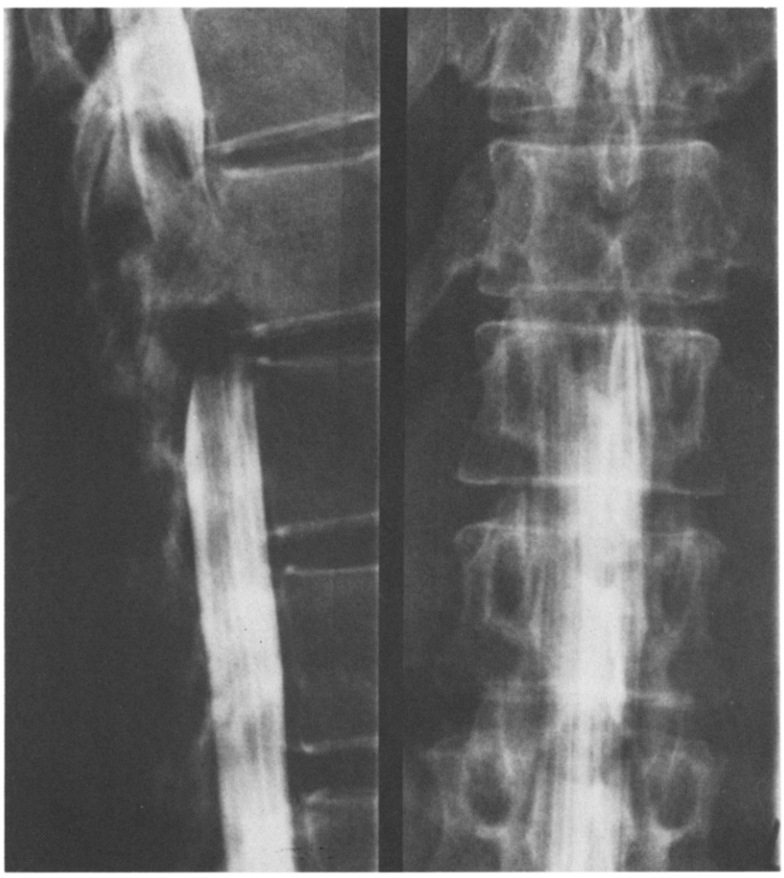

Fig. 1. Epidural metastasis at T12.

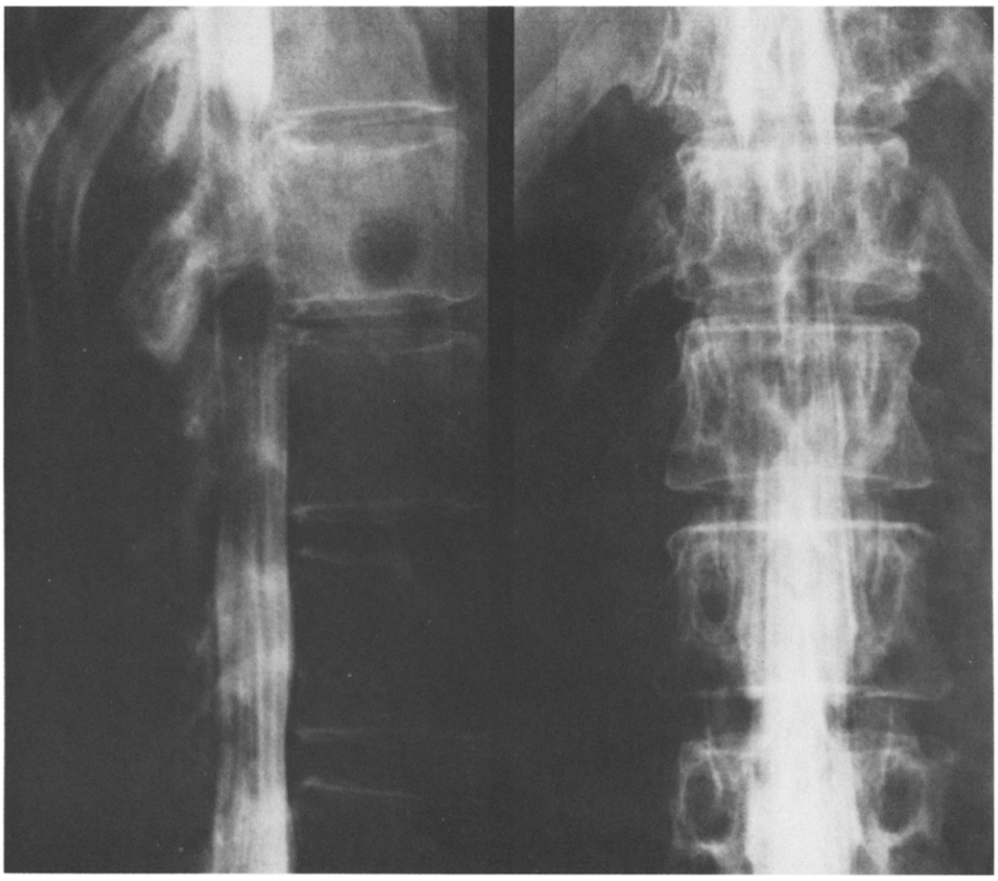

Fig. 2. Six months after radiotherapy: epidural metastasis at T12, extending to L1–L2 level.

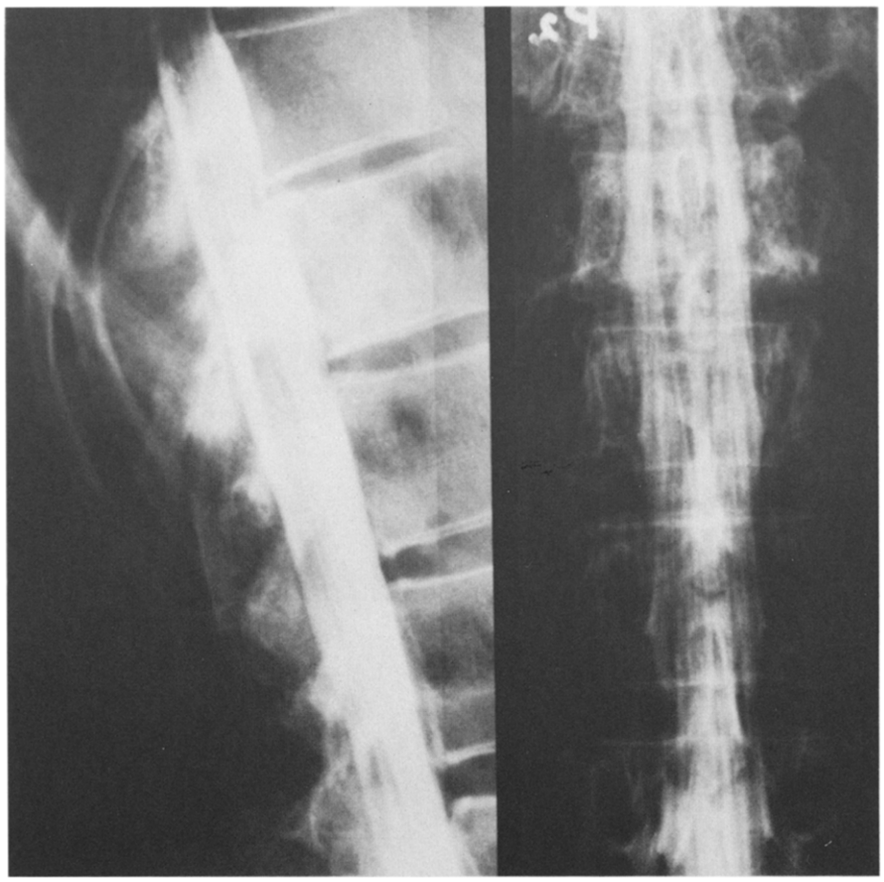

Fig. 3. Six months after chemotherapy: sclerotic aspect of T12, no epidural tumor.

or surgery is regarded as hazardous or impossible. Particularly in patients with minor neurological deficit due to a small and only slowly progressive epidural metastasis, systemic therapy might be tried as primary treatment instead of radiotherapy. Moreover, the risk of 'recurrence' of epidural tumor after radiotherapy due to outgrowth of epidural skipped lesions outside the original treatment field [15] will be reduced by using systemic therapy. The exact place of this kind of treatment, however, still has to be defined. Under these circumstances, early detection and close neurological observation will be even more important than usual.

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