CEREBRAL METASTASES FROM MULTIPLE MYELOMA

Multiple myeloma can secondarily affect the central nervous system (CNS) and many cases of intracranial plasmacytoma arising from skull or dura mater have been reported. Isolated myelomatous meningeal infiltration is less common. Intraparenchymal brain plasmacytoma without bone or dural attachment seems to be very rare and only a few cases have been reported (1).

In the following we report a patient with multiple intracerebral lesions from myeloma. The case also demonstrates that myeloma is a radiosensitive tumour and that radiotherapy is important to keep in mind when intracranial lesions are revealed.

Case report. A 67-year-old woman who had suffered from rheumatic fever in young days developed a diffuse tumour on the sternum in 1980. A blood test showed a high ESR in March 1981. A biopsy taken in October 1986 revealed malignant myeloma. Further examinations showed osteolytic bone lesions, anemia, hypercalcemia and a bone marrow, nearly totally infiltrated with plasma cells. Bence Jones protein was present in the urine. Serum electrophoresis revealed no monoclonal immunoglobulin component. The patient was treated with a standard melphalan/prednisone regimen. The treatment was stopped due to increasing number of osteolytic lesions in August 1989. Radiotherapy was given to lesions in the right tibia in October 1989 to prevent pathological fracture.

In February 1990 she was brought unconscious to the hospital. A cranial CT scan revealed cerebral edema with compression of the side ventricles and at least three cerebral lesions (Fig. 1). Dexamethasone was given at a dose of 4 mg q.i.d. The patient regained consciousness and complained of headache. Total brain irradiation was given from February to March 1990, with 10 fractions over 14 days and a total midpoint dose of 30 Gy. After treatment her memory normalized and her headache disappeared. A CT scan three weeks after the treatment showed considerable regression. The lateral ventricles were now normal in size and position. A CT scan control in May 1990 confirmed continuous remission (Fig. 2). She is now (December 1990) well and living at home with her husband ten months after the irradiation.

Discussion. The development of intracranial metastasis is suggested by Warner & Krueger (2) to be due to circulating lymphocytes carrying the idiotypic determinant of the myeloma protein. When seeded to CNS the tumor cells may escape the effect of chemoterapeutic agents because of the blood—brain barrier (3).

Clarke (4) divided the manifestations of intracranial involvement into the following three groups: A) Syndromes of cranial nerve palsies, B) intracranial tumor syndromes and C) intraorbital tumor syndromes.

The brain plasmacytomas reported have seldom occurred without cranial or dural attachment. To our knowledge there are only six cases reported of intraparenchymal brain plasmocytomas without bone or dural attachment (1).

Our patient had multiple bone lesions in the skull but none of these were in direct connection with the intracranial metastases. The intracranial myeloma lesions were not confirmed histologically and the diagnosis was based on CT. Systemic multiple myeloma is frequently accompanied with cancers of other sites (5, 6), and hence it could be argued that the cerebal lesions were metastases from a second cancer. However, no second cancer was found and the radiographic findings were similar to prior reports (3). The very good remission after radiotherapy is in good agreement with the well-known radiosensitivity of myeloma (7).

In spite of the fact the myeloma is a very radiosensible disease, many of the patients reported in the literature were not treated with

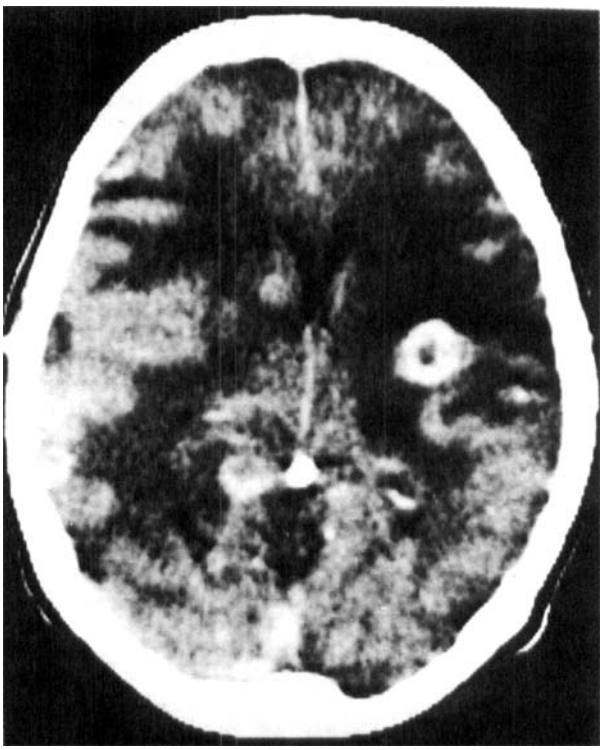

Fig. 1. CT of head showing bilateral edematous changes with compression of the lateral ventricles. There are at least three areas of contrast enhancement appearing as metastases. The largest one is about 2 cm in diameter.

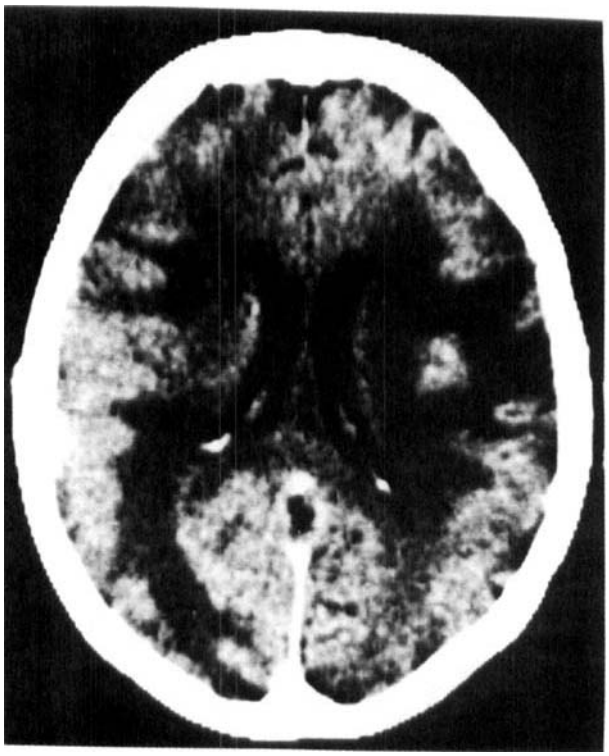

Fig. 2. CT of head $2\frac{1}{2}$ month after radiation treatment revealing pronounced regression of tumors and edematous changes.

radiation and died within few weeks (3, 7, 8). Konick et al. (3) treated their patient with dexamethasone and diuretics. The patient died after four days. A combination regimen with vincristine, BCNU, cyclophosphamide, melphalan and prednisone has also been tried without success (9). Rostom et al. (7) reported a patient treated with upper hemibody irradiation, who died seven weeks after treatment due to brain involvement. In eight cases a mean survival of five weeks was reported (3). Patients with solitary intracranial plasmocytomas are reported to have a more favorable clinical course than those with generalized myeloma (10).

Excellent results have been reported with radiotherapy (10, 11). Jordan et al. (10) observed almost totally disappearance of an intracranial plasmacytoma seven weeks after radiation treatment with 20 Gy over 5 days in combination with intravenous chemotherapy vincristine. The survival time for this patient is not mentioned. The patient reported by us is still alive and well after ten months.

Surgical treatment is reported to be of value when myelomas extend from the skull into the epidural area causing intracranial hypertension (12). Several authors have reported long remissions following complete or incomplete tumor resection and radiation therapy (10).

Key words: Myeloma, intracerebral lesions, radiotherapy.

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EPIRUBICIN IN PATIENTS WITH INOPERABLE NON-SMALL CELL LUNG CANCER—A PHASE II STUDY

Recommendations regarding treatment of inoperable non-small cell lung cancer (NSCLC) range from aggressive chemotherapy to supportive care only. However, during the past 10 years, data have appeared showing that a variety of chemotherapy regimens produce responses in NSCLC (1). Anthracyclines play a major role in those regimens at present (2). Recently there has been considerable interest in newer anthracyclines with, for instance less cardiac toxicity. Epirubicin (4'-epidoxorubicin), a derivative of doxorubicin, has been extensively investigated in a wide variety of tumors. It has been reported to have a more favorable therapeutic index than doxorubicin. There is less hematologic or cardiac toxicity at comparable doses (3–5). Clinical studies are continuing to define the optimal administration schedule and to assess its role in combination chemotherapy regimens. The aim of our study was to evaluate the efficacy and toxicity of epirubicin in patients with inoperable NSCLC.

Material and methods. Patients with histologically or cytologically proven, measurable, non-operable NSCLC were enrolled into the study. To be eligible, patients had to have a Karnofsky index $\geq 60\%$, an age ≤ 70 years and adequate hemathologic, renal and hepatic functions. Epirubicin was administered in escalating doses of 90 mg/m^2, 100 mg/m^2 and 120 mg/m^2 intravenously every 4 weeks for 3 cycles and thereafter 120 mg/m^2 until progression or a maximum of 6 months. WHO criteria (6) for evaluation of response and toxicity were used. Patients were evaluable for response after a minimum of two chemotherapy cycles. All patients, who received chemotherapy (CT) were evaluable for toxicity. The duration of remission and survival time were measured by the product-limit method of Kaplan and Meier.

Results. From March 1985 until November 1986, 32 patients entered into the trail. Patient characteristics are shown in the Table. Twenty-six patients were considered as evaluable for response. The reasons for not being evaluable were early death ($n = 3$) and other treatment ($n = 3$). Half of the patients (16/32) had previously been treated and only 5 had M0 disease when entering into the study. Median number of epirubicin cycles was three (range 1–6). Median cumulative dose of epirubicin was of 285 mg/m^2 ranging from 78 to 656 mg/m^2.

There were two partial responses (PR) in previously untreated patients with M0 disease, stable disease (SD) in 21 patients, and 3 patients with progressive disease (PD). Both responding tumors were adenocarcinomas. The median duration of the objective responses were 9 months and 3 months respectively. The survival of the patients with PR was 17 months and 5 months respectively. Median survival time for all 32 patients was 5 months. One-year and 2-year survival rates were 20% and 0% respectively. Out of the 29 patients evaluable for toxicity, 12 (41%) patients had no side-effects during the treatment while 17 (59%) patients had some kind of side-effects. Of them, 14 had leukopenia (WHO grade 2 ($n = 5$), grade 3 ($n = 8$), and grade 4 ($n = 1$)). Only 3 patients had thrombocytopenia of grade 1. The patient who had severe