Short reports

Pleural mesothelioma treated by fast neutron therapy

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The incidence of malignant mesothelioma of the pleura is rising—there were 254 deaths from this cause in England and Wales in 1982.¹ Despite the fact that isolated claims have been made for radical surgery,² chemotherapy,³ and megavoltage therapy⁴ there is no good evidence that any of these forms of treatment improve the outlook in mesothelioma and most clinicians would subscribe to the view that those patients who have the least active treatment do best.⁶ We report a patient who has done well with fast neutron therapy.

Case report

A 56 year old housewife presented to her general practitioner in January 1976 complaining of persistent cough. A chest radiograph showed a small pleural effusion but pleural biopsy yielded no evidence of malignancy and bronchoscopy showed nothing. Subsequently the effusion subsided. In April 1977 she noticed a subcutaneous mass at the pleural biopsy site. Excision and histological examination of this mass revealed the appearances of a malignant mesothelioma, which was confirmed by electron microscopy, when no epithelial elements could be seen. By July 1977 there was further local recurrence and an increase in the pleural effusion. Chest radiography and computed tomography showed a mass 45×50 mm in the left paravertebral region extending from the seventh to the twelfth thoracic vertebra (fig 1). The patient had no history of exposure to asbestos fibre.

On referral to the fast neutron clinic she was found to have in addition to a left basal effusion a firm subcutaneous mass, 74×59 mm on the lower left posterior chest wall. There was no evidence of distant metastases. In July and August 1977 she underwent neutron therapy for the subcutaneous and intrathoracic disease, a three field technique being used; she received 1650 cGy (rad) in 12 fractions over 35 days.

Over the four months after treatment the subcutaneous mass regressed completely and became impalpable. In March 1978 a 10×10 mm nodule of tumour grew adjacent to the lower border of the neutron treated area. This regressed after 4900 cGy of cobalt radiation in 12 fractions over 27 days, a biological dose similar to that of the neutron therapy.⁷ The pleural effusion at first increased, requir-

ing five aspirations, but then did not recur and since April 1978 there has only been a small left basal opacity, which has remained unchanged to the present day. There is now no sign of recurrent disease 78 months after treatment (fig 2).

Discussion

Most patients with mesothelioma present with advanced disease affecting large areas of pleura. In addition to the "radioresistance" of the tumour it is technically difficult to deliver a high dose to the tumour while sparing the underlying lung. Our patient is unusual in presenting with a bulky mass localised to half the pleural cavity. The visual evidence of regression of the superficial extension of tumour, however, and the long disease free survival after neutron therapy is encouraging.

Fast neutrons are produced by a cyclotron and interact with matter in a different manner from x rays. They have been used for the treatment of locally advanced tumours at the Medical Research Council Cyclotron Unit, Hammersmith Hospital, for the past 14 years. The main rationale for their use is the greater effectiveness of fast neutrons against hypoxic, radioresistant cells, which are thought to be present in large tumours and may provide a source of recurrence. The high rates of complete regression, how-

Fig 1 Computed tomography scan, July 1977, showing the pleural effusion (PF) and the mesothelioma lying as localised tumour (T) behind the heart adjacent to the aorta (A).

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Fig 2 Lateral chest radiograph, 12 January 1984, showing a persistent left basal opacity unchanged for six years.

ever, achieved in a variety of histological types of tumour suggests that fast neutrons may have other biological properties. Complete regression rates of 82% and 75% have been achieved with well and poorly differentiated soft tissue sarcomas and of over 70% with other radioresistant tumours, such as adenocarcinoma, melanoma, and malignant salivary gland tumours.^{8,9} Recurrence after complete regression has occurred in less than 15% of patients. Unfortunately the neutron beam at Hammersmith Hospital is of comparatively low energy and has poor tissue penetration, similar to that of outmoded orthovoltage x ray machines. Delivery of an adequate dose to tumours of the mediastinal pleura is possible only in thin patients with limited disease. The patient reported here is the only patient referred to us with a mesothelioma which could be

adequately covered by the radiation field and for whom a radical course of treatment has been attempted.

In this patient neutron therapy has controlled extensive stage II bulk disease for 78 months without sign of recurrence and a similar biological dose of cobalt radiation has controlled a small nodule. Modern high energy cyclotrons can produce neutron beams with a penetration similar to that of present day megavoltage x ray apparatus. With improved penetration and using techniques designed to spare underlying lung it should be possible to treat radically patients with larger or more deep seated mesotheliomas and to compare the results of treatment with fast neutrons with those of x ray treatment.

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