treatment is therefore warranted based on clinical suspicions and the results of imaging studies. For example, in a patient with a clinically non-invasive anterior mediastinal mass, primary surgical excision without prior biopsy is recommended. In fact, incisional (needle or scalpel) biopsy of a clinically localised (stage I or II) thymoma is contraindicated since violation of the tumour capsule may jeopardise the chances for the excellent surgical result expected with this lesion.⁷ Nagasaka *et al* recently reported a case of needle tract implantation of thymoma after transthoracic needle biopsy which, of necessity, violated the tumour capsule.⁹ If the mass is clearly invasive and unresectable, then needle biopsy is indicated unless there is a strong suspicion of lymphoma, since even core needle biopsy does not usually provide sufficient tissue alone for complete histological classification. Suspected germ cell tumours may be candidates for needle biopsy alone if biochemical markers are positive. Masses felt to represent metastatic disease may be the best candidates for needle biopsy since the sensitivity rate and positive predictive value are virtually 100% when diagnostic tissue is obtained.¹

As a general rule, if sound clinical judgement suggests a lesion that may be unequivocally

diagnosed by tissue obtained with a needle thereby avoiding an open surgical biopsy, then a percutaneous needle biopsy of the mediastinal mass is a reasonable first choice. If the clinical suspicion is of a lesion requiring a larger amount of tissue for diagnosis, then the clinician should forgo the initial needle biopsy and proceed with open biopsy or possibly a complete resection.

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Recall lung pneumonitis due to carmustine after radiotherapy

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Abstract

A patient who developed pneumonitis immediately after the administration of carmustine (BCNU), within exactly the same field as previous irradiation, is presented. The patient responded partially to corticosteroids. This case suggests that irradiation causes subclinical sensitisation of the lung and can therefore have an additive effect in precipitating lung damage when another pulmonary toxin is encountered at a later date.

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Keywords: recall pneumonitis, carmustine, radiotherapy.

BCNU (carmustine; 1,3-bis(2-chloroethyl)-1-nitrosourea) is a nitrosourea capable of in-

hibiting nucleic acid and protein synthesis. Pulmonary toxicity has been described after the administration of 1.2-1.5 g/m² of the drug.¹ BCNU is not known to have a preference for any particular zone of the lung, nor are pre-existing insults known to predispose to this side effect. Pneumonitis and fibrosis after lung irradiation are well described.² Pneumonitis usually occurs 6-12 weeks after the first fraction and often progresses to pulmonary fibrosis by two years. Lymphocyte activity may be seen in areas of lung outside the field of radiation, but most radiographic change is within the treatment zone.

A combination of these two agents would be expected to increase the risk of serious lung damage and we present a case of such toxicity.

Case report

A 51 year old woman developed a subcutaneous mass on the right chest wall which was diagnosed as a localised high grade non-Hodgkin's lymphoma from a right axillary lymph node biopsy.

She was treated over the course of the next three months with three cycles of combination chemotherapy (CHOP: cyclophosphamide (total 4.6 g), adriamycin, vincristine, and prednisolone) with limited response and eventual disease progression. A further course of chemotherapy was tried at approximately nine months after presentation (ifosfamide (total 6.9 g), methotrexate (total 45 mg), and etoposide).

Posteroanterior chest radiograph showing shadowing in the right lung with a linear upper border which corresponded to the upper limit of the radiotherapy field. A little shadowing can also be seen at the left costophrenic angle.

For pain and disease progression at 12 months, however, she required local radiotherapy to the axilla, right breast and chest wall using parallel opposed fields totalling 40 Gy in 20 fractions over 28 days. At 14 months a further 30 Gy in 10 fractions over 12 days using a tangential field to the right chest wall was given, the upper border of which was a horizontal line just below the right clavicle. She noted no ill effect from the radiation. A palliative course of chemotherapy was tried at 14 months (prednisolone, mitozanthrone, etoposide, chlorambucil and cisplatin). Disease progression at 18 months was noted and therefore a course of BCNU (96 mg, i.e. 60 mg/m², day 1), cytarabine 160 mg and etoposide 120 mg (day 2), melphalan 46 mg (day 6) was given. A chest radiograph demonstrating normal lung fields was obtained on the day before the chemotherapy when a central venous line was inserted. Seven days after receiving the BCNU the patient developed a rash and fever, and two days later she noted dry cough and breathlessness. There were inspiratory crepitations over the right chest and the chest radiograph was as shown in the figure. A small left pleural effusion was seen, together with marked diffuse right lung shadowing which spared the apex with a clear horizontal upper border. This did not correspond to any anatomical boundaries, but coincided exactly with the upper border of the tangential radiotherapy. The patient had resting hypoxaemia with an SaO₂ of 92% breathing air. Her serum biochemistry was normal, haemoglobin was 10.3 g/dl, WBC 4.2 × 10⁹/l (90% neutrophils), platelets 59 × 10⁹/l. Blood, urine and throat swabs grew no pathogens. Serological studies showed no rise in antibody titres to respiratory pathogens. She was treated with ampicillin, erythromycin, acyclovir and amphotericin. Bronchoscopic lavage showed no evidence of infection by either common, atypical, fungal, mycobacterial, or viral pathogens. Differential cytology of the lavage showed 47.8% macrophages, 3% neutrophils, 6.7%

eosinophils, and 35.8% lymphocytes, none obviously lymphomatous. Brushings and biopsies were not attempted in view of concurrent thrombocytopenia.

In addition to the above antibiotics, she was treated with high dose methylprednisolone, 1 g for five days followed by prednisolone 60 mg per day reducing to 40 mg over the following week. She became less breathless over the next four days with a normal SaO₂ on air, but her chest radiograph showed no significant improvement. She was well enough to be allowed home a week later. The lymphoma showed further signs of progression; both the patient and her physicians felt that further attempts at treatment would not be appropriate and she died four weeks later. A request for post mortem examination was refused.

Discussion

The acute onset of pulmonary inflammation or pneumonitis shortly after the admission of BCNU strongly implicates this agent as the precipitating cause of the pulmonary toxicity in this patient. The drug is well described as causing pneumonitis and fibrosis. The distribution, however, is clearly delineated by the upper radiation portal (figure) with a straight edge effect which has been previously described in association with radiotherapy alone.³ It has been known for some years that chemotherapeutic agents can potentiate radiation lung injury, which has been shown in experimental models using cyclophosphamide, bleomycin, and vincristine. Concomitant bleomycin given with radiotherapy appeared to be more likely to produce pulmonary fibrosis in those treated for small cell carcinoma.⁴ The same reaction has been described in patients having simultaneous chemotherapy and irradiation with both actinomycin D and doxorubicin.^{5,6} Our patient was somewhat different in that her irradiation was completed three months before the chemotherapy. No single agent can conclusively be implicated in the development of the disease, but BCNU is known to cause pneumonitis and eventual fibrosis.¹⁷ The dose of BCNU given to this patient was much lower (60 mg/m²) than the usual level associated with pulmonary toxicity (1.2–1.5 g/m²), supporting the hypothesis that this is an additive or synergistic effect of both BCNU and radiotherapy. It is possible that the radiation was the sole cause of the response. However, the patient had no previous symptoms or signs, and the chest radiograph one day before administration of the BCNU was normal, which would be unlikely if such florid disease was developing. A pathogen may be difficult to detect in such a situation,⁸ but the distribution and response to corticosteroids after cessation of antimicrobials would make an infection unlikely.

We would hypothesise that the association of lung pneumonitis after BCNU administration within the distribution of previous radiation implies a priming or sensitising event, not detectable by radiology. Roberts *et al*⁹ have previously shown that, after irradiation,

lymphocytes are actively recruited into the lung including areas outside the treatment field. They suggested that, in addition to post-radiation vasculitis, lymphocytes are involved in a hypersensitivity reaction. Certainly there is an increase in the pulmonary CD4+ helper T lymphocytes and it is possible that self-antigen release occurs with the induction of autoreactive lymphocyte clones. The combination of this reaction with a drug which is also able to cause vasculitis may aid such antigen recognition, creating a "recall" pneumonitis.

We would like to thank Professor Catovsky for permission to report his patient.

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Management of residual thymic cysts in patients treated for mediastinal Hodgkin's disease

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Abstract

The pathogenesis of residual thymic cysts after treatment for mediastinal Hodgkin's disease is uncertain. Their presence after adequate treatment often presents the oncologist and the thoracic surgeon with a therapeutic dilemma. Two patients with residual thymic cysts after curative treatment for mediastinal Hodgkin's disease are described and the management discussed.

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Keywords: Hodgkin's disease, thymic cysts, radiotherapy, chemotherapy.

Thymic cysts are occasionally found after the completion of planned treatment for patients with mediastinal Hodgkin's disease. Their presence on chest radiographs or computed tomographic (CT) scans may indicate either residual or recurrent disease or a benign lesion.

Surgical excision followed by histological examination is the most reliable method of evaluating the possibility of viable tumour within the residual thymic cysts, but this may be dangerous and unnecessary. Needle biopsy, although safer, can produce false negative results. Further chemotherapy and/or radiotherapy may be given to these residual thymic cysts without pathological confirmation, which could be unnecessarily harmful and may even lead to

death in patients with no viable lymphoma cells.

We report two patients who received no supplementary treatment for residual thymic cysts and who remain alive and well 2-6 years after their initial treatment.

Case reports

CASE 1

A 28 year old man presented with enlargement of the right cervical lymph nodes. A biopsy specimen demonstrated nodular sclerotic Hodgkin's disease. The chest radiograph showed mediastinal widening and a computed tomographic (CT) scan of the chest showed a thymic cyst in addition to the mediastinal lymphomatous masses (fig 1A).

The patient was treated with three courses of chemotherapy (adriamycin, bleomycin, vinblastine and DTIC) followed by a radical course of radiotherapy to the mediastinum and cervical and axillary regions. The follow up CT scan approximately nine months after commencing treatment showed complete resolution of the lymphomatous masses in the neck and the mediastinum but no change in the cystic mass. Annual CT scans were performed and the CT scans taken three years and six years after treatment serve to confirm that the patient remains in complete remission (fig 1B).

CASE 2

A 26 year old woman presented with left supraclavicular lymphadenopathy. A biopsy specimen showed nodular sclerotic Hodgkin's disease. A chest radiograph showed mediastinal widening and a CT scan confirmed the mediastinal lymphadenopathy and also a thymic cyst.

The patient was given six courses of chemotherapy consisting of epirubicin, bleomycin, vinblastine, and prednisolone. The thymic cyst at initial presentation was 7 × 4 cm; 3-6 months follow up CT scans showed considerable reduction in size to 2.3 × 1.2 cm 10 months later. The cyst has remained the same size on the two year follow up CT scan.

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