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Case reports

A commentary on the following four case reports appears on pages 1121–3.

Fallibility of transthoracic needle biopsy of anterior mediastinal masses

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Abstract

Percutaneous transthoracic core needle biopsy has been advocated as a highly accurate technique for the diagnosis of anterior mediastinal masses. A patient is described with a large anterior mediastinal mass in whom the diagnosis of mediastinal carcinoid tumour was made by transthoracic core needle biopsy. At definitive surgical resection the tumour proved to be a B cell lymphoma. This case illustrates one of the important limitations of needle biopsy with its potential for sampling error.

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Keywords: needle biopsy, B cell lymphoma, mediastinal neoplasms.

The development of the minimally invasive technique of percutaneous needle biopsy has proved to be invaluable in obtaining diagnostic tissue from most body compartments. The use of this technique has risen dramatically with the evolution of sophisticated imaging techniques especially computed tomographic (CT) scanning. The most recent anatomical area to be targeted for needle biopsy is the mediastinum. The literature is replete with multiple series advocating not only fine needle aspiration, but now core needle biopsy of lesions in this body compartment including the anterior mediastinum with its diverse population of potential tumours.[1–3] The following case report illustrates the diagnostic fallibility of core needle biopsies, particularly of histologically similar, hypercellular anterior mediastinal neoplasms, that influence subsequent definitive therapy.

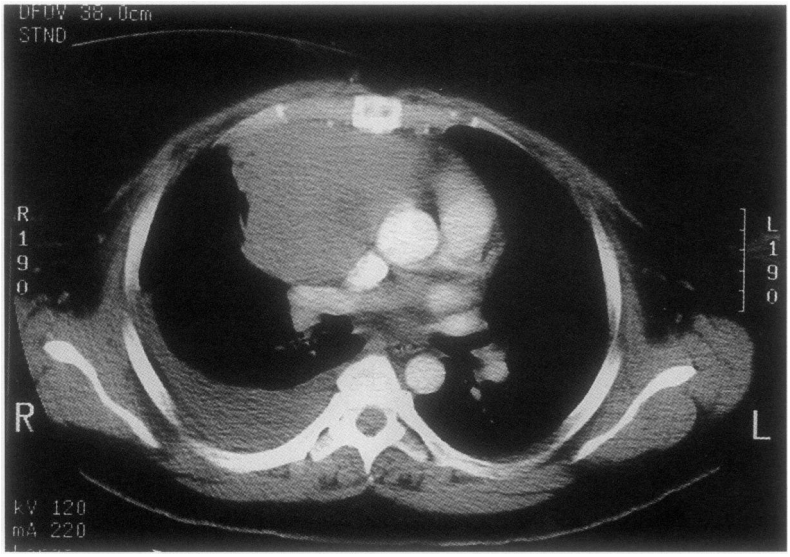

Figure 1 Representative image from a contrast enhanced computed tomographic scan of the chest taken at a level 2 cm inferior to the carina. A 10 cm × 10 cm × 8 cm homogenous mass can be seen in the anterior mediastinum that abuts, and possibly invades, the sternum and chest wall, displacing the great vessels and heart to the left. A moderate sized right pleural effusion is also present.

Case report

A 37 year old white woman presented with a six week history of a tight full sensation in her chest accompanied by right anterolateral chest pain which was worsened by alcohol ingestion. During the previous two weeks she had noted some dyspnoea on exertion, a non-productive cough, and a 3 kg weight loss. She also reported some diarrhoea for several weeks but this had resolved. She smoked one pack of cigarettes per day. She had no history of flushing, fever, night sweats, pruritus or other constitutional symptoms, or any other significant medical problems. She had a strong family history of a variety of cancers in three uncles and a grandmother. Her physical examination was normal.

A chest radiograph demonstrated a large anterior and middle mediastinal mass. CT scans of the chest and abdomen (fig 1) showed a 10 cm × 10 cm × 8 cm anterior mediastinal mass abutting the chest wall and displacing the superior mediastinal structures and heart to the left, accompanied by a moderate sized right pleural effusion. Pericardial and pleural thickening was evident, suggesting local invasion. The right upper lobe bronchus was narrowed with some distal pulmonary consolidation. There was no mediastinal or abdominal adenopathy.

A transthoracic core needle biopsy of the mass was performed and showed histological characteristics of a carcinoid tumour (fig 2A). She was referred for further evaluation and therapy. Review of the biopsy specimen was performed, including an immunohistochemical stain for chromogranin which was interpreted as positive, and a leucocyte common antigen (LCA) stain (CD45, a pan-leucocyte marker)[4] which was felt to be negative. A barium enema, upper gastrointestinal and small bowel barium series, and bronchoscopic examination were all normal. Pulmonary function studies showed a mild restrictive process. Urinary 5-HIAA levels,

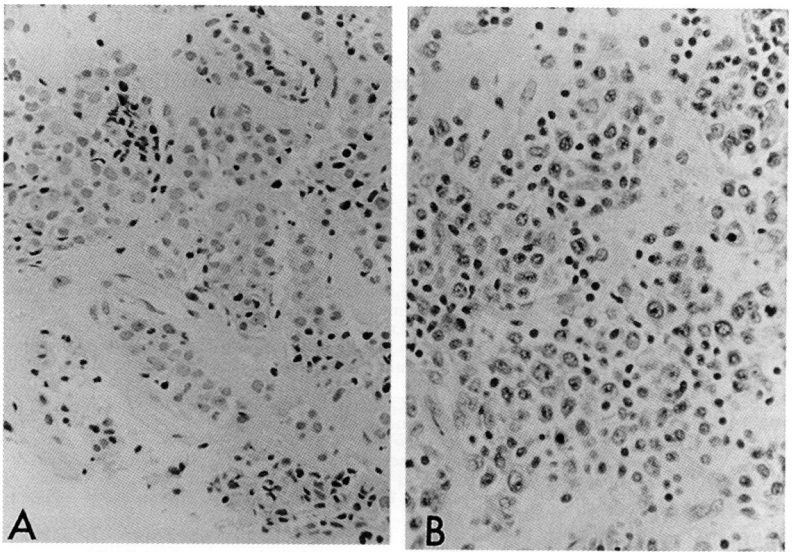

Figure 2 (A) Haematoxylin and eosin stained photomicrograph from the preoperative transthoracic core needle biopsy specimen of the mediastinal mass showing cells with uniform nuclear chromatin arranged in packets and separated by fibrous tissue. This is consistent with a diagnosis of carcinoid tumour. (B) Representative haematoxylin and eosin stained section from the mediastinal mass removed at surgery showing cells with peripheral nucleoli and irregular chromatin arranged in packets and sheets separated by fibrous tissue, considered to be similar to (A). The cells in (A) had positive immunohistochemical staining for chromogranin (not shown). However, only the cells in (B) subsequently stained positive with leucocyte common antigen (not shown), verifying the final pathological diagnosis of non-Hodgkin's lymphoma, large cell (B cell) type diffuse with sclerosis. Original magnification × 150, reduced to 63% in origination.

complete blood count, liver function tests, serum cortisol, adrenocorticotrophic hormone, serum glucose and other blood chemicals were all normal.

Following a review of the literature on primary mediastinal carcinoid tumours,[5] aggressive surgical resection of this rare but locally invasive neoplasm was performed by median sternotomy. The tumour invaded the pericardium, superior mediastinum, right pleural apex, the medial aspect of the entire right lung including the hilar vessels, and the chest wall. A subtotal resection of approximately 95% of the mass was accomplished. The patient had an uneventful course following surgery and was discharged on the eighth postoperative day.

Pathological evaluation of the surgical specimen revealed non-Hodgkin's lymphoma, large cell (B cell) type diffuse with sclerosis, verified by positive LCA staining. In addition, there were small foci of organoid-appearing cell clusters similar to the biopsy specimen, but they represented only a small percentage of the tumour. A representative microscopic section from the surgical specimen (fig 2B) demonstrated similarity to the core needle biopsy, particularly when the section was obtained in a few particular locations. The needle biopsy tissue was probably obtained from these small areas of the tumour resulting in a significant sampling error and a misleading diagnosis. However, it was not felt that carcinoid tumour was present in the neoplasm. The patient is currently undergoing chemotherapy for non-Hodgkin's lymphoma.

Discussion

The diagnostic evaluation of mediastinal masses often presents a challenge due to the variety of primary tumours as well as inflammatory, vascular, or metastatic masses that may occur in this area. In one collected series,[6] 54% of mediastinal masses occurred in the anterosuperior compartment. Located in this area were thymomas (30%), lymphomas (20%), germ cell tumours (18%), carcinomas (13%), and a variety of other lesions in the remaining 19%.

On initial presentation approximately one third of all lesions are symptomatic in adults,[7] with malignant tumours causing symptoms in approximately 85%.[6] The anterior mediastinum contains the greatest number of malignant masses (40% of the total) and symptomatic lesions.[7] Diagnostic investigation of mediastinal masses was greatly enhanced by CT scanning and magnetic resonance imaging, often supplemented by markers such as α-fetoprotein, placental alkaline phosphatase, and β-human chorionic gonadotropin levels. Radionuclide scanning may occasionally be helpful for localisation of masses such as pheochromocytomas, or for an indication of benign versus malignant neoplasms suggested by gallium scintigraphy.[7]

Invasive diagnostic procedures often play a valuable part in staging and providing tissue for pathological study in order to plan treatment. Mediastinoscopy and parasternal mediastinotomy have traditionally filled this role.[7] However, percutaneous fine needle aspiration and, more recently, core biopsies with large bore needles guided by CT scanning or ultrasound have also been advocated for the diagnostic examination of mediastinal lesions.[1-3]

Numerous series using transthoracic needle biopsy techniques for mediastinal masses report that a definite histological diagnosis is obtained in as many as 89% of patients with core biopsy specimens.[3] Despite the excellent safety and low complication rate with this technique, the nature of the common tumours found in the anterosuperior compartment tends to limit its accuracy. Although core specimens are obtained, tissue amounts are frequently inadequate to classify lymphocytic thymomas, small lymphocyte lymphomas, and Hodgkin's disease. Because malignant Reed-Sternberg cells are rare but are necessary for the diagnosis of Hodgkin's disease, the needle biopsy tissue sample is frequently inadequate to find these cells. Though core biopsy samples may provide the general diagnosis of non-Hodgkin's or Hodgkin's lymphoma, further classification with additional tissue from a surgical biopsy specimen is usually necessary before instituting treatment.[2] In addition, malignant germ cell tumours often have more than one component and this may not be represented by a core needle biopsy alone.[1]

As with any diagnostic procedure, there are definite advantages as well as limitations to transthoracic needle biopsies of mediastinal masses, especially in the anterior compartment. Ferguson *et al* in a series of patients with anterior mediastinal masses found that, based on histological findings, non-resectional therapy was the most appropriate treatment in 61% of cases.[8] A selective approach to diagnosis and

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 inhibiting nucleic acid and protein synthesis. Pulmonary toxicity has been described after the administration of 1·2–1·5 g/m^2 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 (ifosphamide (total 6·9 g), methotrexate (total 45 mg), and etoposide).