CASE FOR DIAGNOSIS

Chest pains complicating an artificial therapeutic pneumothorax

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Case report

A 56 yr old nonsmoking woman was admitted to hospital in 1985 with left sided chest pain and weight loss. She had a history of pulmonary tuberculosis 35 yrs previously. An extrapleural therapeutic pneumothorax had been performed at that time and was complicated several years later by chronic pyothorax. On admission in 1985, she had no dyspnoea or cough. Physical exam-

ination showed decreased breath sounds in the upper left chest. No superficial lymphadenopathy was found. A peripheral white cell count revealed $10.5 \times 10^9 \cdot L^{-1}$ leucocytes, of which $9.15 \times 10^9 \cdot L^{-1}$ were polymorphonuclear cells and $0.6 \times 10^9 \cdot L^{-1}$ were lymphocytes. The erythrocyte sedimentation rate was 60 mm in the first hour.

A chest radiograph (fig. 1) and computed tomographic (CT) scan (fig. 2) are shown.

Fig. 1. — Chest radiograph showing pleural thickening in the upper left pleural space.

Fig. 2. — Computed tomographic scan of the chest demonstrating an encapsulated pleural effusion.

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BEFORE TURNING THE PAGE: INTERPRET THE CHEST RADIOGRAPH AND CT SCAN, SUGGEST A DIAGNOSIS AND PROPOSE USEFUL COMPLEMENTARY INVESTIGATIONS.

Interpretation of the chest radiograph and CT scan

The chest radiograph demonstrates pleural thickening in the left upper pleural space. The CT scan of the chest shows an encapsulated pleural effusion, without pulmonary or mediastinal lymph node involvement.

Further investigations

Bronchoscopy revealed external compression of the left upper lobe bronchus. Pleural aspiration was performed, and haemorrhagic fluid was obtained. No malignant cells were seen. Cultures of the pleural and bronchial fluids for acid-fast bacteria were negative.

A posterolateral thoracotomy was performed, and an encapsulated lesion containing necrotic tissue was removed from the extrapleural space. Histological findings revealed large atypical lymphoid cell proliferation with necrosis and haemorrhage (fig. 3). Immunohistochemistry showed a non-Hodgkin's lymphoma (NHL) of the diffuse large B-cell type using monoclonal antibodies DBB42 (Immunotech, Marseille, France), and MB2 (Euro-diagnostics, Apeldoorn, The Netherlands). *In situ* hybridization with an Epstein-Bar virus (EBV)-encoded small ribonucleic acid (RNA) (EBER-1) oligonucleotide probe (Dako, Glostrup, Denmark), demonstrated positive nuclear staining for EBV gene expression (fig. 4).

Bone marrow biopsy did not show lymphoid cell infiltration. Other investigations for extrapleural extension remained negative.

DIAGNOSIS: "Pleural B-cell malignant lymphoma associated with an artificial therapeutic pneumothorax"

Treatment and evolution

The patient received combination chemotherapy (four courses of vincristine, cisplatin, chlormethine, and prednisone every month) plus left upper pulmonary-mediastinal radiotherapy (46 Grays (Gy)).

The patient died of squamous cell carcinoma which developed 10 yrs later in the left upper bronchus. This may have been related to previous chemotherapy and radiotherapy received, as she had never smoked.

Discussion

To our knowledge isolated pleural NHL has been reported only in association with chronic pyothorax or artificial therapeutic pneumothorax. Pleural NHL is a rare complication of chronic pyothorax. LUCHI *et al.* [1] reported three cases in a series of 134 tuberculous pyothoraces (2%). NHL with chronic pyothorax is cytomorphologically and immunohistochemically exclusively

Fig 3. – Pleural histological findings show large atypical lymphoid cell proliferation (arrow). (Internal scale bar = 10 μ M).

Fig 4. – *In situ* hybridization with an Epstein-Bar virus encoded small ribonucleic acid (EBER-1) oligonucleotide probe of pleural lymphoma. Most tumour cells show a strong nuclear signal (arrow) (Internal scale bar = 10 μ M).

of B-cell lymphoma cell-type [2]. Most cases have been reported from Japan and Taiwan [1, 2]. An environmental factor for the development of pleural NHL has thus been suspected [3].

Pleural effusions are rarely found in Hodgkin's disease at the time of diagnosis, but more frequently in NHL [4]. At autopsy, patients with NHL frequently have pleural effusion. Evidence of pleural malignant cellular infiltration is obtained in 30% of cases. Direct pleural infiltration appears to be the predominant cause of effusion in NHL. Pleural effusion usually occurs in the presence of disease elsewhere. However, isolated pleural effusion is unlikely to be due to lymphoma, once staging has been completed [1]. A primary and isolated pleural effusion of NHL is reported in <1% of cases [3].

We report here a new case of pleural B-cell NHL associated with a clinical history of chronic inflammation of the pleura resulting from therapeutic artificial pneumothorax. Previously, three similar cases have been reported from European countries [5]. The low frequency of pleural NHL in Western countries might be explained by the rarity of chronic pyothorax in these cases. Differential diagnoses such as malignant mesothelioma [6], soft tissue sarcoma [7], and squamous cell carcinoma [8] have been reported to complicate chronic pyothorax. However, lymphomas are the most frequent tumour arising in such a context [2]. Usually the interval between the development of malignancy and the initial chronic tuberculous pyothorax is more than 20 yrs. Mechanisms of oncogenesis remain unclear, but recent *in situ* hybridization experiments have shown that pleural B-cell lymphomas had high levels of EBV gene expression [5]. Relationships between EBV and NHL development are incompletely understood. Chronic pleural inflammation could have favoured a clonal evolution of EBV-infected B-cells through the production of growth factors or immunosuppressive cytokines produced by inflammatory cells [5]. Finally, an autoimmune pathophysiological association such as lymphocytic thyroiditis has been proposed [9]. In our case, we have been not found such an association with an auto-immune disorder.

Chest pain and new weight loss are the most common clinical features at presentation. Usually, uncomplicated chronic pyothorax is free of symptoms [3, 10]. The possibility of malignant transformation must be considered when chronic pyothorax becomes symptomatic. The success rates of needle biopsy and pleural fluid cytology depend on tumour extent. They appear particularly low in localized tumours [11]. Some authors emphasize the usefulness of thoracotomy to investigate suspected pleural involvement [2, 3]. Thoracoscopy appears to be a very useful diagnostic tool for malignant pleural effusion. In large series, thoracoscopy provided the pathological diagnosis of chronic malignant pleural effusion in 92–97% of cases. These results are dependent on the skill of the practitioner [12, 13].

In a Japanese series, treatment included chemotherapy alone or combined chemo and radiotherapy. Survival rates of 2 yrs were poor (32–42%) [10]. The unusual long term of survival in our case could be due to an encapsulated tumour without pulmonary or thoracic wall extension. Primary complete surgical resection could be an important prognostic factor.

Keywords: B-cell malignant lymphoma, chronic tuberculous pyothorax, Epstein-Barr virus, *in situ* hybridization.

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