A variant of pyothorax-associated lymphoma

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Summary

A case of pleural lymphoma that developed after an episode of empyema is described. This may be a variant presentation of the rare yet distinct condition termed pyothorax-associated lymphoma. This condition was first recognised in Japan; there have been only a few reports in Western countries to date. A feature of this case is the relatively short interval between diagnosis of empyema and subsequent development of lymphoma.

Keywords: lymphoma; pyothorax-associated lymphoma; empyema

The entity 'pyothorax-associated lymphoma' was first reported by Aozasa in 1987, after reviewing 37 cases of pleural lymphoma in Japan. The presentation of this special subtype of lymphoma was characteristically preceded by 20–30 years of pleural irritation (pyothorax/artificial pneumothorax for tuberculosis treatment).¹ There have been sporadic reports of this condition since, with the majority of cases described being immunoblastic or large cell types.^{2,3} The current case describes the development of pleural lymphoma within a short time frame after diagnosis and surgical drainage of an empyema.

Case report

A 70-year-old Caucasian man presented to the St George Hospital in December 1996, with a one-month history of increasing shortness of breath and left pleuritic chest pain. Further history revealed a weight loss of 3 kg, anorexia, and night sweats. The chest X-ray showed a large left pleural effusion. Percutaneous aspiration of the effusion yielded only 15 ml of white turbid fluid. Computed tomography (CT) of the chest showed a large loculated fluid collection occupying most of the left hemithorax.

The patient's history included mild hereditary spherocytosis, mild hypertension controlled with an angiotensin-converting enzyme (ACE) inhibitor, and localised transitional cell carcinoma of the bladder, which required adjuvant pelvic radiotherapy at time of diagnosis in 1993, with no subsequent recurrence on follow-up cystoscopies. He was homosexual, but on repeated testing had been HIV negative.

The patient underwent open thoracotomy, evacuation of the empyema, and decortication of the left lung in December 1996. At operation, a thick-walled empyema with 800 ml of pus was evacuated. Postoperative recovery

was uneventful. Routine microscopy and cultures for bacteria and acid-fast bacilli were unable to identify a causal organism.

Over the subsequent few months the patient was followed up as an out-patient. Persistent left lower lobe atelectasis prompted two bronchoscopic examinations. On each occasion, a slit-like narrowing of the apical segmental bronchus of the left lower lobe was noted. Bronchial biopsy showed inflammatory changes, including lymphoid infiltrates. Bronchial washings were negative for acid-fast bacilli and malignant cells.

At follow-up in December 1997, the patient was well and routine haematology and biochemistry tests were normal. The chest X-ray and thoracic CT scan, however, showed several right-sided pleural-based mass lesions of variable size, the largest measuring 3 × 2 cm adjacent to the right heart border. One of these lesions had extended into the spinal canal in the upper thoracic region. There was also a mass lesion in the right mid zone with several smaller nodules in the right lung. On the left side, there was chronic collapse of the lower lobe, and pleural thickening at the lung base, consistent with a previous empyema drainage. Fine needle aspiration biopsy of one of the right-sided pleural lesions yielded atypical lymphoid cells, of mixed small and large cell types. While highly suspicious of lymphoma, the findings were insufficient for diagnosis.

A repeat CT scan, including the abdomen as part of the staging process, confirmed the soft tissue masses on the right chest wall and collapse of the left lower lobe. No mediastinal or axillary lymphadenopathy was present. Homogenous splenomegaly was noted, consistent with the history of hereditary spherocytosis. There was no other abnormality in the abdomen. A second fine needle pleural biopsy showed a population of large malignant lymphoid cells on cytology. Immunocytochemistry confirmed B cell monoclonality.

Further investigations included a bone marrow biopsy, which showed no evidence of lymphomatous infiltration. A gallium scan showed gallium avid disease confined within the thorax, which correlated with the lymphoma deposits visible on the CT scans.

The patient was commenced on combination chemotherapy, consisting of chlorambucil, vincristine, procarbazine, and prednisone (LOPP), which was tolerated very well. After five treatment cycles given on a monthly basis, the restaging CT scan demonstrated resolution of the right pleural masses, and repeat gallium scan confirmed this improvement. At the time

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of this report, the patient is in clinical remission from lymphoma.

Discussion

The majority of cases of pyothorax-associated lymphoma (PAL) described in the literature occurred in Japan; there have been less than 10 cases reported in Western countries.² Environmental factors such as Epstein-Barr virus exposure,³ or other as yet undetermined factors, may be a crucial trigger to malignant transformation, thus explaining the geographical variation in incidence. One relatively constant feature of PAL appears to be the presence of inflammation or irritation of the pleura prior to development of lymphoma. Tuberculosis, or artificial pneumothorax used for treatment thereof, is a common culprit.¹ Association with Epstein-Barr virus genome within tumour cells has been noted.¹⁻³ Several authors have been able to demonstrate unusual cytokine concentrations in the lymphoma-induced pleural effusion fluids. Interleukins 6 and 10 have been implicated.⁴⁻⁶ Cytokine stimulation exerted on local cells may be the key to de-differentiation of normal reactive lymphocytes. In addition, high frequencies of p53 mutations have also been found in lymphoma cells of this type.¹⁻⁵

In the present case, there was no history of exposure to tuberculosis, and examination of the empyema fluid for *M tuberculosis* was negative. The causal organism of the empyema eluded identification. The radiotherapy that

Learning points

- a pleural lymphoma developing subsequent to local inflammation may belong to a distinct subtype called 'pyothorax-associated lymphoma'
- cytokines associated with the inflammatory process have been implicated in the malignant transformation
- such a lymphoma is responsive to chemotherapy, and remission can be achieved

the patient received for carcinoma of the bladder was limited to the pelvic region, and probably has no bearing on the chest pathology.

While the bulk of the lymphoma was in the right hemithorax, the initial site of disease was probably at the slit-like narrowing of the left lower lobe segmental bronchus. This lesion predated the other right-sided pleural masses, and showed atypical lymphoid infiltrates on bronchial biopsy. Empyema-induced local inflammation in the left lower lobe could, as postulated in the literature, have led to de-differentiation and malignant transformation of reactive lymphocytes.

The fact that the lymphoma was the second malignancy in this patient, may imply some form of predisposition towards malignancy development, be it inherited or acquired. In turn, this could explain the unusually short interval between the episode of empyema and the subsequent development of lymphoma.

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