

## Massive pleural effusion: an unusual presentation of Castleman's disease

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*Massive pleural effusion: an unusual presentation of Castleman's disease. S.P. Reynolds, A.R. Gibbs, R. Weeks, H. Adams, B.H. Davies.*

**ABSTRACT:** Giant lymph node hyperplasia (Castleman's Disease) is a rare cause of pleural effusion. We report the case of a 51 yr old West Indian male, who presented with a recurrent massive pleural effusion, due to a tumour arising from the pleura. He underwent parietal pleurectomy and subtotal excision of the tumour. Histological analysis of the specimen showed the features of multicentric Castleman's disease. Nine months following surgery he remains well, with no recurrence of the effusion.

*Eur Respir J*, 1992, 5, 1150-1153.

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Keywords: Castleman's disease; paraproteinaemia; pleural effusion.

Received: January 20 1992

Accepted after revision May 19 1992

### Case report

A 51 yr old West Indian male, who had lived in the UK for 30 yrs, presented to hospital with increasing breathlessness, night sweats and loss of 10 kg in weight, which had developed over 12 months. He had been hypertensive for 10 yrs and was well controlled on nifedipine and bendrofluazide. There was no exposure to asbestos or contact with tuberculosis. He was a lifelong nonsmoker and denied excessive alcohol intake.

On examination he was afebrile, with a respiratory rate of 28·min<sup>-1</sup>. There was clubbing and a 1 cm diameter firm, non-tender, palpable lymph node in his right axilla. There was evidence of a large right pleural effusion. Abdominal examination revealed a 2 cm smooth, non-tender hepatomegaly.

Laboratory investigations showed normal blood count and full biochemical screen. Arterial blood gases on air were oxygen tension (P<sub>O<sub>2</sub></sub>) 9.9 kPa, carbon dioxide tension (P<sub>CO<sub>2</sub></sub>) 5.7 kPa and O<sub>2</sub> saturation 95%. The patient's liver function tests showed albumin 46 (normal 35-48) g·l<sup>-1</sup>, total protein 87 (normal 60-80) g·l<sup>-1</sup>, bilirubin 24 (normal 1-17) μmol·l<sup>-1</sup>, Gamma GT 115 (normal 5-35) U·l<sup>-1</sup>, alkaline phosphatase 60 (normal 40-110) U·l<sup>-1</sup> and aspartate transaminase 44 (normal 12-30) U·l<sup>-1</sup>. Serum protein electrophoresis revealed a polyclonal increase in immunoglobulin G (IgG) of 25.6 g·l<sup>-1</sup> and in immunoglobulin M (IgM) lambda paraprotein of 3 g·l<sup>-1</sup>. Light chains were not present in the urine. Permission for bone marrow aspiration was denied. Intradermal tuberculin test was positive at 1 in 1,000 with 11 mm of induration after 48 h.

The chest X-ray (fig. 1) confirmed a massive right-sided pleural effusion with mediastinal shift to the left. Thoracic echocardiography revealed a small anterior and posterior pericardial effusion with no signs of cardiac tamponade.

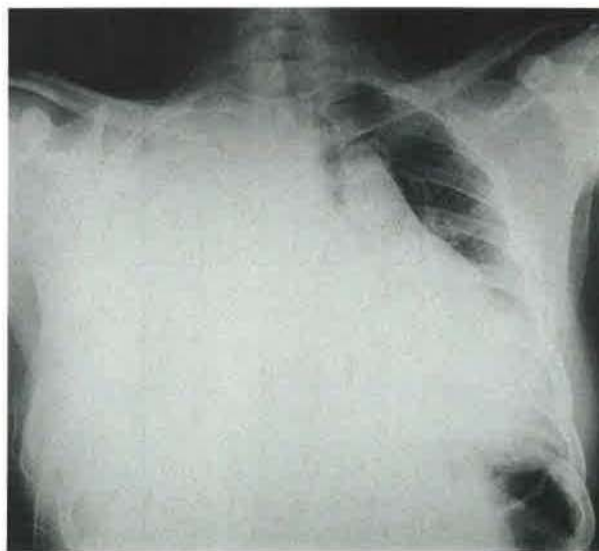


Fig. 1. - The chest radiograph shows massive right pleural effusion causing mediastinal shift.

A chest drain was inserted and 7 l of straw-coloured liquid was drained over three days. Protein concentration of the pleural fluid was 73 g·l<sup>-1</sup> confirming an exudative effusion. Cytology, microscopy, Ziehl Neelsen staining and culture of the fluid for *Mycobacterium tuberculosis* were all negative. Pleural and

axillary node biopsy showed reactive changes with no evidence of granulomata or malignancy.

A post-aspiration chest radiograph revealed an irregular right heart border. Computed tomography (fig. 2) of the thorax demonstrated a small homogeneous mass adjacent to the right atrium. Fluoroscopy-guided fine needle aspiration of the mass was attempted as thoracoscopic exploration of the pleural space was not available. Cytology revealed blood-stained fluid with no evidence of malignant cells.

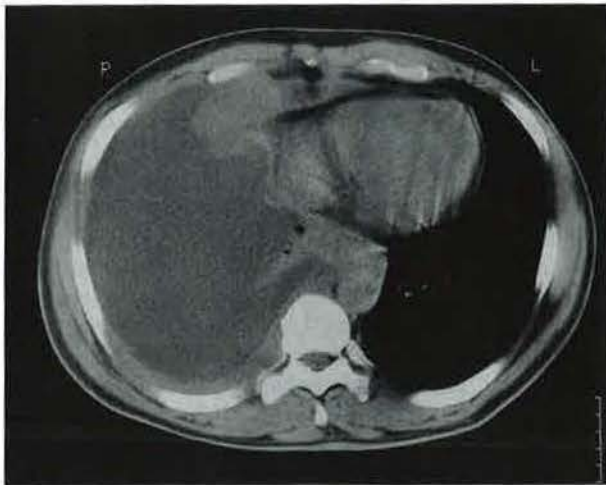


Fig. 2. - Computerized tomograph (CT) through the lower thorax showing a massive pleural effusion. A mass is present adjacent to the right atrium.

An exploratory thoracotomy was performed one week later to obtain a tissue diagnosis. At thoracotomy, 3 l of straw-coloured fluid had reaccumulated. Inspection of the right hemithorax confirmed a mass anteriorly, at the cardiophrenic angle, adherent to the right pericardium and involving the phrenic nerve. Tumour was observed to have spread posteriorly over the right hemidiaphragm and onto the chest wall. Excision of the mass was attempted but was incomplete due to proximity to the phrenic nerve. A parietal pleurectomy was performed.

The tissue removed at thoracotomy consisted of an oval piece of fairly homogeneous grey firm tissue (tumour) measuring 3.5x2.5x1.5 cm and multiple pieces of thickened, slightly nodular, grey pleura, together approximately 10x3.5x2 cm (fig. 3). Microscopically, the oval piece of tissue was composed of sheets of small lymphocytes with finely dispersed granular chromatin and occasional large lymphoid cells with central nucleoli and slightly open chromatin (fig. 4). There were scattered small germinal centres and numerous hyalinized vessels throughout the lesion. There were patchy foci, where plasma cells were the predominant cells, but they were not evenly dispersed throughout the lesion. The pleura separate from the nodule showed a similar lymphoid infiltrate, with germinal centres and occasional hyalinized vessels (fig. 5).



Fig. 3. - The homogeneous grey nodule can be seen on cut section. On the left is thickened pleura attached to the nodule.

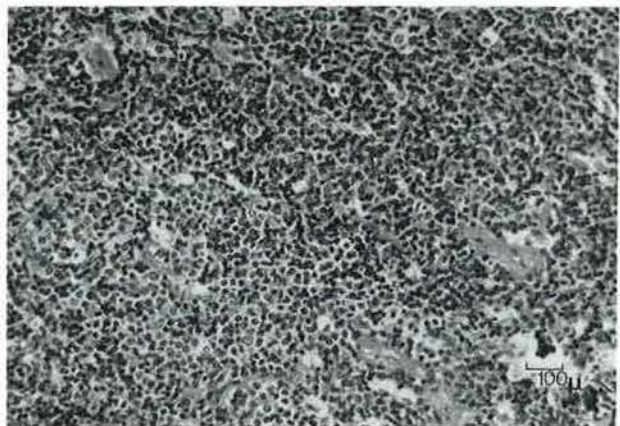


Fig. 4. - This microscopic section is obtained from the nodule and shows small lymphocytes, plasma cells and a smaller component of large lymphocytes. There are several hyalinized vessels present.

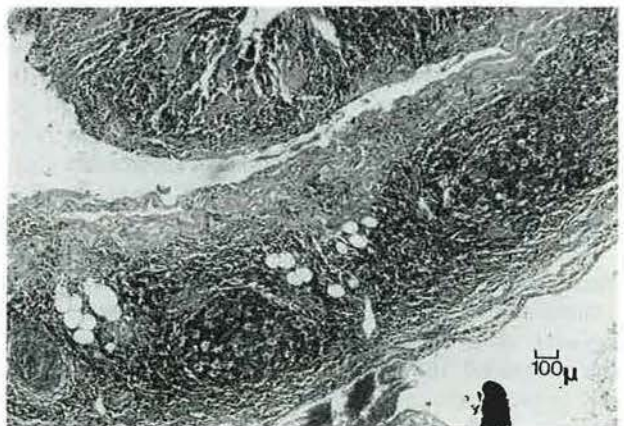


Fig. 5. - The pleura shows a lymphocytic infiltrate with germinal centres and hyalinized vessels.

Immunohistochemistry showed mainly B-lymphocytes with polyclonality for lambda and kappa chains in the oval lesion. A diagnosis of Castleman's disease of mixed or transitional type was made.

The patient recovered quickly following the operation and was discharged home. On regular review extending to 9 months, he has remained well with no systemic complaints. Serum electrophoresis has continued to show an increase in IgM lambda paraprotein at  $10 \text{ g} \cdot \text{l}^{-1}$ . However, the chest radiograph did not show any reaccumulation of pleural fluid.

### Discussion

Castleman's disease, also referred to as lymph node hyperplasia [1], lymph node hamartoma [2] or angiofollicular lymph node hyperplasia [3] is an eponymous term, which was first given to a lymphoid tumour of the mediastinum [4]. Although the majority of lesions occur within the chest as asymptomatic masses [1], less commonly other sites including the neck, pelvis, retroperitoneum and axilla may be involved [5]. There is no significant sex predominance and no identifiable risk factors in the development of the disease [1]. Three histological types have now been described: hyaline vascular, plasma cell and transitional (mixed) type [6].

The first two types are usually localized diseases, whereas the transitional type is usually multicentric. The rare multicentric form with associated systemic disorders may have an aggressive and sometimes fatal clinical course [7-10]. In a few cases, malignant lymphoma, colonic carcinoma or Kaposi sarcoma have developed [9-11].

Similar histological findings to the multicentric form of Castleman's disease have been reported in association with the POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy and skin changes) and some authors consider them to be overlapping entities [12].

We report a multicentric form of Castleman's disease in association with a massive pleural effusion, clubbing, a small pericardial effusion and an IgM paraproteinaemia. Clubbing has been reported in association with the POEMS syndrome [12] but the finding of a pleural effusion in Castleman's disease is rare. We have found only six reports of small to moderate sized pleural effusions [1, 12-14]. In two, these were bilateral but not clinically detectable [12, 13]. In a few reports, however, these effusions were several litres in volume [1, 12, 14].

Pericardial effusions are uncommon in Castleman's disease and are not usually detectable clinically [15].

Immunohistochemical studies on tumour tissue from patients with Castleman's disease have frequently demonstrated the presence of polyclonal plasma cell populations and polyclonal hypergammaglobulinaemia [16]. The occurrence of hypergammaglobulinaemia may be due to release of factors from hyperplastic lymph node cells, known to be involved

in the activation process of B-cells. In this context, large amounts of B-cell differentiation factor activity and interleukin-6 have been measured in unstimulated lymph node suspensions [17, 18].

Less often, lesions contain a monoclonal plasma cell population, usually IgG or IgA lambda, with a paraproteinaemia corresponding to the Ig type of the proliferated cells [16]. Although polyclonal staining for IgG and IgM was present within excised tissue from our patient, in addition to a polyclonal IgG hypergammaglobulinaemia, there was also an IgM paraproteinaemia. Presumably, there existed a clone of IgM lambda producing cells within the tumour as well as a population of reactive cells responsible for increased serum polyclonal IgG production. The IgM lambda paraprotein has risen slowly following subtotal resection of the tumour and suggests the continued existence of a monoclonal plasma cell population. Despite evidence of monoclonality, the patient has not demonstrated any obvious signs of malignancy during a short follow-up period.

In cases of localized Castleman's disease, complete surgical excision is the treatment of choice. However, if this is not possible, partial excision may be useful [1]. A variety of drugs including prednisolone, chlorambucil and cyclophosphamide have been used in the multicentric form, alone or in combination, with variable results [9, 11, 19].

In conclusion, we report a unique case of multicentric Castleman's disease, presenting with a massive pleural effusion, in a man of West Indian extraction. Surgical pleurodesis in addition to subtotal excision of the tumour appears to have prevented recurrence of his symptoms and pleural effusion.

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