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- A high index of suspicion along with knowledge of the diagnostic criteria is essential to avoid misdiagnosis.
- The co-morbidities of older people may render clinical diagnosis difficult.
- s-IBM should be considered in treatment-resistant polymyositis over 50 years, disproportionate quadriceps, finger/wrist flexor weakness, unexplained dysphagia and in atypical motor neuron disease.
- Repeated biopsies may have to be done to demonstrate the features of IBM.
- Steroid treatment must not be continued for more than 3–6 months as it is not effective and also carries a risk of steroid-induced myopathy, which worsens the condition.
- In life-threatening oesophageal impairment, a course of IVIg + steroids is beneficial.

References

The very long list of references supporting this article has meant that only the ten most important are listed here and are represented by bold type throughout the text. The full list of references is available in the supplementary data on the journal’s website (http://www.ageing.oxfordjournals.org) along with a description of the diagnostic criteria and mechanisms and the theories of pathogenesis of IBM (Appendices II and III).


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An unusual cause of pleural effusion

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Abstract

Primary effusion lymphoma (PEL) is a unique clinicopathological entity associated with human herpesvirus-8 (HHV-8) infection, occurring almost exclusively in human immunodeficiency virus (HIV)-infected individuals. We report a rare case of HHV-8-negative PEL in an HIV-negative elderly patient who presented with pleural effusion. The patient was treated with CHOP and Rituximab. As opposed to the general poor outcome of this disease, our patient achieved complete remission and is still without signs of disease 11 months after the last treatment.

Keywords: primary effusion lymphoma, human herpesvirus-8, Rituximab, human immunodeficiency virus, CHOP
Introduction

Primary effusion lymphoma (PEL) represents an unusual entity of B-cell neoplasm, predominantly described in human immunodeficiency virus (HIV)-infected individuals. This body cavity-based lymphoma was originally reported to be associated with infection of human herpesvirus-8 (HHV-8) and in the majority of cases with Epstein–Barr virus (EBV) as well. Recently, however, some cases of PEL in HIV-negative patients have been reported, some of them not associated with HHV-8 [1–5]. The causative agent or aetiological background associated with this distinctive disease remains unclear. Whether PEL develops in immunocompromised patients or not the prognosis remains strikingly poor, regardless of the involvement of HHV-8, with a reported median survival of 3 months in most series so far [1]. Here we describe an unusual case of an elderly patient with HIV, HHV-8 and EBV-negative PEL that was successfully treated with a combination of CHOP and Rituximab.

An 88-year-old man was admitted to our hospital because of progressive weakness and exertional dyspnoea that developed 10 days prior to his hospitalization. His previous medical history included ischaemic heart disease for which he was treated pharmacologically with satisfactory results. Physical examination revealed diminished breath sounds over the left lung and moderate pitting oedema of both legs, but was otherwise unremarkable. Chest radiography showed a massive left pleural effusion (Figure 1).

Computed tomography scan of the chest and abdomen showed the same pleural effusion, but no mass or pathological lymph nodes were detected.

Echocardiography revealed a moderate pericardial effusion, normal contractility of both ventricles, and overall acceptable diastolic and systolic function. The patient’s laboratory data was unremarkable except for the following abnormalities: blood chemistry showed an elevated serum lactate dehydrogenase of 670 IU/l, arterial blood gases found the PO2 to be 54 mmHg, the PCO2 33 mmHg and pH 7.46. The blood count was without any abnormal findings. The patient had an elevated ESR (65 mm/h) and C-reactive protein (90 mg/l). Serological tests were negative for HIV (Trinity Biotech Uni-Gold Recombigen HIV rapid test, later confirmed by Bio-Rad Genetic System’s Western blot), hepatitis-B virus (core and surface antigens excluded by Roche Diagnostics Cobas Core and Elecsys Modular Kits, Basel, Switzerland, respectively), hepatitis-C virus (Abbott AXSYM), EBV and CMV (Enzygnost, Dade Behnking, Atterbury, UK). The patient underwent pleurocentesis that produced 3,000 cm3 of bloody fluid that was characterized as exudative by a high protein content and a high lactate dehydrogenase. Cytological analysis of the pleural effusion revealed large lymphoid cells with prominent round or lobulated nuclei, basophilic cytoplasm and a few vacuoles. Immunohistochemistry showed the neoplastic cells to be positive for CD-20, CD-30, CD-79a and leukocyte common antigen CD-45 (LCA). Flow cytometry analysis of the fluid supported the above findings that are all consistent with a large B-cell lymphoma. Polymerase chain reaction (PCR) and nested PCR were negative for HHV-8 DNA (done as described previously by Shimazaki et al. [2] trying to detect the KS330123 and KS330153). Bone marrow aspiration and biopsy demonstrated a slightly hypocellular bone marrow but was without any evidence of malignancy. A Gallium-67 scintigram showed an abnormal diffuse uptake over the left hemithorax.

The patient was treated with a full dose CHOP regimen: cyclophosphamide 750 mg/m2 on day 1, doxorubicin hydrochloride 50 mg/m2 on day 1, vincristine sulfate 1.4 mg/m2 on day 1 and prednisone 100 mg on days 1–5. In addition to this standard regimen, we added 375 mg/m2 of Rituximab on day (–1). A week after the first course, the patient was found to have a significant clinical improvement and was released without any complaints except general weakness. He underwent two more identical cycles without significant side effects and on his last follow-up was without any clinical or radiological evidence of disease. A follow-up Gallium-67 scintigram showed no abnormal uptake 9 months after the treatment.

Discussion

We have described a case of B-cell lymphoma with massive pleural effusion in an elderly HIV, HHV-8 and EBV-negative patient. Throughout the clinical course, physical examination, ultrasonography, computed tomography scan and Gallium scintigraphy failed to reveal a contiguous solid mass. The absence of a mass or lymph nodes, combined with the characteristic clinical and cytomorphological features, made us consider the case to be PEL. PEL was originally described in HIV-infected individuals (some authors even consider PEL to be an AIDS-defining illness) and was characterized by HHV-8 infection of the neoplastic cells [4]. Subsequently, PEL was described in immunocompetent patients as well, and to date 22 cases have been described in HIV-negative patients who were negative for HHV-8 as well [1, 3]. Twelve of these cases were reported to be associated
with EBV infection, and six cases involved the hepatitis-C virus. The median age of onset of HIV, HHV-8-negative PEL was 71, and the pleural space was the most commonly involved body cavity. The prognosis is poor regardless of the HHV-8 status—between 3 and 6 months median survival in different series [1, 2, 4]. To date, no optimal chemotherapeutic regimen has been established for the disease. CHOP therapy, a standard therapeutic regimen for aggressive large B-cell lymphoma, is the usual first-line treatment. Lately, Inoue et al. [1] reported achieving durable remission using the newly developed oral bis-dioxopiperazine sobuzoxane in a patient with pericardial PEL that responded partially to CHOP. In our case, the neoplastic cells expressed the CD-20 antigen, suggesting the possible benefit of the monoclonal chimeric antibody Rituximab in addition to the standard treatment.

The CD-20 cell-surface molecule is detectable from the pre-B-cell stage till late in the differentiation of B-cells. It is highly expressed (over 100,000 molecules per cell) and it is not generally present in soluble form, making it an effective target for B-cell depletion [6]. Several trials have shown the advantage of adding Rituximab to the standard chemotherapeutic regimen when treating patients with large-B-cell lymphoma, and lately Coiffier et al. [7] showed the combination of CHOP and Rituximab to increase response rates in elderly patients without increasing toxicity.

Our patient responded with a complete remission and to date, 11 months after the treatment, no evidence of recurrent disease has been detected.

Key points

- Primary effusion lymphoma is a rare B-cell lymphoma found mostly in HIV positive patients and is associated with HHV-8. Even so several reports have been made of this unique entity in elderly HIV negative patients.

- Primary effusion lymphoma, as other lymphomas in the elderly population, is associated with a poor prognosis.

- Addition of Rituximab to the standard chemotherapeutic treatment has been proven effective in elderly patients with CD-20 positive B-cell lymphomas. Our case suggests that patients diagnosed with primary effusion lymphoma could also benefit from this combination.

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