Unclassifiable B-cell lymphoma occurring after necrotizing pneumonia

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INTRODUCTION

Grey zone lymphomas (GZLs) are a rare specific entity of lymphomas, mostly demonstrating features of both classical nodular sclerosing Hodgkin’s lymphoma (cHL-NS) and mediastinal large B-cell lymphoma (MLBCL) [1]. There is no consensus on the optimal treatment, and patients generally have a poor prognosis.

CASE REPORT

A 47-year-old man was referred with a necrotizing pneumonia of the right lower lobe, destroying most of the lung parenchyma of the lower lobe. Underlying malignancy was suspected. He had never smoked, and his medical history only mentioned allergic conjunctivitis and slight bronchial hyperreactivity. Computed tomography (CT) of the chest showed complete opacification of the right lower lobe. Integrated 18F-fluorodeoxyglucose positron emission-computerized tomography (18F-FDG PET/CT) demonstrated isotope uptake in the mediobasal segment of the right lower lobe (Fig. 1). The hilar and right paratracheal lymph node stations were also positive on PET/CT scans. Group C Streptococcus and Pseudomonas were isolated from culture specimens of the bronchial aspirate. Initially, the patient was treated with broad-spectrum antibiotics and steroids with some resolution. CT showed a partial aeration of the lower lobe with a minor reduction in the size of the hilar and mediastinal lymph nodes. However, control 18F-FDG PET/CT showed persistent radionuclide uptake in pretracheal and paratracheal lymph nodes. Cervical mediastinoscopy was negative, so the patient underwent an exploratory thoracotomy. Lymphoma was suspected on frozen section analysis of the tumour in the right lower lobe, and a bilobectomy of the middle and lower lobes was necessary to remove the whole tumour. A systematic lymph node dissection was performed.

On pathological examination, the diagnosis of a CD20+ GZL with Reed Sternberg cells was confirmed. CD20, CD30 and EBV were positive in nearly all tumour cells, and CD15 was positive in some of them. However, some neoplastic cells were CD20 negative. Weak expression of PAX-5, MUM1 and BCL-2 was found, whereas EMA and CD45 were negative. The pathological examination of the systematic nodal dissection showed the presence of B-cell lymphoma in lymph node station 11 (anterior in major fissure); all other lymph node stations including the mediastinal were inflammatory, with the presence of eosinophilic granulocytes. The patient was subsequently treated with six cycles of R-BEACOPP (rituximab, cyclophosphamide, doxorubicin, etoposide, procarbazine, prednisone, bleomycin and vincristine), which was well tolerated. Because of the poor prognosis, the patient subsequently underwent autologous peripheral-blood stem-cell transplantation after high-dose chemotherapy with excellent results. Control PET/CT after 4 months showed an encapsulated fluid collection of the right pleura, but no remaining active lesions. After a clinical follow-up of 9 months, the patient is in good general condition without signs of recurrent disease and will soon return to work.

DISCUSSION

GZL involving the lung is a rare entity and, in most reported patients, a mediastinal localization was present. No relationship between GZL and necrotizing pneumonia could be found in the literature. There are several types of GZLs. Primary MLBCL, a grey zone between classical Hodgkin lymphoma (CHL) and diffuse...
large B-cell lymphoma (DLBCL); grey zone between CHL and anaplastic lymphoma kinase-negative anaplastic large cell lymphoma and/or peripheral T-cell lymphoma and a grey zone between CHL or nodular lymphocyte predominant Hodgkin lymphoma and T-cell/histiocyte-rich large B-cell lymphoma [2]. The most frequent GZL demonstrates characteristics of both cHL-NS and MLBCL, whereas the GZL with overlapping features of CHL and DLBCL is the most problematic area, which was the fact in our case.

There is a difference in the gene expression profile of MLBCL and DLBCL occurring at extra-mediastinal sites, but there are common features with CHL [2]. The aetiology of GZL is unknown, and only 20% or fewer cases are EBV-positive [1].

The histological workup of MGZL involves evaluation by pathological, immunohistochemical and molecular analyses (Table 1) [1, 3]. Immunohistochemical stains, in particular CD30 and CD15, are used routinely for the confirmation of CHL. However, there are cases where CD15 is either negative or only focally positive in association with strong CD20 positivity. In these cases, large B-cell lymphoma (LBCL) also comes into differential diagnosis as this tumour usually also co-expresses CD30 (an activation marker not specific for HL) and rarely, CD15 as well. Antibodies for EBV like LMP are also useful in many cases of CHL show nuclear staining for this antibody [1, 3]. Despite all these immunohistochemical markers, there are some cases in which the diagnosis of either CHL or LBCL cannot be confirmed, labelling these cases as GZL.

CD15-negative and CD30-positive cases are more common in the Indian population. These Indian patients also have a worse prognosis in comparison with Caucasian patients with a CD15-negative and CD30-positive lymphoma [4].

<table>
<thead>
<tr>
<th>Kind of lymphoma</th>
<th>Markers</th>
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<tbody>
<tr>
<td>CHL</td>
<td>CD15+, CD30+, CD20+, EBV-LMP+, BOB 1–, OCT-2–</td>
</tr>
<tr>
<td>DLBCL</td>
<td>CD15+, CD20+, CD30+, BOB 1+, OCT-2+</td>
</tr>
<tr>
<td>GZL (CHL + DLBCL)</td>
<td>CD15+, PAX-5+, MUM1+, BOB 1+, CD20+, CD30+, EBV+, OCT-2+, EBER+</td>
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</tbody>
</table>


DLBCL, a type of GZL occurring at extra-mediastinal sites, carries a worse prognosis than primary mediastinal thymic large B-cell lymphoma, requiring more aggressive treatment [5]. However, there is still little evidence about the optimal treatment and no specific guidelines are available.

BEACOPP is the standard treatment for CHL, whereas rituximab is added for DLBCL as it improves the outcome [1, 5]. This explains the choice of treatment in our current case.

**CONCLUSION**

GZLs are a rare specific entity of lymphomas showing overlapping features of different types of lymphomas.

In our case, the GZL showed common characteristics of CHL and DLBCL. The aetiology of GZL is unknown. The diagnosis is...
confirmed by pathological, immunohistochemical and molecular analyses. Useful immunohistochemical markers in confirming the diagnosis of either CHL or DLBCL are CD15 and CD30. Despite all these immunohistochemical markers, there are some cases in which the diagnosis of either CHL or LBCL cannot be confirmed, labelling these cases as GZL. There is still no consensus on the optimal treatment, and further study is warranted.

Generally, these patients have a poor prognosis.

Conflict of interest: none declared.

REFERENCES