CASE REPORT

Bowel perforation from occult ileal involvement after diagnosis in a case of primary mediastinal large B-cell lymphoma

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SUMMARY

Primary mediastinal large B-cell lymphoma (PMBCL) is confined to the mediastinum or contiguous nodal areas in most cases. Extramediastinal and abdominal involvement, especially at diagnosis, is extremely rare. Our case describes the first case of histologically proven ileal involvement of PMBCL at diagnosis that led to ileal perforation. Positron emission tomography CT could increase the sensitivity of staging by detecting unusual sites of disease localisation, and could impact clinical management.

BACKGROUND

Primary mediastinal large B-cell lymphoma (PMBCL) is a distinct clinical and pathological subtype of diffuse large B-cell lymphoma (DLBCL). It arises from a small population of B cells within the thymus.^{1 2} PMBCL is a rare lymphoma, and represents 2–4% of all non-Hodgkin's lymphomas and 6–12% of all DLBCLs.¹

PMBCL is characterised by a rapidly growing mediastinal mass, frequently accompanied by local invasiveness. Patients often present with cough, dyspnoea, chest pain and superior vena cava syndrome. Extramediastinal involvement at diagnosis is rare.³ When present, the involvement of the stomach,⁴ kidneys, adrenal glands, liver and central nervous system (CNS) has been described. Conversely, these organs are very frequently involved at the time of disease relapse.^{1 3 5}

The diagnostic approach to PMBCL has classically relied on whole body CT scan, and histological confirmation through core or surgical biopsies.³ According to WHO,⁶ PMBCL expresses B-cell markers (CD19, CD20, CD22 and CD79a) but lacks surface immunoglobulins. CD30 is present in more than 80% of cases, but its expression is usually weak and/or heterogeneous. Positron emission tomography CT (PET-CT) scan has recently been recommended at presentation to increase the sensitivity of staging, and improve the response assessment after therapy.⁷ However, this has led to some uncertainty about the impact of PET-positive disease at subdiaphragmatic sites on management and prognosis.^{4 8}

Supporting the utility of a more accurate staging, this case illustrates a unique presentation of PMBCL with asymptomatic ileal involvement that was not identified by CT scan at diagnosis and led to bowel perforation at the start of steroid treatment.

CASE PRESENTATION

A 44-year-old male patient presented to the emergency room with shortness of breath, chest discomfort and prominent facial swelling, which had arisen few days before and progressively worsened. He denied having fever, chills, night sweats and weight loss in the previous weeks. Physical examination revealed significant facial, neck and upper trunk oedema, and visible engorged vessels consistent with superior vena cava syndrome. Physical examination did not reveal any abdominal mass or hepatosplenomegaly, abdominal tenderness or palpable lymphadenopathy. A complete blood count was only notable for mild neutrophilic leucocytosis (white cell count 13 600/L). Serum lactate dehydrogenase, β -2-microglobulin and uric acid were normal. A chest X-ray demonstrated a large anterior mediastinal mass. CT scan showed a large anterior mass, from a likely neoplastic origin, measuring 12×12 cm with effacement of the superior vena cava and impairing ventilation of the middle lobe of the lung. There was moderate left pleural effusion and some pathological mediastinal lymphnodes, of which the largest was in the right paratracheal region and measured 19 mm. CT scan also showed a 3.3 cm mass in the left adrenal gland, ascribed to the same process underlying the mediastinal mass in the first instance. No other pathological findings were reported by CT scan. Histological examination of a CT-guided core biopsy of the mediastinal mass showed a diffuse infiltrate of large lymphoid cells with prominent sclerosis. Immunostaining was positive for CD20, CD45, CD23, IRF4/MUM1 and CD30^{dim} (figure 1A). The neoplastic cells were negative for CD15, CD3 and CD10. Diagnosis of PMBCL was made according to the current WHO criteria.⁶

Following the diagnosis and before the staging could be completed with a total-body PET-CT scan, steroid therapy (dexamethasone 4 mg two times a day) was quickly started to manage symptoms of superior vena cava syndrome. After 10 days, the patient manifested severe abdominal pain and obstructive symptoms for which he was admitted to the emergency room. An urgent laparoscopic surgery was performed that revealed an ileal perforation. Therefore, the patient underwent a small bowel resection with end-to-end anastomosis. The surgical specimen was sent for histological examination which surprisingly revealed infiltration by large lymphoid cells involving all the intestinal wall layers with the same immunohistochemical

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Figure 1 (A) Diffuse infiltrate of large pleomorphic cells with relatively clear large cytoplasm and fibrosis (H&E $\times 20$) in a mediastinal core needle biopsy (Ai) showing diffuse positivity for the B cell-associated antigen CD20 (Aii, peroxidase immunostaining). (B) Diffuse infiltrate of large pleomorphic cells with relatively clear large cytoplasm (H&E $\times 40$) in an intestinal surgical sample (Bi) showing diffuse positivity for the IRF4/MUM1 molecule (Bii, alkaline phosphatase immunostaining)

features of the mediastinal sample, indicative of ileal localisation of PMBCL (figure 1B).

Staging was then finalised with a PET-CT showing a highly fluoro-deoxyglucose (^{18}F FDG)-avid mediastinal mass and diffuse hypermetabolic mediastinal adenopathies involving the paratracheal, Baretty and hilar areas, and measuring about 1 cm in diameter. In the abdomen, PET-CT showed a hypermetabolic lesion in the left adrenal gland, interpreted as a disease localisation site, and a low-grade diffuse uptake of small bowel, which was most likely a non-specific finding from the recent surgery. Bone marrow trephine biopsy and cerebrospinal fluid analysis were negative. Eastern Cooperative Oncology Group performance status was 0. According to these data, the clinical stage was IVA and the International Prognostic Index (IPI) was 2, while the age-adjusted IPI was 1; thus, both were in the intermediate low-risk group.⁹

TREATMENT

The patient received six cycles of dose-adjusted rituximab-etoposide, prednisone, vincristine, cyclophosphamide and doxorubicin (R-EPOCH).¹⁰ Owing to the high risk of developing CNS disease in patients with involvement of more than one extranodal site, triple intrathecal prophylaxis was administered with cytosine arabinoside, methotrexate and dexamethasone at each cycle.¹¹

OUTCOME AND FOLLOW-UP

Interim response assessment after three cycles with a CT scan revealed $>50\%$ disease reduction, indicating a partial response to

treatment. A final assessment at the end of treatment with CT and PET scans showed complete response. The patient is currently in complete remission 7 months after completion of treatment.

DISCUSSION

Our case describes an unusual presentation of PMBCL with extensive intra-abdominal involvement. While PMBCL typically shows propensity to early intrathoracic extension to adjacent organs, in most cases the disease is confined to the mediastinum or contiguous nodal areas. Only a minority of patients show extrathoracic disease at presentation.^{3 5 12} Nevertheless, the prognostic role of extranodal and subdiaphragmatic involvement is still uncertain. We selected the dose-adjusted combination chemotherapy regimen R-EPOCH based on results reported by Dunleavy *et al* showing 93% event-free survival and 97% overall survival at 5 years. In that study, 15 patients (29%) had stage IV disease and 27 (53%) had involvement of extranodal sites; however, no different outcome in these subgroups was reported.¹⁰

Gastrointestinal localisation of PMBCL at diagnosis is extremely rare. An early report⁵ found stomach involvement in 1 in 23 patients. In a more recent study,⁴ only 1 in 204 patients showed evidence of gastric involvement of PMBCL that was confirmed from histology specimens; this was clinically evident because of spontaneous gastrointestinal haemorrhage. In the same study, PET-CT at diagnosis was performed on 14 patients and highlighted stomach hypermetabolic activity in one, who was eventually found to have a second lymphoma, namely a gastric marginal B-cell lymphoma, mucosa-associated lymphoid tissue type, in addition to the PMBCL.

To the best of our knowledge, no studies to date have reported cases of ileal localisation of PMBCL at diagnosis. In our patient, who presented without abdominal symptoms, we found a histologically proven small intestine localisation. Ileal involvement was not diagnosed by CT scan staging at baseline, and was eventually discovered because steroid treatment likely promoted tumour necrosis which in turn caused an ileal perforation. Unfortunately, we could not perform a PET-CT scan before steroid therapy was started owing to the urgent need for symptom control. Nevertheless, we believe that the ileal lesion would have been as metabolically active as the mediastinal and adrenal gland lesions.

PET-CT-based staging could detect gastrointestinal involvement in rare asymptomatic patients where the CT scan staging is negative. Aside from prognostic value, awareness of such unusual localisations may change the clinical approach to the patient, supporting the inclusion of PET-CT at diagnosis. Given the low frequency of extramediastinal involvement of PMBCL, gastrointestinal lesions discovered during PET-CT staging should prompt the need for histological confirmation to exclude the presence of two different neoplasms in the same patient. Moreover, the clinician should be aware of visceral localisation of PMBCL so that he can plan a closer follow-up during earlier phases of treatment or for unexpected complications, such as bowel perforation.

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Contributors CDP and MCDC cared for the patient, collected clinical data and wrote the manuscript. ES performed pathology analysis NB supervised clinical care, conceived the project and wrote the manuscript.

Competing interests None declared.

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Learning points

- ▶ Gastrointestinal involvement of primary mediastinal large B-cell lymphoma (PMBCL) at diagnosis is extremely rare, but may cause serious complications.
- ▶ Positron emission tomography CT (PET-CT) could increase the sensitivity of staging by detecting unusual sites of disease localisation.
- ▶ Upstaging of PMBCL by PET-CT could impact clinical management, even though the prognostic value of extrathoracic disease is still uncertain.

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