Circulating lymphoma cells of double-hit lymphoma

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DESCRIPTION
A Caucasian man aged 65 years presented with generalised weakness, 20 pounds weight loss and occult gastrointestinal (GI) bleeding. Laboratory findings revealed pancytopenia with WCC of 2500/mm³, haemoglobin of 7.4 g/dL and platelets of 86 000/mm³. Peripheral smear revealed characteristic immature lymphoid cells (figure 1A). Flow cytometry of peripheral blood confirmed the presence of abnormal monoclonal B-cells representing lymphoma cells. Full-body CT scan showed bilateral pleural effusions, splenomegaly, kidney lesions and presacral mass. Upper GI endoscopy revealed gastric ulcers. Bone marrow biopsy established the diagnosis of B-cell lymphoma, unclassifiable, with features intermediate between diffuse large B-cell lymphoma and Burkitt lymphoma (BCLU) (figures 1B, C and 2B). Biopsy of gastric ulcers (figure 1D), presacral mass and pleural fluid cytology showed the presence of lymphoma. Immunohistochemical stains showed the tumour cells to be positive for CD10 and CD20, while tumour cells were negative for CD3 and TdT. BCL-2 expression showed high background and was equivocal (figure 2A). Ki-67 staining showed a proliferative fraction of ~80–90% (figure 2C). Cyclin D1 was also negative (figure 2D). FISH analysis showed gene rearrangement of BCL-2 and c-MYC, confirming double-hit lymphoma. The patient was started on dose-adjusted EPOCH-R (Etoposide, Prednisone, Vincristine, Doxorubicin, Cyclophosphamide, Rituximab). PET scan showed complete response after four cycles of chemotherapy along with intrathecal-methotrexate for central nervous system prophylaxis.

Double-hit lymphoma is a very aggressive form of non-Hodgkin’s lymphoma with extremely poor prognosis. Dose-adjusted EPOCH-R is considered to be the most effective treatment regimen. Our case highlights the aggressiveness of this lymphoma, its response to DA-EPOCH-R and also emphasis the importance of checking peripheral smear. Circulating lymphoma cells were the hallmark of this case.

Learning points
- Gene rearrangement for BCL-2, BCL-6 and c-MYC should always be checked in aggressive B-cell lymphoma to rule out double-hit lymphoma.
- Dose-adjusted EPOCH-R is the treatment of choice for double-hit lymphoma.
- Peripheral smear should always be reviewed in all cases of pancytopenia.

Contributors UK wrote the manuscript and obtained the images. CD wrote the manuscript and did proofreading.

Competing interests None declared.

Patient consent Obtained.

Figure 1 (A) Peripheral smear showing lymphoma cells. (B and C) Bone marrow biopsy. (D) Gastric biopsy showing lymphoma infiltration.

Figure 2 (A) BCL-2 expression. (B) H&E stain of bone marrow biopsy. (C) Ki-67 of 80–90%. (D) Negative cyclin D1 expression.
REFERENCES
