Burkitt-like lymphoma with 11q aberration

Alice C Westwood
Hebah Ali

Abstract
Burkitt-like lymphoma with 11q aberration (BLL-11q) is a newly recognized entity in the revised 4th (2017) edition of the WHO Classification of Tumours of Haematopoietic neoplasms. These tumours lack the MYC rearrangement seen in Burkitt lymphoma and instead have the hallmark 11q-gain/loss pattern detected on fluorescence in situ hybridization (FISH). We report a case of BLL-11q in a 33-year-old male with an ileocaecal mass and associated abdominal lymphadenopathy. Microscopy showed tumour morphology and immunoprofile in keeping with Burkitt lymphoma, however, no MYC rearrangement was detected and instead 11q aberration was found on FISH analysis. We also report characteristics of cases diagnosed as BLL-11q from Leeds Haematological Malignancy Diagnostic Service.

Keywords 11q aberration; Burkitt-like; high grade B-cell lymphoma

Case report
A 33-year-old male was referred to haematology with a suspicion of lymphoma. Colonoscopy revealed an ileocaecal mass and further investigations showed associated abdominal lymphadenopathy. The mass was biopsied and the local histopathology report suggested a diagnosis of Burkitt lymphoma (BL). The case was referred to the Haematological Malignancy Diagnostic Service (HMDS) for review. Microscopic examination showed diffuse dense lymphoid infiltration with Burkitt-like morphology and immunoprofile. The lesional cells were medium to large with relatively uniform nuclei, small nucleoli, thin rims of cytoplasm, frequent mitoses and apoptotic bodies, with focally interspersed macrophages and sparse small T-cells (Figure 1a). By immunohistochemistry, tumour cells expressed an abnormal germinal centre (GC) B-cell phenotype with diffuse strong positivity for CD20, CD10 and BCL6, lack of BCL2 and MUM1/IRF4. Similarly to classic BL, BCL2 staining is typically negative; only one biopsy showed weak patchy BCL2 expression. Proliferation fraction by Ki-67 is always high with most cases amounting to 100%.

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Discussion
BL is a highly aggressive B-cell lymphoma with characteristic morphological, immunophenotypic and molecular features, with the hallmark MYC gene rearrangement. Patients frequently present with involvement of extra-nodal sites with most cases of sporadic BL presenting with an abdominal mass.1 Lymphomas showing pathological features consistent with BL, with a similar gene expression profile, but lacking a detectable MYC gene rearrangement do exist. In the previous 2008 WHO classification, 5–10% of BL were believed to lack the characteristic t (8:14) (q24;q32).2 Such cases were usually considered by pathologists as MYC-negative BL.

Literature has described a particular subset of MYC-negative, high-grade B-cell lymphomas sharing similarities with, but not being BL. Instead, these cases show a peculiar 11q aberration characterized by proximal 11q gains and distal 11q loss.3 This entity has recently been recognized in the revised 4th (2017) edition of the WHO Classification of Tumours of Haematopoietic neoplasms as BLL-11q.1

There are few studies of BLL-11q but the diagnosis appears to be rare; one study including adults and children identified 3% of molecularly defined BL to be BLL-11q.3 Although optimal clinical management remains undefined, of the limited cases described, the prognosis and clinical course appears to be similar to that of BL.1 From our experience (Table 1), the disease predominantly affects adults with a median age in the sixth decade and a male preference. BLL-11q shows extra-nodal as well as, unlike BL, nodal involvement. The former presentation is commonly a colon or an abdominal/pelvic mass. Abdominal, neck and groin nodal groups are often affected.

The majority of cases reveal histological features indistinguishable from BL with medium sized, highly proliferative cells with a starry sky appearance; however, two biopsies exhibited a diffuse large B-cell lymphoma (DLBCL) like morphology. The phenotype is consistently an aberrant GC B-cell. Apart from one CD10-negative case, the lesional cells strongly and diffusely express CD20, CD10, BCL6 and lack MUM1/IRF4. Similarly to classic BL, BCL2 staining is typically negative; only one biopsy showed weak patchy BCL2 expression. Proliferation fraction by Ki-67 is always high with most cases amounting to 100%. Immunohistochemistry for LMO2 and MYC is variable.

Figure 1 (a) H & E section of ileocaecal biopsy viewed at x 20 magnification showing dense infiltration by atypical medium to large tumour cells, frequent mitoses and apoptotic bodies with focally interspersed macrophages. (b–f) Immunohistochemistry showing expression of CD10 and BCL6 but lacking BCL2 and IRF4. Ki67 is 100%.

Presentation and pathological features of the reported case (index) and all Burkitt-like lymphoma with 11q aberration cases in HMDS Leeds 2018–2020. LN, lymph node; +, positive; -, negative; DLBCL, diffuse large B-cell lymphoma; BL, Burkitt lymphoma HMDS; Haematological Malignancy Diagnostic Service.

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Sex</th>
<th>Sample</th>
<th>Presentation</th>
<th>Phenotype by immunohistochemistry</th>
<th>Morphology</th>
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<td>71</td>
<td>M</td>
<td>LN, groin</td>
<td>Pelvic mass and lymphadenopathy</td>
<td>CD20⁺, BCL-2⁺, BCL-6⁺, IRF4⁺, Ki6795⁺, LMO2⁺, MYC⁺</td>
<td>DLBCL</td>
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<td>2</td>
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<td>BL</td>
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<tr>
<td>3</td>
<td>73</td>
<td>M</td>
<td>Colon</td>
<td>Colon mass</td>
<td>CD20⁺, BCL-2⁺, BCL-6⁺, CD10⁺, IRF4⁺, Ki6795⁺, LMO2⁺⁺, MYC⁺</td>
<td>BL</td>
</tr>
<tr>
<td>4</td>
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<td>Colon</td>
<td>Caecal mass</td>
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<td>DLBCL</td>
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<tr>
<td>5</td>
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<td>M</td>
<td>LN, neck</td>
<td>Lymphadenopathy</td>
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<td>Abdominal mass</td>
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<td>Caecal mass and lymphadenopathy</td>
<td>CD20⁺, BCL-2⁺, BCL-6⁺, CD10⁺, IRF4⁺, Ki6795⁺, LMO2⁺⁺, MYC⁺</td>
<td>BL</td>
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BLL 11q shows genetic features distinct from classic BL. They lack MYC rearrangement and the presence of the typical 11q-gain/loss pattern is the hallmark that defines this entity. These findings can be detected by FISH analysis. There are no pathognomonic histological or immunohistochemical features to distinguish this entity from BL. A useful way to detect BLL 11q is performing FISH for 11q aberration in all MYC-negative high-grade B-cell lymphomas (HGBCL) that otherwise resemble BL both in morphology and phenotype.

Whether this lymphoma is a distinct category or a particular variant of other entities is controversial. A recent study questioned the specificity of 11q aberration to BLL-11q as they found that 11q gain/loss also occurred in MYC-positive BL and HGBCL not otherwise specified. After all, the BLL-11q might not actually be ‘Burkitt-like’ at molecular level!

**Conclusion**

We report a case of BLL-11q in a 33-year old male alongside a case series. Although BLL-11q appears to be relatively rare, it is important that trainees consider this as a potential diagnosis in all MYC-negative HGBCL that otherwise resemble BL, and that FISH analysis for 11q aberration is subsequently performed.

**REFERENCES**

5. Grygalewicz B, Woroniecka R, Rymkiewicz G, et al. The 11q-gain/loss aberration occurs recurrently in MYC-negative Burkitt-like...
lymphoma with 11q aberration, as well as MYC-positive Burkitt lymphoma and MYC-positive high-grade B-cell lymphoma, NOS. *Am J Clin Pathol* 2017; **149**: 17–28.
