Burkitt-like lymphoma with 11q aberration

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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

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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 expression, and a Ki-67 proliferation index of 100% (Figure 1b–f). Staining for MYC was however negative. Fluorescence in situ hybridization (FISH) was performed and showed no evidence of *MYC*, *BCL2* or *BCL6* gene rearrangements. Further FISH analysis showed 11q aberration (gain of 11q23 and loss of 11q24). These results confirmed the diagnosis of the new entity of Burkitt-like lymphoma with 11q aberration (BLL-11q).

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.[4]

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-negtaive 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.

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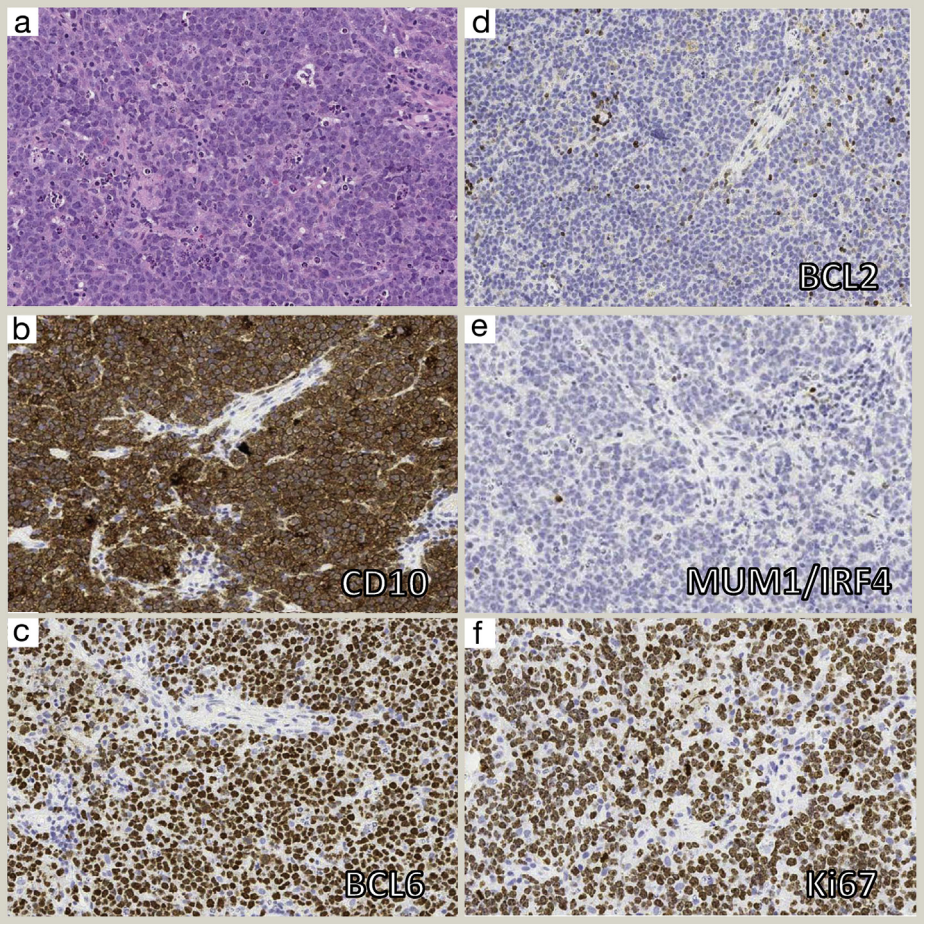

Figure 1 (**a**) H & E section of ileocaecal biopsy viewed at x 20 magnification showing dense infiltration by atypical medium to large tumour cells, frequent mitoses and apoptotic bodies with focally interspersed macrophages. (**b**–**f**) Immunohistochemistry showing expression of CD10 and BCL6 but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

Case	Age	Sex	Sample	Presentation	Phenotype by immunohistochemistry	Morphology
1	71	M	LN, groin	Pelvic mass and lymphadenopathy	$CD20^{+}$, $BCL\text{-}2^{-}$, $CD10^{-}$, $BCL\text{-}6^{+}$, $IRF4^{-}$, $Ki67^{60}$, $LMO2^{+}$, MYC^{-}	DLBCL
2	70	M	LN, groin	Lymphadenopathy	$CD20^{+}$, $BCL\text{-}2^{-}$, $CD10^{+}$, $BCL\text{-}6^{+}$, $IRF4^{-}$, $Ki67^{90}$, $LMO2^{+/-}$, MYC^{+}	BL
3	73	M	Colon	Colon mass	$CD20^{+}$, $BCL\text{-}2^{-}$, $BCL\text{-}6^{+}$, $CD10^{+}$, $IRF4^{-}$, $Ki67^{90}$, $LMO2^{+/-}$, MYC^{-}	BL
4	68	M	Colon	Caecal mass	$CD20^{+}$, $BCL\text{-}2^{-}$, $BCL\text{-}6^{-}$, $CD10^{+}$, $IRF4^{-}$, $Ki67^{60}$, $LMO2^{-}$, MYC^{-}	DLBCL
5	79	M	LN, neck	Lymphadenopathy	$CD20^{+}$, $BCL\text{-}2^{+/-}$, $BCL\text{-}6^{+}$, $CD10^{+}$, $IRF4^{-}$, $Ki67^{100}$, $LMO2^{+}$, MYC^{+}	BL
6	41	M	Abdominal mass	Abdominal mass	$CD20^{+}$, $BCL\text{-}2^{-}$, $BCL\text{-}6^{+}$, $CD10^{+}$, $IRF4^{-}$, $Ki67^{100}$, $LMO2^{+/-}$, MYC^{+}	BL
7, Index case	33	M	Colon	Caecal mass and lymphadenopathy	$CD20^{+}$, $BCL\text{-}2^{-}$, $BCL\text{-}6^{+}$, $CD10^{+}$, $IRF4^{-}$, $Ki67^{100}$, $LMO2^{-}$, MYC^{-}	BL

(*continued on next page*)

Table 1 (*continued*)

Case	Age	Sex	Sample	Presentation	Phenotype by immunohistochemistry	Morphology
8	24	M	Abdominal mass	Abdominal mass	*CD20*$^{+}$, *BCL-2*$^{-}$, *BCL-6*$^{+}$, *CD10*$^{+}$, *IRF4*$^{-}$, *Ki67*^{100}, *LMO2*$^{-}$, *MYC*$^{+/-}$	BL
9	71	M	LN, neck	Lymphadenopathy	*CD20*$^{+}$, *BCL-2*$^{-}$, *BCL-6*$^{+}$, *CD10*$^{+}$, *IRF4*$^{-}$, *Ki67*^{90}, *LMO2*$^{+}$, *MYC*$^{+}$	BL
10	75	M	LN, neck	Small bowel, adrenals and left kidney masses and lymphadenopathy	*CD20*$^{+}$, *BCL-2*$^{-}$, *BCL-6*$^{+}$, *CD10*$^{+}$, *IRF4*$^{-}$, *Ki67*^{90}, *LMO2*$^{+}$, *MYC*$^{+/-}$	BL

Table 1

Multiple choice questions

1. Immunoprofile of Burkitt-like lymphoma with 11q aberration is:

A) High grade ABC B-cell phenotype
B) High grade GC B-cell phenotype
C) Low grade GC B-cell phenotype

Correct answer (B)

2. MYC rearrangement can be detected in the following but:

A) Burkitt-like lymphoma with 11q aberration
B) Double hit lymphoma
C) Burkitt lymphoma

Correct answer (A)

3. Gain of 11q23 and loss of 11q24 is characteristic of:

A) Burkitt lymphoma
B) Double hit lymphoma
C) Burkitt-like lymphoma with 11q aberration

Correct answer (C)

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.[5] Further studies showed that BLL-11q shows a mutational landscape distinct from that of sporadic BL and closer to those of HGBCL or GC DLBCL rather than BL with 11q gain/loss.[6,7] 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. ◆

Practice points

Pathological features:

- Burkitt or DLBCL-like morphology: Diffuse infiltration, frequent mitoses and scarce infiltrating reactive lymphocytes.

Phenotypic features:

- Burkitt-like immunoprofile: Aberrant GC B-cell phenotype CD20+ CD10+ BCL6 + BCL2-and high Ki-67.

Molecular features:

- Lack of *MYC* rearrangement and presence of 11q aberration.

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