Case Report

Spinal lesion as the first manifestation of high-grade B-cell lymphoma, with MYC and BCL2 rearrangements

Yunxia Ye, Wenyan Zhang, Sha Zhao, Lili Jiang, Weiping Liu, Yanhong Long, Ying Wan

Department of Pathology, West China Hospital of Sichuan University, Chengdu, Sichuan Province, China

Received May 14, 2017; Accepted June 20, 2017; Epub August 1, 2017; Published August 15, 2017

Abstract: High-grade B-cell lymphoma with MYC and BCL2 rearrangements is a rare lymphoma which has highly aggressive clinical manifestations. The reporting case is a 72-year-old female presented with lumbago and weakness in the lower limb due to a mass at T8-10 revealed by computed tomography (CT) scan. Histological feature of the lesion shows an abundant and diffuse large lymphoid cells infiltration. Immunophenotype meets with germ center B cell (GCB) lymphoma (Hans algorithm). C-MYC and BCL2 gene rearrangements are detected by fluorescence in situ hybridization (FISH). It’s a rare and typical case of high-grade B-cell lymphoma with MYC and BCL2 rearrangements with uncommon clinical manifestation.

Keywords: Spinal, high-grade B-cell lymphoma, MYC, BCL2, gene rearrangement

Introduction

Diffuse large B-cell lymphoma (DLBCL) is the most common type of lymphoid neoplasm, accounting for 35~40% non-Hodgkin lymphoma (NHL). High-grade B-cell lymphoma with MYC and BCL2 and/or BCL6 rearrangements once termed as double hit (or triple-hit) B-cell lymphoma (DHL/THL) has the similar morphology and immunophenotype to DLBCL, but it presents more aggressive clinical behavior than latter. However, high-grade B-cell lymphoma with MYC and BCL2 and/or BCL6 rearrangements is rare. Only 5~10% of DLBCL can be defined as it. Making diagnosis of high-grade B-cell lymphoma with MYC and BCL2 and/or BCL6 rearrangements (DHL/THL) is very challenging and genetic analysis should be necessary.

The known clinicopathological characteristics of high-grade B-cell lymphoma with MYC and BCL2 rearrangements are limited due to few cases having been studied. Herein we report an extremely rare case of high-grade B-cell lymphoma with MYC and BCL2 rearrangements presenting as spinal mass.

Materials and methods

Case collection

A 72-year-old Chinese woman who complained of lumbago for 2 months and weakness in the lower limb for 4 days visited West China Hospital of Sichuan University, and took an excision of a mass at T8-10.

Pathological study

Histological study

4 μm-thicken formalin fixed paraffin embedded (FFPE) tissue section series were prepared for H&E and following immunohistochemical staining.

Immunohistochemical analysis

EnVision or Elivision DAB systems were used for immunohistochemical reaction. For antigen retrieval, the slides were heated at 97°C for 25 minutes in citrate buffer at pH 6.0 or in EDTA buffer at pH 9.0. Endogenous peroxidase activity was blocked with 3% hydrogen peroxide in methanol. CD20, CD3ε, CD5, CD10, BCL-6,
Spinal lesion as the first manifestation of high-grade B-cell lymphoma

A 72-year-old Chinese women presented with lumbago for 2 months and weakness in the lower limb for 4 days. Fever, night sweat, or weight loss were denied. Laboratory findings were hydrothorax and elevated LDH. A computed tomography (CT) scan revealed a mass at T8-10 with ambiguous boundaries (Figure 1), and then was resected.

**Histopathologic findings**

Histological examination showed a diffuse infiltration of lymphoid cells. The lymphoid cells were large and centroblasts-like. The nuclei were round or oval and have rough chromatin. Neoplastic cells had visible nucleoli. Apoptosis and necrosis were easily observed (Figure 2).

**Immunophenotype**

The lymphoid cells expressed CD20 (Figure 4), CD79a, CD10, BCL-6, NF-κB (P65), P53 and C-myc, and were negative for CD3ε, Cyclin D1, mum-1, bcl-2, CD5 and CD30. The proliferative index, demonstrated by Ki67 stain, was more than 80% (Figure 3).

**Follow-up**

The patient was diagnosed as high-grade B-cell lymphoma with MYC and BCL2 rearrangements, germ center B-cell-like (GCB) phenotype (Hans algorithm) according to World Health Organization (WHO) classification of hematopoietic and lymphoid tumors (2016 revision) [2]. The patient was evaluated as IV B stage (Ann Arbor stage) and IPI 5 and then received 6 courses of EPOCH chemotherapy and got partial remission (PR) with relieving of signs and symptoms.

**Discussion**

Diffuse large B-cell lymphoma (DLBCL) actually has heterogeneous features implying differ-
Spinal lesion as the first manifestation of high-grade B-cell lymphoma

Figure 2. Hematoxylin and eosin-stained section of high-grade B-cell lymphoma with MYC and BCL2 rearrangements. A. Diffuse lymphoid cells infiltrate (HE×100). B. An abundant and diffuse large lymphoid cells infiltrate (HE×400).

ent biological behavior. It is recognized as ger-
minal center B-cell like (GCB) and activated
B-cell-like (ABC) molecular 'subgroups' based
on gene expression profile (GEP). BCL2 gene
rearrangement is associated with GCB-DLBCL
and has been identified as an adverse prognos-
tic factor in DLBCL [1, 3, 4].

MYC is a powerful oncogene initially identified
as the target of the t(8;14)(q24;q32) chromo-
some translocation in Burkitt lymphoma (BL).
MYC gene rearrangement have been identified
in many mature B-cell lymphomas that are usu-
ally associated with an aggressive clinical be-
havior [5]. For example, MYC rearrangement
can be observed in approximately 10% of de
novo DLBCL and correlates with a worse out-
come [5, 6]. B-cell lymphoma carrying MYC
rearrangement combination with rearrange-
ment involving either BCL2, BCL6, or rarely
other known oncogenes is regarded as dou-
ble hit (or triple-hit) B-cell lymphoma (DHL/THL)
[7, 8]. DHL/THL is strictly defined by the pres-
ence of rearrangement and breakpoints at the
sites of both MYC and BCL2 and/or BCL6 ge-
ne mutation, low level copy number increase, or
high-level amplification without a concurring
breakpoint and rearrangements should not be
interpreted as such. The definition is also con-
ined de-novo DLBCL [9]. About 5-10% of DL-
BCLs fulfill the criteria for DHL/THL [8].

In addition to the adverse clinical impact of
rearrangement of MYC gene combined with
rearrangement involving either BCL2 and/or
BCL6, high stage, elevated lactate dehydro-
genase (LDH), extranodal involvement (CNS
involvement included), high IPI score are more
common in DNL/THLs than in other lympho-
mas [10]. GEP studies have shown the GCB

group have a better prognosis than the ABC
group. Although most of MYC/BCL2 DHLs arise
within the GCB group, there is discordance
between prognosis and the cell of origin (COO)
subtypes [2].

DLBCL accounts for about 40% of all non-Hodg-
kin lymphomas. Most patients present with
rapidly enlarged lymph nodes or tumor masses
localized in extranodal sites. About 30% of
patients present with the extranodal lesions,
and 71% have extranodal involvement during
the course of the disease. Common prima-
ry extranodal sites include the gastroin-
testinal tract and Waldeyer’s, but practically
any organ can be involved, including bone
[11]. Lymphoma is definitely less than myelo-
ma involves spine. Since high-grade B-cell
lymphoma, with MYC and BCL2 rearrangements
is a rare variant of DLBCL, it is a great chal-
lenge to making correct diagnose of this disease
before the surgical pathology and ensure the
patient receiving appropriate therapy. This rare
case implies that lymphoma can involve any
site and presents as any symptom or sign.

Acknowledgements

This study was supported by a grant founded
by Health and Family Planning Commission of
Sichuan Province (NO. 16PJ337), and a grant of
Application Basic Research Project founded by
Science & Technology Department of Sichuan
Province (NO. 2017JY0266).
Figure 3. The lymphoid cells are positive for CD20 (A, ×400), CD10 (B, ×400) and bcl-6 (C, ×400), but negative for MUM-1 (D, ×400). More than 80% of tumor cells are positive for Ki-67 staining (E, ×400).
Figure 4. Detection of MYC and BCL2 gene rearrangement with dual color break apart probe respectively. The MYC (A) and BCL2 (B) gene rearrangement is indicated by separation of the red and green signals.

Disclosure of conflict of interest

None.

Address correspondence to: Wenyan Zhang, Department of Pathology, West China Hospital of Sichuan University, Guoxue Alley No. 37, Chengdu 610001, Sichuan Province, China. Tel: +86-28-85423848; +86-18980601864; E-mail: zhangwenyanpath@163.com

References


