A B-cell lymphoma case that is unclassifiable, and intermediate between diffuse large B-cell lymphoma and Burkitt lymphoma of lacrimal gland

Tatsuya Yunoki 1
Jun Murakami 2
Yukihiro Imagawa 3
Takahiko Nakajima 4
Atsushi Hayashi 1

1 Department of Ophthalmology, Graduate School of Medicine and Pharmaceutical Sciences, University of Toyama, Toyama, Japan
2 Department of Ophthalmology, Osaka Kaisei Hospital, Osaka, Japan
3 Department of Diagnostic Pathology, Graduate School of Medicine and Pharmaceutical Sciences, University of Toyama, Toyama, Japan

Abstract: A 60-year-old woman presented with acute eyelid swelling and a subcutaneous hemorrhage in the right eye. Magnetic resonance imaging showed a spherical tumor of the lacrimal gland. The tumor was removed by the Kroenlein method. We diagnosed as a B-cell lymphoma that is unclassifiable, and intermediate between diffuse large B-cell lymphoma (DLBCL) and Burkitt lymphoma (BL) (intermediate DLBCL/BL) based on its immunohistopathological examination and c-MYC/IgH rearrangement. We administered six cycles of dose-adjusted-EPOCH-R (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin hydrochloride, and rituximab) therapy, and remission of the lymphoma was obtained. This is the first case of an intermediate DLBCL/BL of a lacrimal gland.

Keywords: diffuse large B-cell lymphoma, Burkitt lymphoma, c-MYC gene, fluorescence in situ hybridization

Introduction
According to the 2008 World Health Organization Classification of Tumors of Haematopoietic and Lymphoid Tissues, the morphological and genetic features of diffuse large B-cell lymphoma (DLBCL) overlap with those of Burkitt lymphoma (BL). 1 Intermediate DLBCL/BL, a B-cell non-Hodgkin lymphoma, is highly aggressive. 2 It has a high malignancy grade, and as it is a very rare lymphoma subtype in adults, standard treatment has not yet been established. A previous study has reported that intermediate DLBCL/BL has poor outcomes, with a median overall survival of only 9 months and a 5-year overall survival rate of 30%. 2 The rapid progression of an aggressive orbital lymphoma can cause optic nerve disorders and sometimes a life-threatening crisis. Thus, early diagnosis and appropriate treatment of this condition are crucial. 3, 4

In this case report, we describe a case of intermediate DLBCL/BL of the lacrimal gland that presented with subcutaneous hemorrhage and orbital hematomas. To the best of our knowledge, this is the first report of an intermediate DLBCL/BL of the lacrimal gland.

Case report
Patient characteristics and clinical examination
The patient was a 60-year-old Japanese woman who presented with acute eyelid swelling and a subcutaneous hemorrhage in the right eye. She has no history of acute eye trauma. At the time of the first medical examination, the best-corrected
visual acuity of both eyes was 1.2, and no abnormality was
detected on slit lamp microscopy and fundoscopy. It was
difficult for the patient to open her right eye because of
eyelid swelling and subcutaneous hemorrhage (Figure 1A).
The Hess chart results indicated an ocular motility dis-
order (Figure 1B). Magnetic resonance imaging revealed
a spherical tumor of the lacrimal gland (Figure 1C and
D). There was no tumor involvement of the temporalis
fossa or the skin of the eyelid. Furthermore, hemorrhage
occurred within and around the tumor, probably owing to
intratumoral bleeding. The patient did not have a history of
autoimmune diseases such as Sjögren’s syndrome, which
could underlie the development of malignant lymphoma.
Written informed consent was obtained from the patient
for publication of this case report and accompanying
images.

Immunohistochemistry and gene profiling
Under general anesthesia, the patient underwent surgical
removal of the tumor using the Kroenlein method, and we
attempted to extract as much of the tumor mass as possible.
Hematoxylin and eosin (H&E) staining of the tumor sample
revealed a starry sky pattern, and immunohistochemical
analysis revealed that the tissue was positive for leukocyte
common antigen, CD20, CD10, and Bcl-6 staining; and
negative for Bcl-2, CD3, and MUM1 staining, with a MiB1
labeling index of 90–95% (Figure 2). A fluorescence in situ
hybridization (FISH) examination revealed reciprocal trans-
location (81.5%) of the $c$-MYC gene and the immunoglobulin
gene ($IgH$), and $IgH$-Bcl-2 fusion and Bcl-6 split signal were
negative. G-banding was not performed, but the t(8; 14)
translocation was detected by FISH-based visualization of
the $c$-MYC/IgH rearrangement. This rearrangement is very
rare in cases of DLBCL.

Diagnosis and treatment
This case could have been diagnosed as BL on the basis
of its immunoprofile and the $c$-MYC/IgH rearrangement.
However, because the lymphoma was composed of proli-
erating cells with medium to large pleomorphic nucleoli,
we defined it as an intermediate DLBCL/BL of the lacrimal
gland according to the 2008 WHO Classification of Tumors
of Haematopoietic and Lymphoid Tissues.1 Positron emission
tomography/computed tomography images showed intense fluorine-18 deoxyglucose uptake in the porta hepatis, in addition to that in the orbit. We administered six cycles of dose-adjusted-EPOCH-R (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin hydrochloride, and rituximab) therapy, which resulted in remission of the lymphoma. We followed the patient’s progress carefully, and no visual function problems have been observed at 6 months after the completion of chemotherapy.

Discussion

In the current case, on the basis of the morphology of the lymphoma cells and the presence of c-MYC/IgH rearrangement by FISH, we concluded that this was not a case of either BL or DLBCL, but a case of intermediate DLBCL/BL in an otherwise healthy adult Japanese woman.

It is very rare for an orbital lymphoma that is an intermediate DLBCL/BL and a subcutaneous and orbital hematoma to present clinically with rapid eyelid swelling. Clinicians must consider the possibility of an orbital intermediate DLBCL/BL when these symptoms are observed. Early treatment and appropriate management are crucial to maintain the patient’s visual function and to improve the likelihood of survival. The rapid progression of an aggressive orbital lymphoma results in various clinical symptoms such as painful proptosis and vision loss.1 If an orbital lymphoma, such as BL and intermediate DLBCL/BL, is suspected, the diagnosis must be confirmed as soon as possible by using methods such as tissue biopsy.

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Disclosure

The authors report no conflicts of interest in this work.

References