Bilateral orbital marginal zone B-cell lymphoma of the mucosa-associated lymphoid tissue in a patient with hepatitis B virus infection

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Article Info

Article history:
Received 1 December 2016
Received in revised form 31 March 2017
Accepted 16 May 2017
Available online 18 May 2017

Keywords:
Marginal zone B-Cell lymphoma of mucosa-associated lymphoid tissue
Hepatitis B virus
Bilateral
Superolateral orbit

Abstract

Purpose: To report a case of marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma) in the bilateral orbit with chronic hepatitis B virus (HBV) infection.

Observations: A 72-year-old man with chronic HBV infection presented with a bilateral proptosis with slight restriction of ocular motility for 9 months. Computed tomographic images showed well-defined, isodense masses in the bilateral superolateral orbit. Magnetic resonance images showed isointense on T1- and hyperintense on T2-weighted images, with bilateral involvements of the lateral rectus muscles reaching the superior orbital fissures. These masses molded along the globe contour. Incisional biopsies via upper eyelid crease were performed on both lesions. The immunohistopathological diagnosis was MALT lymphoma.

Conclusions and importance: This case showed a possible association between orbital MALT lymphoma and HBV.

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1. Introduction

Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma) is a type of low grade non-Hodgkin’s lymphoma, which comprises the most common malignancy of the orbit.1 The pathogenesis of MALT lymphoma has been known to be associated with the environmental factors and its corresponding host immune response.2 Certain microorganisms are known to be linked in the development of MALT lymphoma. These include Helicobacter pylori with gastric MALT lymphoma, Borrelia burgdorferi with cutaneous MALT lymphoma, and Chlamydia psittaci with ocular adnexal MALT lymphoma. As well, hepatitis C virus (HCV) is associated with marginal zone B cell lymphomas.2

A recent study has shown an association between hepatitis B virus (HBV) and non-Hodgkin’s lymphoma.3 However, there has been no report describing an association of HBV and orbital MALT lymphoma. We, here, report a case of bilateral orbital MALT lymphoma associated with chronic HBV infection.

2. Case report

A 72-year-old man presented with a bilateral proptosis with slight restriction of ocular motility for 9 months (Fig. 1). His visual acuity was 20/20 in both eyes. Computed tomographic (CT) images showed well-defined, isodense masses measuring 21 × 23 × 26 mm in the bilateral superolateral orbit (Fig. 2). Magnetic resonance images showed isointense on T1- and hyperintense on T2-weighted images, with bilateral involvements of the lateral rectus muscles reaching the superior orbital fissures (Fig. 3). These masses molded along the globe contour.

He was infected with HBV 32 years ago. Blood examination showed that he was an asymptomatic carrier of HBV [positive for HBV surface antigen (HBsAg), HBV envelope antigen (HBeAg), and anti-HBeAg antibody (HBeAb) and negative for serum anti-HBsAg antibody (HBsAb)]. Other viral serological tests, such as human immunodeficiency virus and HCV, were negative.

Incisional biopsies were performed via upper eyelid crease on both lesions. Similar appearing soft, pinkish-gray masses were
encountered at the sites of bilateral lacrimal gland. The intraoperative frozen sections of both masses showed malignant lymphoma.

Post-operative immunohistopathological examination revealed an infiltration of small round to cleaved lymphocytes in the lacrimal gland, with a few germinal centers (Fig. 4A and B). Tumor cells were positive for CD20, CD79a, and bcl-2 but negative for CD3, CD5, CD10, bcl-6, cyclin-D1 (Fig. 4C and D). Clonal rearrangement of the immunoglobulin heavy chain gene was found by Southern blotting. The definitive diagnosis was MALT lymphoma. There was no systemic involvement which was confirmed by CT, positron emission tomography, and bone marrow aspiration.

After a 15-day course of regional radiation therapy with 30 Gy, the tumor regressed dramatically. Six months after the radiation therapy, no recurrence was shown in the orbit.

3. Discussion

We have reported the first case of bilateral orbital MALT lymphoma with chronic HBV infection. Although HBV is a hepatotropic virus and replicates within hepatocytes, it also transfers into the peripheral blood, bone marrow, spleen, lymph node, and thymus.\(^5\) As regards lymphocytes, HBV binds to peripheral blood mononuclear cells (PBMC) with HBV DNA integration in PBMCs.\(^5\) HBV integrates in the host genome, which leads to overexpression of cellular oncogenes or downregulation of the expression of the tumor suppressor gene. As well, since HBV infection 32 years ago, HBV antigen had induced chronic antigen stimulation, which may predispose to genetic aberrations and then autonomously induce neoplastic transformation and proliferation.\(^5\) Gene regulation and chronic antigen stimulation are proposed to be linked to a lymphomagenesis in anywhere in the body including the orbit.\(^5\)

Anti-HCV-positive lymphomas have reported to respond well to antiviral therapy.\(^6\) However, no similar therapeutic protocol has been established about HBV-associated non-Hodgkin’s lymphoma. In the latter entity, neoplastic proliferation requires support of ongoing viral replication, which is present on patients with positive HBeAg and HBeAb.\(^7\) We, therefore, recommend on future studies to investigate whether HBV-positive non-Hodgkin’s lymphoma patients could undergo clinical response upon treatment with antiviral therapy.

The patient did not show systemic lymphoma during 6-month follow-up period. However, patients with orbital lymphoid tumor have a 33% risk for developing systemic lymphoma in 10 years. This risk increases to 72% in bilateral orbital tumor, by contrast to 12% in

![Fig. 1. Pre-operative patient’s face photo showing bilateral proptosis.](image)

![Fig. 2. Pre-operative (A) axial, (B) coronal, and (C) sagittal sections of computed tomographic images. Well-defined, isodense masses measuring 21 × 23 × 26 mm are shown in the bilateral superolateral orbit, which are molded along the globe contour (arrows).](image)
unilateral orbital tumor. Bilaterality is a significant predictor for poorer disease-specific survival, local control, and distant control. These facts suggest that patients with bilateral orbital lymphoid tumor need to be followed up closely.

4. Conclusions

We presented a case of bilateral orbital MALT lymphoma in a patient with chronic HBV infection. This case showed a possible association between orbital MALT lymphoma and HBV. The
patients with bilateral orbital lymphoma need to be followed up closely because of its high risk to developing systemic lymphoma.

Patient consent

The Institutional Review Board of the Ethics Committee of Aichi Medical University Hospital approved this retrospective case report, which adhered to the tenets of the 1964 Declaration of Helsinki. Written informed consent was also obtained from the patient for the publication of this case report and any accompanying images.

Funding

No funding or grant support.

Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Conflict of interest

The authors have no competing interests to declare.

Acknowledgements

None.

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