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Detection of *Chlamydia pneumoniae* in a Bilateral Orbital Mucosa-Associated Lymphoid Tissue Lymphoma

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Abstract

PURPOSE—To detect *Chlamydia pneumoniae* (*C. pneumoniae*) gene in a patient with bilateral orbital musoca-associated lymphoid tissue (MALT) lymphoma.

DESIGN—Interventional case report.

METHODS—A 47-year-old Chinese man with recurrent bilateral orbital masses underwent surgical biopsy. Ophthalmologic and radiographic examinations, routine histology, immunohistochemistry, and molecular analysis for immunoglobulin heavy chain (IgH), *bcl-2/IgH* gene translocation, and *Chlamydia* genes were performed.

RESULTS—Pathology revealed orbital MALT lymphoma with B-cell monoclonality. In addition to *IgH* gene rearrangement, *C. pneumoniae* DNA was detected in the lymphoma.

CONCLUSIONS—The finding of *C. pneumoniae* molecular signatures in this case suggests a possible association of *Chlamydia* and orbital MALT lymphoma. The infection may contribute to the development of the lymphoma.

Bilateral orbital lymphoid lesions include a wide spectrum of diseases from benign pseudotumor to malignant lymphomas.¹ Orbital lymphomas generally have an insidious onset without overt inflammatory signs. The etiology of primary orbital lymphoma is unknown. An association between *Chlamydia psittaci* (*C. psittaci*) and ocular adnexal lymphoma is recently reported in Italy,² although other investigators in the USA could not replicate this finding.³ This study detects *C. pneumoniae* gene in a case of orbital lymphoma that was once misdiagnosed and treated as an inflammation.

A 47-year-old Chinese male was seen in Hong Kong with bilateral proptosis, lid swelling, and conjunctival chemosis that recurred three times in one year. He was diagnosed with “inflammatory pseudotumor” and treated with systemic corticosteroids with partial response; however, the disease recurred in a few months. An axial CT scan demonstrated bilateral retrobulbar masses, which wrapped around the optic nerves and displaced the globes forward (Figure 1). Both cavernous sinuses appeared slightly bulky, especially on the left side attributable to tumor infiltration.

Biopsies were performed on both orbits through transcutaneous anterior orbitotomies. The biopsies disclosed multiple clusters of mainly small lymphocytes. Plasmacytic differentiation with Russell and Dutcher bodies was prominent (Figure 2). The mitotic activity was low. Most cells stained positively for B cell markers (Figure 2). Molecular analysis of the microdissected

tumor cells showed *IgH* gene rearrangement and translocation of *bcl-2/IgH* gene (Figure 3). A diagnosis of orbital low-grade B-cell mucosa-associated lymphoid tissue (MALT) lymphoma was made.

A multiplex touchdown, enzyme time-release polymerase chain reaction, designed to simultaneously detect *Chlamydia trachomatis* (*C. trachomatis*), *pneumoniae*, and *psittaci* DNA² was performed and found *C. pneumoniae* (Figure 3). The patient was treated with chemotherapy including several cycles of chlorambucil and prednisone. His disease was in control with daily 4 mg chlorambucil during four years of follow-up.

The molecular signature of *C. pneumoniae*, not *C. psittaci*, is detected in recurrent orbital MALT lymphomas from a patient in Hong Kong. Chronic antigen stimulation is implicated as a causative agent in the development of mature B-cell proliferation and MALT lymphomas. For example, *Helicobacter pylori* (*H. pylori*) plays an important role in the development of gastric MALT lymphoma,⁴ and may have a role in conjunctival MALT lymphoma.⁵ Eradication of pertinent microorganisms such as *H. pylori* is effective in many gastric and ocular adnexal MALT lymphomas.^{2,4,6}

The different results between this particular Hong Kong patient and other Italian or US patients may relate to geographic differences in *Chlamydia* infection. For example, the nature of orbital lymphomas shows a relatively high proportion of T-cell lymphomas in Hong Kong compared with the Caucasian population.⁷ There may also possibly be other unknown genetic and environmental co-factors. Additional surveys for *C. pneumoniae* and *C. psittaci* in orbital MALT lymphomas in Chinese and other populations may help to clarify the discrepancy. Other microorganisms or chronic antigenic stimulation should also be considered and investigated.

C. pneumoniae is demonstrated in a bilateral orbital MALT lymphoma of a Hong Kong patient. *Chlamydia* infection may contribute to the development of MALT lymphoma in the orbits. Additional antibiotic therapy may prevent the need for systemic chemotherapy or irradiation for some select orbital MALT lymphomas.⁶

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FIGURE 1.

Orbital CT scan showing bilateral tumor invasion. CT scan demonstrates bilateral infiltrative orbital masses with extraconal and intraconal orbital involvements that molded over the globes and bones without bone destruction.

FIGURE 2.

Microphotograph showing typical MALT lymphoma. There is a monotonous population of small atypical lymphocytes, some with plasmacytic differentiation. Occasional Russell and Dutcher bodies are present (purple red color). Inset. Most cells are positive (black color) for CD20. (hematoxylin and eosin and avidin-biotin immunoperoxidase (inset); original magnification, $\times 100$).

FIGURE 3.

Polymerase chain reaction (PCR) products showing *C. pneumoniae* DNA in orbital MALT lymphoma. *IgH* gene rearrangement at the CDR3 region and *bcl-2/IgH* gene translocation (t(14;18), as well as *C. pneumoniae* gene are detected in the microdissected MALT lymphoma cells (lane 1, patient; lane 2, negative control; lane 3, positive control).