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SHORT COMMUNICATION

Cytomegalovirus Retinitis in Chinese Patients of non-Hodgkin Lymphoma with Normal CD4 Counts

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A B S T R A C T

Objective: To manifested the clinic features in two cases of cytomegalovirus(CMV) retinitis in Chinese patients of non-Hodgkin lymphoma with normal CD4 counts.

Methods: Two patients with non-Hodgkin lymphoma presented with floaters and vision reduction in affected eyes. The patient underwent eye examination and blood investigation, and vitreous was extracted for CMV-DNA polymerase chain reaction (PCR). The patient was treated with intravenous and intravitreal ganciclovir.

Results: Fundoscopy showed typical yellow and white lesions in the retina of affected eyes. Blood investigation showed HIV(-), CMV- IgG (+) IgM (-),and CD4 T-cell counts more than 300 cells/ul. CMV DNA PCR(+) of vitreous sample supported the diagnosis of CMV retinitis. Retinitis regressed after the treatment of ganciclovir.

Conclusions: CMV retinitis occurred in non-HIV disease such as non-Hodgkin lymphoma with normal CD4 counts. These cases showed CMV-DNA PCR of vitreous may be a good marker for CMV retinitis and intravitreal ganciclovir may be an effective treatment.

INTRODUCTION

Cytomegalovirus (CMV) retinitis is a severe ocular infectious disease characterized by progressive retina inflammation and necrosis. It is the most frequent ocular opportunistic infection among patients with acquired immunodeficiency syndrome (AIDS) who infected with human immunodeficiency virus (HIV) [1-3]. CMV retinitis usually became clinically evident at CD4 T-cells counts less than 50 cells/ul [4]. Although rare, CMV retinitis was also seen in patients with non-HIV diseases in conditions of immunosuppression. We here presented two cases of CMV retinitis with non-Hodgkin lymphoma in Chinese patients with normal CD4 cell counts.

CASE 1

A 43-year-old chinese male presented with floaters and gradual reduction of vision in both eyes during hospitalization for diagnosed non-Hodgkin lymphoma (peripheral T-cell lymphoma). The patient developed eye symptoms after fourteen cycles of combination chemotherapy with hyper CVAD-A or B regimen.

Best corrected visual acuity (BCVA) was right eye: 20/500 and left eye: 20/20. In the right eye, there were only few flares in anterior chamber. Fundus examination showed retinal hemorrhage, scatted yellow and white retinal necrosis lesions and vessel white sheath in the right eye (figure 1A), and only few small hemorrhagic spots beside the optic disc in the

left eye (figure 1B). Vision of the left eye decreased three month later. BCVA was right eye: light perception (LP) and left eye: 20/400. The inflammation of retina progressed in both eyes(figure 1C,D).Serology showed CMV-IgM 0.2 (-) IgG 204.1(+) (reference value<6AU/ml), HIV(-), herpes simplex HSV-I/II-IgG(-), IgM(-), toxoplasm IgG(-), IgM(-), syphilis RPR(-), and CRP(70.5), ESR (93) increased,. Blood investigation revealed CD4 counts of 419 cells/ul. Vitreous biopsy was positive for CMV DNA by polymerase chain reaction (PCR). The diagnosis of CMV retinitis was proposed by the typical clinic features, and confirmed by a positive PCR for CMV of vitreous.

The patient was treated with intravenous ganciclovir (5 mg/kg every 12 h) for 3 weeks. Retinitis regressed (Figure 1E,F) prominently and visual acuity of left eye improved to 20/60. The treatment had to be stopped for the serious pancytopaenia (WBC 1.3×10E9/L, Pt 46×10E9/L, Hb 106g/L). The retinitis relapsed with reappearance of retinal lesions (figure 1G,H) and decreased visual acuity. The patient was treated with intravitreal ganciclovir (0.2mg/0.1ml) twice a week. Progression of CMV retinitis was halted, but the follow-up was discontinued for the worse of the lymphoma and general conditions of the patient.

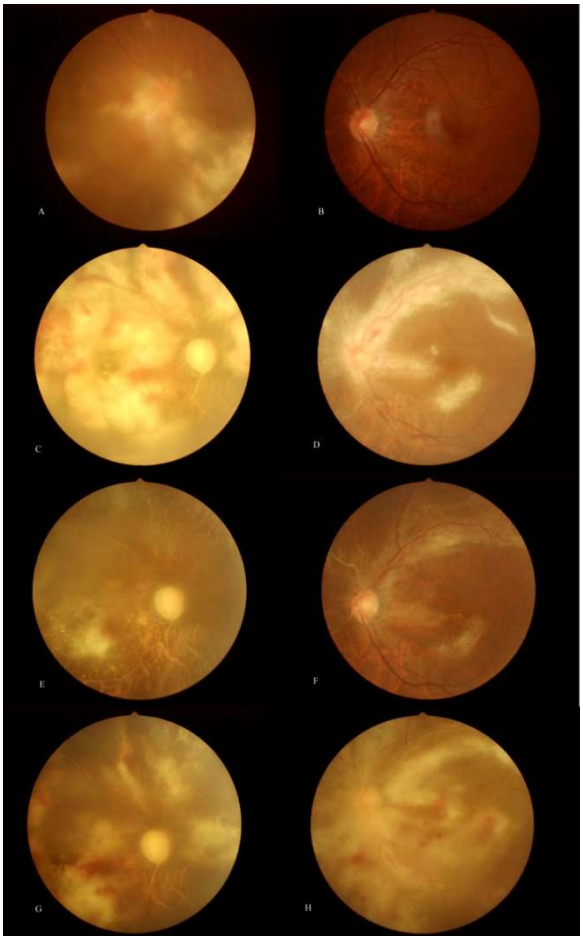

Figure 1: Fundus photographs showed vitreous opacities, scatted yellow and white lesions, retinal necrosis and vessel white sheath in the right eye (A), and only small hemorrhagic spot beside the optic disc in the left eye(B). Retinitis progressed three month later(C, D). CMV retinitis regressed in both eyes after treatment of intravenous ganciclovir (E, F). Retinitis relapsed after withdraw of intravenous ganciclovir(G, H).

CASE 2

A 60-year-old married male presented with black shadow and blurred vision in the left eye. He suffered from non-Hodgkin lymphoma (diffuse large B-cell lymphoma) for half a year and had been treated with six cycles of chemotherapy (hyper CVAD-A regimen).

BCVA was left eye: 20/50 and right eye: 20/20. There were no flares in anterior chamber and only little opacity in vitreous in the affected eye. Fundus examination showed retinal infiltrate and necrosis lesions with hemorrhage in the nasal and superior quadrants, vessels occlusion with white sheath (figure 5). Blood investigation showed CRP(22), ESR(24.5) increased, HIV(-), CMV- IgG (+)IgM (-), HSV-IgG/IgM(-), toxoplasm IgG/IgM(-), syphilis RPR(-),CD4 counts 347 cells/ul. Vitreous sample was positive for CMV DNA by PCR, but CMV DNA-PCR of blood sample was negative.

The patient was treated with intravenous ganciclovir (5 mg/kg every 12 h) and intravitreal ganciclovir (0.2mg/0.1ml)once a week and topical eyedrops (steroid and mydriatics). Lesion in the retina shrinked and CMV retinitis began to remit.

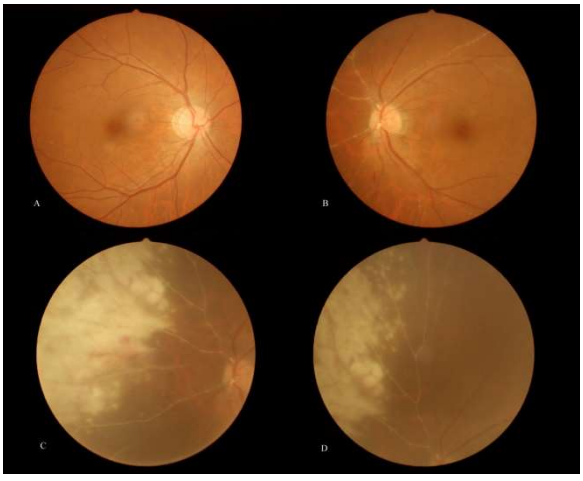

Figure 2: Fundus photographs showed retinal infliatrate and necrosis with hemorrhage in the nasal and superior quadrants, vessels occlusion with white sheath in all quadrants in the left eye (B,C,D), and retained normal in right eye(A).

DISCUSSION

CMV retinitis is a serious sigh-threatening eye disease which mainly affects AIDS patients, and it accounts for 75-85% of CMV infection in AIDS patients. Although rare, CMV retinitis may also occurred in patients with immunosuppresion,

The major issue of CMV retinitis was found in patients with allogeneic stem-cell transplantation or organ transplantation [5, 6], and the incidence of it in nontransplantation patitents is relatively small. There were few literatures about CMV retinitis occurred in leukemia [7], systemic lupus erythematosus (SLE) [8] and Wegener's granulomatosis [9]. We here presented two cases of CMV retinitis with non-Hodgkin lymphoma in Chinese population, and the clinic features were summarized.

In our cases, CMV retinitis occurred after several courses of chemotherapy with combined cytotoxic medicines. The diagnosis of CMV retinitis was first clinical. Typical extensive yellow retinal infiltrates, hemorrhages, necrosis lesions, inflammatory and occluded vessels were found in fundus examination. The diagnosis was confirmed by the vitreous biopsy. CMV PCR were positive in both patients, while PCR of blood samples were negative in the second patient. Serology showed CMV IgG(+) but IgM (-) ,which is usually a symbol of current infection. These indicated that CMV-DNA PCR of vitreous might be a sensitive marker for the disease instead of CMV antibodies.

Immune recovery uveitis (IRU) is always considered as the differential diagnosis of CMV retinitis. IRU occurred in CMV retinitis patients (always AIDS patients) who experienced immune reconstitution by using highly active antiretroviral therapy [10]. It is usually characterized by vitreous opacities and macular edema, and usually manifesting a good response to steroid medicine. In our cases, there was little or no inflammation in vitreous and no antiretroviral therapy used before retinitis arose, in early stage it response poor to the treatment of steroid. Vitreous CMV PCR positive also excluded the diagnosis of IRU.

In patients with AIDS, CD4 T-cell counts (<50 cells/ul) is a high risk factor for development of CMV retinitis, and with counts>100 cells/ul the incidence of CMV retinitis is minimal [11]. But in our cases CMV retinitis developed with normal CD4 counts in both first episode and relapse. The postulated reasons might be the dysfunction of abnormal T cells in lymphoma patients. And it might suggest CD4 T-cell counts might not be a good marker for indicating the CMV retinitis in non-HIV patients, and similar result was found in SLE patients [8].

In most cases of CMV retinitis, ganciclovir and foscarnet are recommended as effective medicines [12, 13]. In our cases, intravenous ganciclovir was the effective treatment, but it usually had to be stopped for its side-effects of myelosuppression and pancytopaenia. Intravitreal injection of ganciclovir manifested it effectiveness in our cases and it might be a recommendable method for its minor systemic complication [13].

Along with the increased use of immunosuppression drugs, the incidence of CMV retinitis in non-HIV patients would rise. Enough vigilance, early diagnosis and effective treatment of CMV retinitis may result in better prognosis and visual outcome.

Competing interests: The authors declare that they have no competing interests.

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