미만성 거대 B 세포 림프종 환자에서 발병한 거대세포바이러스 망막염

Cytomegalovirus Retinitis in Patients with Diffuse Large B-cell Lymphoma

강혜민

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Purpose: To report two cases of cytomegalovirus (CMV) retinitis in patients with diffuse large B cell lymphoma (DLBCL).

Case summary: A 59-year-old man (patient 1) visited our ophthalmology clinic due to decreased vision in the left eye. The patient had a history of right nephrectomy due to renal cell tumor, which showed complete remission. Best-corrected visual acuity (BCVA) of the left eye was 20/100 according to the Snellen visual acuity chart. Fundus examination revealed yellowish retinal infiltration with retinal hemorrhages, and diagnostic vitrectomy confirmed CMV retinitis. Further systemic evaluation indicated pancytopenia and bone marrow suppression. Positron emission tomography-computed tomography imaging suggested malignant lymphoma, and subsequent biopsy of lymph nodes confirmed DLBCL. In the second case, a 55-year-old woman (patient 2) presented with a sudden decrease in vision in the left eye during systemic chemotherapy for DLBCL. BCVA in the left eye was 20/125 by Snellen visual acuity chart, and the fundus demonstrated diffuse yellowish retinal infiltration with some grainy opacification. After a diagnosis of CMV retinitis, ganciclovir was administered to both patients, leading to improvement of retinal lesions.

Conclusions: CMV retinitis can occur in patients with DLBCL; thus, when patients with DLBCL complain of visual deterioration, CMV retinitis should be suspected.

Keywords: Cytomegalovirus (CMV); CMV retinitis; Diffuse large B-cell lymphoma

Introduction

Cytomegalovirus (CMV) retinitis is the most common opportunistic infection of the eye and can cause profound visual loss [1,2]. Acquired immunodeficiency syndrome caused by human immunodeficiency virus (HIV) is a common underlying disease in CMV retinitis, and was particularly prevalent before the era of highly active antiretroviral therapy [2-4].

CMV retinitis also can occur in the absence of HIV when other conditions lead to systemic immunosuppression, such as after chemotherapy for any malignancy, organ transplantation, or in cases of inherited immunodeficiency [1,5-7]. CMV retinitis has been also reported in various hematologic malignancies including leukemia and lymphoma [5,8-12].

Diffuse large B cell lymphoma (DLBCL) is the most common lymphoid malignancy in adults, and the most common

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subtype of non-Hodgkin's lymphoma (representing approximately one-third of all cases) [13]. DLBCL is most prevalent in middle-aged or elderly subjects, with a mean age at diagnosis in the sixth decade of life. Men are slightly more prone to developing DLBCL than women [13].

Recently, we treated two cases of CMV retinitis in patients with DLBCL, which represent the first cases reported in Korea. In one patient, ophthalmologic confirmation of CMV retinitis led to diagnosis of underlying DLBCL, and the other patient developed CMV retinitis during chemotherapy for DLBCL.

Case Report

Case 1

A 59-year-old male patient visited our ophthalmology clinic due to visual deterioration in the left eye that had progressed over 1 week. The best-corrected visual acuity (BCVA) was 20/20 in the right eye, and 20/100 in the left eye according to the Snellen visual acuity chart. Detailed fundus examination after dilation detected no significant findings in the right eye, whereas in the left eye there was moderate vitreous opacity with retinal infiltration and hemorrhages temporal to the fovea, extending to the temporal periphery (Fig. 1A). The patient had a history of right nephrectomy due to a renal tumor that had been treated at another hospital 15 years prior, which remained in complete remission. The patient did not report experiencing any other diseases. However, baseline blood tests showed generalized hematologic problems including anemia, neutropenia, and decreased platelet cell counts. Other laboratory findings were normal, and an HIV test was negative. The patient's clinical features were suggestive of CMV retinitis and his immune status was not conclusive for immunosuppression, therefore diagnostic vitrectomy was performed on the same day. After diagnostic vitrectomy, systemic administration of ganciclovir was initiated, but due to further deterioration of renal function, treatment was switched to intravitreal ganciclovir injections. PCR analysis of vitreous fluid confirmed CMV retinitis in this patient, and further systemic assessments including bone marrow biopsy were performed. Bone marrow biopsy revealed hypocellular marrow. Subsequent positron emission tomography-computed tomography revealed multiple enlarged lymph nodes with increased fluorodeoxyglucose (FDG) uptake in the bilateral

parotid glands, neck, supraclavicular area, axillary area, mediastinum, paraspinal area, cardiophrenic area, abdomen, retroperitoneum, bilateral iliac changes, and inguinal area.

Figure 1. Representative image of patient 1. (A) Wide fundus photography of a 59-year-old man who visited the ophthalmology clinic with a sudden decrease in vision in the left eye. Dilated fundus examination revealed moderate vitreous opacity with retinal infiltration and hemorrhages temporal to the fovea, extending to the temporal periphery. (B) Wide fundus photography on treatment day 1. After diagnostic vitrectomy, the vitreous opacity was removed. A central shadow due to a posterior subcapsular opacity of the lens could be observed. Retinal infiltration with hemorrhages temporal to the fovea was noted, leading to a diagnosis of cytomegalovirus retinitis. (C) After treatment via intravitreal ganciclovir injection, retinal infiltration subsided, and granular consolidation was achieved.

In addition, the spleen, right nasopharyngeal wall, sternum, thoracic spines, bilateral acetabulum, left pubic bone, and thighs showed increased FDG uptake, suggesting lymphoma. Lymph node biopsy led to a diagnosis of DLBCL stage IVB, IPI 3 in this patient, and systemic chemotherapy was started (rituximab, cyclophosphamide, hydroxydaunorubicin, oncovin and prednisone or prednisolone; R-CHOP). After intravitreal cymevene injections in the left eye, BCVA in the left eye was maintained at 20/100 on the Snellen visual acuity chart, although CMV retinitis itself exhibited repeated stabilization and reactivation over the next 8 months (Fig. 1B, C). Despite systemic chemotherapy, the patient expired 8 months after CMV retinitis diagnosis.

Case 2

A 55-year-old female patient was referred from the hematology department due to a sudden decrease in vision in the left eye. BCVA was 20/25 in the right eye, and 20/125 in the left eye on the Snellen visual acuity chart. The patient had a 7-year history of diabetes mellitus, and had undergone ophthalmologic evaluation in our clinic 7 months prior. BCVA was 20/25 in each eye on the Snellen visual acuity chart. Numerous fine drusen were present, and further assessment showed mild nonproliferative diabetic retinopathy in both eyes (Fig. 2A). Five months prior to visual symptoms, the patient was diagnosed with DLBCL via nasopharyngeal biopsy (stage II EA, IPI 1), and started systemic chemotherapy (R-CHOP). Concurrent with sudden visual deterioration, moderate anterior chamber reaction, mild vitreous haze, diffuse yellowish retinal infiltration, and grainy opacification with some retinal hemorrhages were noted in the left eye (Fig. 2B). Based on the patient's clinical features and systemic condition, she was diagnosed with CMV retinitis and systemic intravenous ganciclovir administration followed by oral administration was started. One month after the initiation of systemic treatment, the anterior chamber reaction was resolved, retinal lesions had stabilized, and BCVA improved to 20/40 in the left eye according to the Snellen visual acuity chart (Fig. 2C). However, the patient expired 7 months after the diagnosis of CMV retinitis due to DLBCL.

Figure 2. Representative image of patient 2. (A) Wide fundus photography of a 55-year-old woman before the development of cytomegalovirus (CMV) retinitis. Due to underlying diabetes mellitus, the patient was referred for routine evaluation for diabetic retinopathy. At that time, fundus examination revealed some drusen over the macula. (B) After diagnosis of diffuse large B-cell lymphoma and development of CMV retinitis, fundus examination demonstrated a mild vitreous haze, diffuse yellowish retinal infiltration, and grainy opacification with some retinal hemorrhages in the left eye. (C) After treatment for CMV retinitis with systemic ganciclovir, retinal infiltration was greatly improved.

Discussion

CMV infection causes retinal whitening or opacification attributable to retinal necrosis and variable edema [14,15]. An

irregular, dry-appearing, granular border, often with characteristic small, isolated satellites at the advancing edge, is the hallmark of untreated CMV retinitis [14,15]. CMV retinitis can be further classified into two variants: a fulminant/edematous type showing marked edema with dense, confluent areas of retinal whitening, which is usually accompanied by moderate-to-severe retinal hemorrhage and vascular sheathing, and an indolent/granular type characterized by less edema, only faint, grainy opacification, and little or no retinal hemorrhage without vascular sheathing [14,15]. CMV retinitis and its complications such as retinal detachment, branch retinal vessel occlusion, and retinal neovascularization can lead to profound vision loss in these patients [14,15]. Because the diagnosis of CMV retinitis is primarily clinical, relying on identification of typical features, clinical suspicion is important for the diagnosis and treatment of CMV retinitis.

This represents the first Korean case report of CMV retinitis, and suggests the importance of clinical suspicion in the diagnosis of this disease for both ophthalmologists and hemato-oncologists. The case of patient 1, clinical suspicion and confirmation of CMV retinitis led to the diagnosis of underlying DLBCL. With this case, we have revalidated the importance of clinical suspicion and a thorough systemic work-up in CMV retinitis patients, even in those who deny the presence of any underlying diseases. By identifying systemic diseases, life-saving treatment in addition to sight-preserving treatment can be administered in a timely manner. In the case of patient 2, we were aware that she was already immunocompromised due to treatment for DLBCL, and timely consultation with the hematology department led to diagnosis of CMV retinitis. CMV retinitis should be suspected when immunocompromised patients report visual disturbances.

We report two cases of CMV retinitis in patients with DLBCL in Korea, and encourage clinical suspicion, timely evaluation and appropriate treatment in such patients.

Conflicts of interest

The authors have no conflicts to disclose.

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