Presumed Bilateral Cytomegalovirus-Induced Optic Neuropathy in an Immunocompetent Person

A Case Report

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Abstract:
Ocular manifestations of an acquired cytomegalovirus (CMV) infection are often associated with the patient being in an immunocompromised state. In the vast majority of cases, the affliction appears as a necrotic retinitis; an isolated optic nerve lesion is seen less frequently. To date, only two cases of CMV retinitis and one case of bilateral acute retinal necrosis have been reported in healthy individuals. We describe a 32-year-old healthy woman who developed bilateral papillitis. Tests were positive for acute CMV infection but negative for an immunocompromised state. We changed the antiviral therapy from acyclovir to foscarnet in association with corticosteroids, and resolution of the papillitis and recovery of visual acuity were obtained.

Key Words: Cytomegalovirus—Papillitis.

The most common clinical manifestation of cytomegalovirus (CMV) infection in healthy hosts beyond the neonatal period is a mononucleosis syndrome. This may occur spontaneously or following transfusion of leukocyte-containing blood products; it presents clinically as a flu-like syndrome. Occasionally, interstitial pneumonia, myocarditis, arthritis, or neurologic involvement (such as Guillain-Barré syndrome or encephalitis) may complicate CMV mononucleosis (1,2). In the course of this syndrome, ocular manifestations are rare (3-5).

We report the case of a 32-year-old woman who developed bilateral papillitis; tests were positive for acute CMV infection. To our knowledge, this is the first report of bilateral CMV papillitis in an immunocompetent person.

CASE REPORT

A 32-year-old woman developed a flu-like syndrome that lasted 1 week. One month later, she began to complain of frontal headache and experienced a progressive loss of vision in her left eye (LE); several days later, her right eye (RE) vision also worsened. There was no pain on movement of either eye.

On examination, the visual acuity was 20/100 in the RE and light perception in the LE. Slit-lamp biomicroscopy examination was normal. Intraocular pressure was 10 mm Hg in both eyes. A left pupillary afferent defect was present. Fundus examination revealed bilateral papilledema, which was more prominent in the LE; intraretinal hem...
or rhages; soft exude in the superior juxta- papillary region of the RE; and venous congestion (Fig. 1). General and neurological examinations were normal.

Tests revealed an erythrocyte sedimentation rate of 18 mm/h [normal value (NV), 1–12], a white blood count of 10.4/mm³ (NV, 4–11), a normal differential count, normal stimulated and atypical lymphocytes, and liver enzyme levels of aspartate amino transferase at 78 U/L (NV, 11–32) and of alanine amino transferase at 143 U/L (NV, 9–36). Chest x-ray film was normal. A cerebral scan showed enlarged optic nerves (Fig. 2). We suspected a herpetic infection and administered i.v. acyclovir, 900 mg, every 8 hours on the day of admission.

Serology for CMV, Epstein–Barr virus, Herpes simplex I/II, Varicella–Zoster virus, Rubella virus, Rubeola virus, Toxoplasmosis, Borrelia burgdorferi, Treponema pallidum, and human immunodeficiency virus (HIV) was positive for anti-CMV IgM (ratio, 4.80; NV, 0.6) and IgG (50 U/ml IgG anti-CMV antibody; NV, 15), and early CMV antigen was detected in the urine. Tests for sarcoidosis and for connective tissue disorders were negative. A lumbar puncture showed a pleocytosis (proteins, 0.29 g/L; white cells, 11/mm³; lymphocytes, 96%) as well as oligoclonal bands; two columns were visible on electrophoresis of the cerebrospinal fluid. Therefore, antigenic stimulation was suspected. Serology of the cerebrospinal fluid was negative. Immunoglobulin electrophoresis, quantitative immunoglobulin levels, tuberculin purified protein derivative (PPD) skin test, CD4 and CD8 T lymphocyte counts, C3–C4, and CH50 examinations were done to establish the diagnosis of an immunocompromised state, but they were within the normal range.

On the basis of the full blood count, the positive serology testing, and the detection of early antigen in the urine, an acute CMV infection was diagnosed; acyclovir was discontinued after 3 days,

FIG. 3. Fundus photographs of the right and left fundi show complete resolution of the papilledema; the intraretinal hemorrhages, soft exudate, and venous congestion that had been previously recorded (see Fig. 1A-B).
and we administered i.v. foscarnet (60 mg/kg) every 8 h for 3 weeks. Methylprednisolone was also introduced (250 mg four times per day, i.v., for 5 days), and then it was replaced by prednisone (1 mg/kg orally at tapering doses for 1 month).

Following 3 weeks of treatment, visual acuity returned to 20/20 in both eyes. This improvement was accompanied by disappearance of the left relative afferent pupillary defect and also by complete resolution of the papilledema, the intraretinal hemorrhages, and the venous congestion (Fig. 3). Cerebral magnetic resonance scan showed that the size of the optic nerves had returned to normal (Fig. 4). Two months later, viral titers revealed a decrease in CMV IgM (ratio, 2.01) and an increase in the CMV IgG to 203 U/ml. Early CMV antigen could no longer be detected in the urine. Liver enzyme levels were normal.

Twelve months later, tests seeking to establish HIV positivity or other immunocompromised states were still negative.

**DISCUSSION**

CMV neuroretinal manifestations, such as retinitis, optic atrophy, and anophthalmia (6–9) appear to occur more often after a congenital infection or as a result of an acquired immunocompromised state, as in chemotherapy, malignancy, or AIDS (1,2).

Foerster first described CMV retinitis in 1959 (10), but CMV as a responsible agent of the disease was suggested by Smith in 1964 (11). Clinically, the ocular condition appears as unilateral or bilateral retinitis composed of scattered yellow–white areas of necrotizing retina with intraretinal hemorrhage and vasculitis; soft exudates and mild vitreous inflammation may be present. These lesions often show a perivascular distribution (12,13). CMV optic nerve involvement (optic neuritis or papillitis) has been described in patients suffering from lymphoma (14) or AIDS (15,16).

The patient described here had a mononucleosis syndrome followed 1 month later by bilateral optic papillitis, abnormal liver enzymes, elevated anti-IgM and -IgG antibodies for CMV, and early CMV antigen in her urine; there was no evidence of an immunocompromised state. Resolution of the papillitis after i.v. foscarnet argues for a diagnosis of CMV papillitis. However, this argument is weakened by the simultaneous use of large doses of systemic corticosteroids. In the recovery period, subsidence of the IgM antibodies to CMV, rise of the IgG antibodies, and absence of early CMV antigen attest to immunocompetence in the patient and the probability that her symptoms were the results of a CMV infection.

This case, along with the description of two cases of CMV retinitis (17,18) and a case of bilateral acute retinal necrosis (19) in the literature, leads us to believe that neuroretinal manifestations (such as retinitis, optic neuritis, and papillitis) may occur in healthy adults suffering from CMV infection. It is impossible to explain why the optic nerves were the only neural tissue affected in this patient, whose cerebral spinal fluid tested was negative. Evidence of CMV infection caused us to change the antiviral therapy to the more specific agent foscarnet; in the absence of direct evidence, CMV etiology must be presumed.

A presumed mechanism for such complications could be the suppressive action of CMV on immunocompetent cells (20,21); indeed, some authors have demonstrated that both mitogen responsiveness and the ability to generate cytotoxic lympho-

**FIG. 2.** Cerebral computed tomography scan (axial views) shows enlarged optic nerves.

**FIG. 4.** Cerebral T1-weighted axial magnetic resonance scan shows that the optic nerves have returned to normal dimensions.
kines is markedly diminished in patients with CMV mononucleosis (22). Some characteristics of the CMV pathogenesis appear to predispose to a transitory immunocompromised state, promoting the appearance of CMV neuroretinal manifestations in certain healthy patients.

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REFERENCES


