Two Cases of Cutaneous Cytomegalovirus Infection in Immunocompromised Patients

Jae Hong Park, M.D., Jeong Joon Oh, M.D., Eil Soo Lee, M.D.

Department of Dermatology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

Cytomegalovirus (CMV) is a major cause of morbidity and mortality in immunocompromised patients. CMV can cause pneumonia, retinitis, gastrointestinal ulcers, and widely disseminated disease, but cutaneous CMV is rare. We report two cases of cutaneous CMV infection presenting as perianal ulcers. A 54 year-old male who had liver transplantation and a 72-year-old male, who was treated with chemotherapy for angioimmunoblastic T-cell lymphoma, presented with perianal ulcers and had systemic symptoms of CMV infection with CMV antigenemia. They had multiple ulcerations with erythematous bases on the perianal area, and histopathologic examinations showed large atypical cytomegalic cells in the dermis, and immunohistochemical stains, with the anti-CMV antibody showed positive reactions. (Ann Dermatol 16(2) 67~70, 2004)

Key Words: Cytomegalovirus, Perianal ulcer

INTRODUCTION

CMV, a member of the Herpesviridae family, is a major cause of morbidity and mortality in immunocompromised patients[1]. The current prevalence of this form of CMV infection is thought to have an iatrogenic basis, and typically, it is associated with neoplasia (especially lymphomas and leukemias), organ transplantation, and other clinical settings in which immunosuppressive therapy is given[2]. In addition to a febrile mononucleosis-like syndrome, CMV infection can produce interstitial pneumonitis and gastrointestinal ulcerations, but involvements of other internal organs occur less frequently. Cutaneous lesions in CMV infection are rare, and are often late manifestations of systemic infection, and usually herald a fatal course[3]. We report two cases of cutaneous CMV infection presenting as perianal ulcers in immunocompromised patients.

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Reprint request to: Eil Soo Lee, M.D., Department of Dermatology, Samsung Medical Center, 50 Ilwon-dong, Kangnam-gu, Seoul 135-710, Korea
Tel. 82-2-3410-6577, Fax: 82-2-3410-3869
E-mail: eslee@smc.samsung.co.kr

CASE REPORT

Case 1

A 54-year-old man consulted to the department of dermatology to evaluate perianal ulcerated lesions. Ten years ago, he was diagnosed with liver cirrhosis and suffered from hepatic encephalitis and variceal bleeding. Four years ago, he underwent cadaveric liver transplantation and thereafter took medicines such as prednisolone, mycophenolate, and cyclosporine. Three months ago, a cough and dyspnea appeared and the perianal ulcerated lesions appeared one month ago. He was taken to an emergency room and laboratory tests showed; WBC 16,700/mm^3, hemoglobin 10.1g/dl, platelet count 71 K/mm^3, AST/ALT 50/58 IU/L, BUN/Cr 47.9/3.8 mg/dl. The CMV culture in peripheral blood was negative but the CMV antigenemia was 57/20,000 WBCs. On the chest CT, air space consolidations were detected in both lower lobes but the CMV culture and PCR with bronchoalveolar lavage fluid was negative. On colonoscopic examination, multiple ulcerations were detected and the immunohistochemical stain with

the anti-CMV antibody of the colon lesion showed a positive reaction. On physical examination, several ulcers with an overlying yellowish crust and surrounding erythema were detected on the perianal area (Fig. 1). Histopathologic examination showed granulomatous infiltrates in the superficial and deep dermis, and owl's eye-appearing atypical cytomegalic cells with eosinophilic intranuclear inclusions (Fig. 2). Immunohistochemical staining with anti-CMV antibody showed scattered intracytoplasmic inclusions within the histiocytes (Fig. 3) and the patient was diagnosed as having cutaneous CMV infection. He was treated daily with 75 mg of intravenous ganciclovir for 2 months, and the lesions have slowly healed.

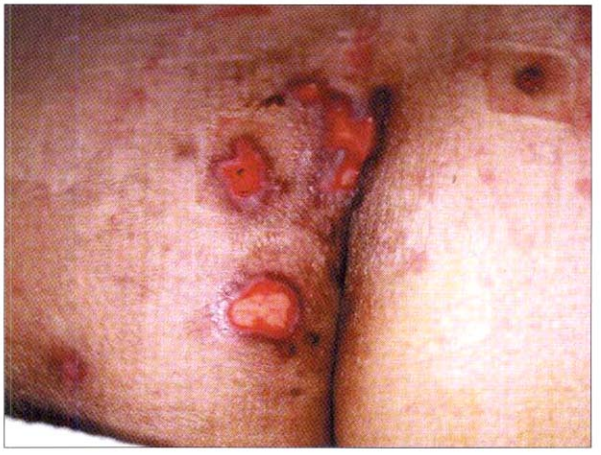

Fig. 1. Several ulcers with an overlying yellowish crust and surrounding erythema on the perianal area.

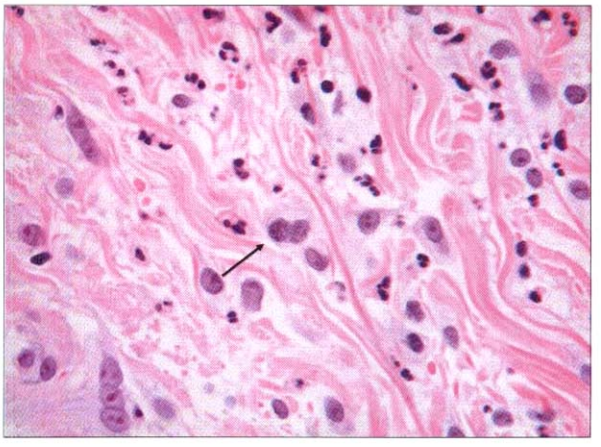

Fig. 2. Owl's eye-appearing atypical cytomegalic cells with eosinophilic intranuclear inclusions (H&E, × 200).

Case 2

A 72-year-old man consulted to the department of dermatology to undergo an evaluation for perianal ulcerated lesions. For many years, he had suffered from hypertension and chronic renal failure. Three months ago, he was diagnosed as suffering from angioimmunoblastic T-cell lymphoma. Threafter, chemotherapy with cyclophosphamide, doxorubicin, vincristine and prednisolone was done. Three weeks ago, the perianal ulcerated lesions appeared. Laboratory tests showed WBC 4,980/mm^3, hemoglobin 10.3 g/dl, AST/ALT 11/4 IU/L, BUN/Cr 114.2/3.6 mg/dl. The CMV culture in peripheral blood was negative but the CMV antigenemia was 57/20,000 WBCs. On sigmoidoscopy, chronic colitis was detected but immunohistochemical staining with anti-CMV antibody of the colon lesion was negative. On physical examination, multiple ulcerated lesions with an erythematous base were detected on the perianal area (Fig. 4). Histopathologic examination showed granulomatous infiltrates in the dermis and atypical cytomegalic cells, which had large nuclei with basophilic intranuclear inclusions body with a perinuclear halo were seen in the upper dermis (Fig. 5). The immunohistochemical stain with anti-CMV antibody was positive and CMV infection was diagnosed. He was treated with 70 mg of intravenous ganciclovir per day for 1 month, however, the patient passed away due to sepsis.

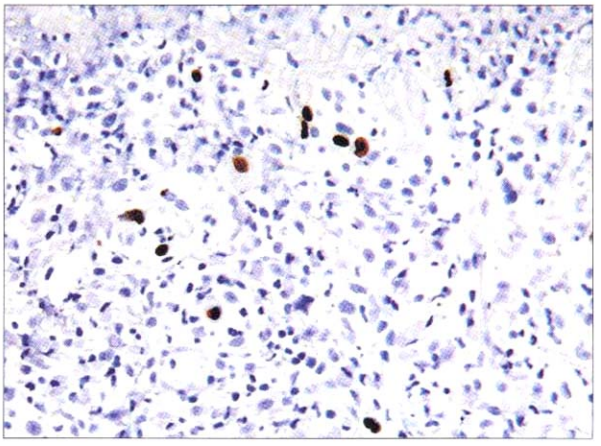

Fig. 3. Immunohistochemical stain with anti-CMV antibody showed scattered intracytoplasmic inclusions within histiocytes (× 200).

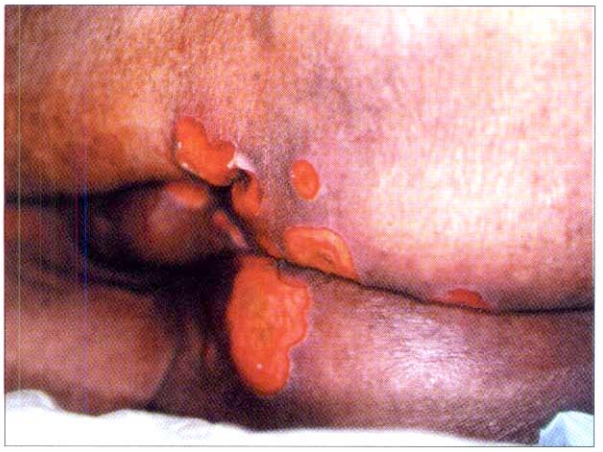

Fig. 4. Multiple ulcerated lesions with erythematous base on the perianal area.

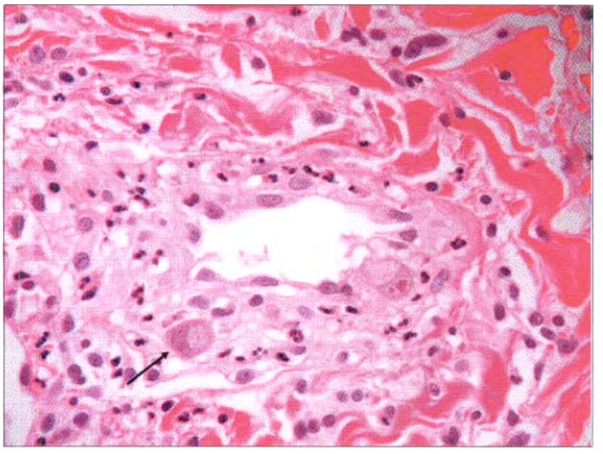

Fig. 5. Atypical cytomegalic cell which had large nuclei with basophilic intranuclear inclusion body with a perinuclear halo (H&E, × 200).

DISCUSSION

Cutaneous CMV has been observed only in the past 30 years, and more than 50% of the cases have been reported in the last 10 years, paralleling the recent increase in immunocompromised patients[1]. In Korea, cutaneous CMV have been reported in patients of acquired immune deficiency syndrome[4], acute lymphocytic leukemia after bone marrow transplantation[5], and after liver transplantation[6]. The small number of case reports of cutaneous CMV may not accurately reflect the true incidence, either due to the nonspecific clinical appearance of the skin lesions or the difficulty in detecting the often sparse viral inclusions on routinely stained sections[1].

In contrast with immunocompetent hosts, CMV infection in immunocompromised patients may represent as mononucleosis, pneumonitis, hepatitis, encephalitis, gastroenteritis, choreoretinits, or cutaneous eruption[7]. The clinical appearances of cutaneous CMV are highly variable. Ulcers[1,3,4,6], indurated plaque[2], purpura[5] may all be presenting signs. The ulcerations appear to have a predilection for the genital and perianal regions[1,4,6], as were seen in our cases. Once CMV affects the skin, the mortality rate is approximately 85% in 6 months[8]. In our cases, the patient of the first case improved after treatment with ganciclovir and the patient of the second case expired after one month of cutaneous CMV infection despite receiving treatment. If cutaneous CMV infection is detected, the evaluation of wide spread disease is important for management and prognosis[9].

Histopathologically, the diagnosis of CMV is made by identifying the characteristic large cytomegalic cell that contains a large, centrally located, round basophilic ("owl's eye"), intranuclear inclusion.[10] Infected cells may also have small, clustered intracytoplasmic viral inclusions, and in our cases, the first case showed owl's eye appearing cells and the second case showed atypical cytomegalic cells with large nuclei and intranuclear inclusions. In most cases of cutaneous CMV infection, inclusion bodies have been found in the endothelial cells of capillaries[2]. It has been suggested that vascular damage is responsible for the initial rash, and if severe enough, results in ulceration of the skin[9]. But generally, histopathologic findings are much less sensitive than those of the culture and immunohistochemical stain[9].

Immunohistochemistry is a widely used, rapid, and sensitive technique to identify a variety of cellular antigens[10]. Monoclonal antibodies, that are directed against nuclear and cytoplasmic CMV antigens, were used in our diagnosis and scattered CMV antigens were detected. In addition, the CMV antigenemia was detected in the serum, but CMV cultures, which have a low sensitivity, were negative.

In situ hybridization and polymerase chain reaction (PCR) by viral DNA are useful methods for the diagnosis of CMV infection. The sensitivity of in situ hybridization is known to be as sensitive as tissue culture[11]. PCR amplification of DNA is the most recent technique and it may be the most valuable

technique because of its high sensitivity and specificity[1].

In summary, CMV infection has an increasing tendency due to AIDS and immunosuppressive treatment. Skin lesions may be clues to the presence of disseminated CMV infections and early diagnosis may lead to a successful outcome. Moreover, the histopathologic finding "owl's eye" is characteristic for CMV infection but its sensitivity is low. Immunohistochemistry, in situ hybridization and PCR can be used for the early diagnosis and treatment with ganciclovir or foscarnet which are known to be effective for CMV infection.

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