

Oral ulcers in heart transplant patient

History

A 40-year-old man, with a history of heart transplantation two years back, presented with painful oral ulcers of three-weeks duration. Physical examination disclosed two large and deep, irregularly shaped ulcers on his lower lip and right buccal mucosa [Figure 1]. No fever or other systemic symptoms were observed. His usual medications included mycophenolate mofetil 360 mg daily and tacrolimus 8 mg daily. Culture specimens were negative for bacteria and herpes simplex virus type I and II. Blood cell counts only showed a mild leukopenia ($3.23 \times 10^9/L$; normal value: $3.80-11.00 \times 10^9/L$) and neutropenia ($1.17 \times 10^9/L$; normal value: $1.80-7.00 \times 10^9/L$); the rest of the analysis were normal. Skin biopsy revealed a dense perivascular and mixed interstitial infiltrate composed of neutrophils, eosinophils, lymphocytes, and plasma cells [Figures 2 and 3]. Endothelial cells demonstrated



Figure 1: Deep, irregularly shaped ulcer on the lower lip

large eosinophilic inclusions, mostly intranuclear and occasionally intracytoplasmic, with some of them showing an “owl’s eye” appearance [Figure 4].

What is Your Diagnosis?

Cytomegalovirus (CMV) oral ulcers.

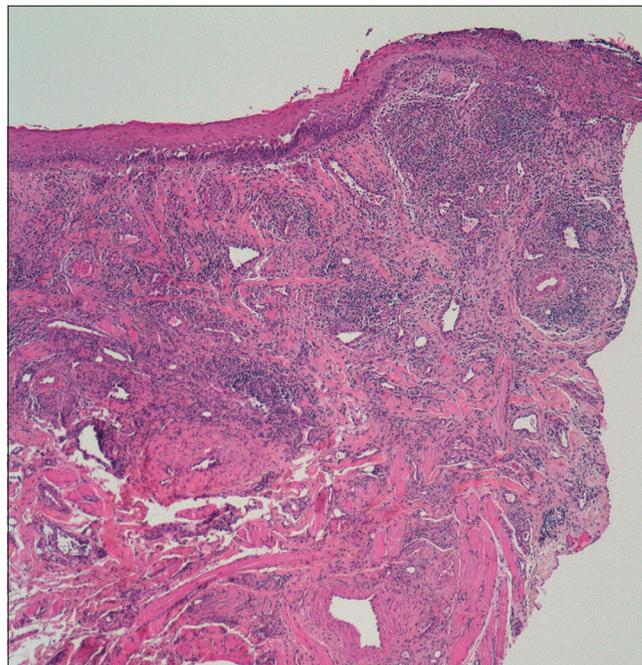


Figure 2: Ulcer with a dense perivascular and mixed interstitial infiltrate of neutrophils, eosinophils, lymphocytes, and plasma cells in the dermis. (H and E, $\times 400$)

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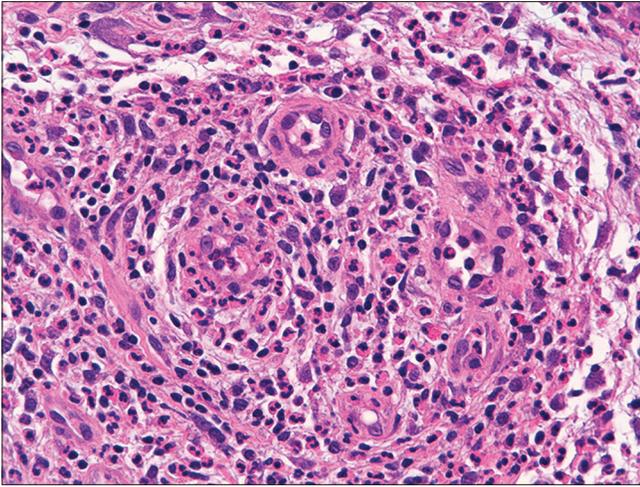


Figure 3: Enlarged endothelial cells with a dense perivascular infiltrate composed of neutrophils, eosinophils, lymphocytes, and plasma cells. (H and E, ×200)

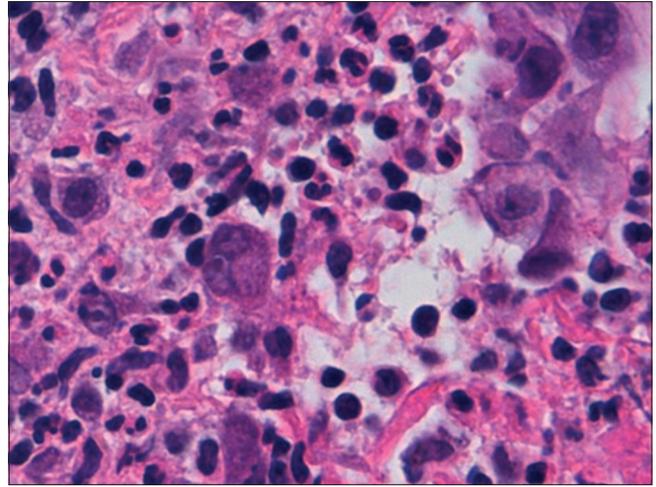


Figure 4: Some of the endothelial cells show large and eosinophilic nuclei which resemble an "owl's eye" (H and E, ×400)

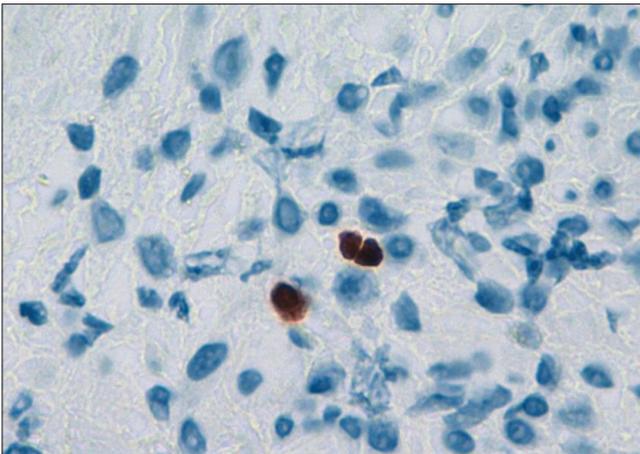


Figure 5: Positive immunoperoxidase staining of cytomegalovirus



Figure 6: Posttreatment ulcer on the lower lip

Answer

Cytomegalovirus (CMV) oral ulcers.

Discussion

CMV is a common opportunistic infection that usually affects immunocompromised patients, particularly those with human immunodeficiency virus infection, hematological malignant neoplasms, and solid-organ or hematopoietic stem cell transplantation recipients.^{1,2} Transmission may occur by body fluids, pregnancy, breastfeeding, blood transfusions, or after solid organ transplantation.^{1,2}

This virus may produce a wide range of diseases including pneumonitis, meningitis, retinitis, hepatitis, esophagitis, colitis, and mucocutaneous diseases. Mucocutaneous manifestations are varied and include oral and cutaneous ulcers, cutaneous nodules, maculopapular and urticarial eruptions, necrotic papules, verrucous plaques, pustules, and localized sclerodermoid changes.³

Oral ulcers secondary to cytomegalovirus infection are uncommon; but, they should be considered in any immunosuppressed patient with nonhealing ulcers, as its recognition may represent the first sign of systemic disease.³ Clinically, they present as solitary or multiple, nonhealing ulcers of variable size and location.^{2,4} These nonspecific clinical features can overlap with several other causes of oral ulcers such as bacterial infections, herpes simplex I and II, drugs, trauma, and neoplasms, making specific investigations a very important aspect of diagnosis.²

Several laboratory tests are available but not all of them are useful for the diagnosis of mucocutaneous disease. Serologic tests determine immunity to the virus; but have no value for the diagnosis of active disease. Antigenemia [detection of viral proteins (pp65) in peripheral blood leukocytes] and quantitative deoxyribonucleic acid (DNA) determinations in blood or plasma by polymerase chain reaction (PCR) may be useful for the diagnosis of visceral involvement, however, low or negative results may be seen in patients with focal disease. A positive culture from tissue biopsy can support the diagnosis,^{4,5} although slow growth of the virus and its low sensitivity limits its use.

Histopathological examination of the lesions is considered the gold standard for diagnosis.^{2,4,5} Tissue invasion is indicated by swollen, vascular endothelial cells with enlarged nuclei, prominent nucleoli, and intranuclear and intracytoplasmic eosinophilic inclusions that resemble an “owl’s eye.”² However, the sensitivity of histopathological examination is usually low as the cytopathological changes of cytomegalovirus infection are typically present only in scattered cells. Sensitivity can be improved in these cases by virus-specific immunohistochemistry staining.^{2,4,5} In our case, PCR and culture specimens were taken from the ulcers; however, all the results were negative and the diagnosis was confirmed by

immunoperoxidase staining with monoclonal anti-cytomegalovirus antibodies of the biopsy specimen [Figure 5].

At present, ganciclovir is considered the primary treatment of this infection.^{1,2} In case of drug resistance, foscarnet and cidofovir may be good alternatives.¹ Our patient was initiated on oral ganciclovir 450 mg daily with rapid improvement and subsequent resolution of the oral ulcers within one month [Figure 6]. CMV prophylaxis was not initiated and mycophenolate mofetil was not discontinued. Monitoring was done weekly, by quantitative DNA estimation, during the first month and every 4 weeks during the next 6 months.

We report an unusual case of cytomegalovirus oral infection in a patient with heart transplantation. Although the clinical appearance is nonspecific, cytomegalovirus infection should be considered in the differential diagnosis of oral ulcers in these patients, to establish a prompt diagnosis and treatment.

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Conflicts of interest

There are no conflicts of interest.

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