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Severe Ulcers in Oral Mucosa Due to Cytomegalovirus in an Immunosuppressed Pediatric Patient

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Abstract

Cutaneous expressions in cytomegalovirus infection are rare and their clinical manifestations in immunosuppressed patients are diverse; for example, ulcerative forms. Therefore, cytomegalovirus infection should be considered in the differential diagnosis of ulcers in immunosuppressed patients.

We reported an immunosuppressed child with severe oral ulcerative lesions of torpid evolution, associated with cytomegalovirus infection, diagnosed by laboratory and histopathological examinations.

Keywords

Cytomegalovirus; Oral Ulcers; Immunosuppressed

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Introduction

Cytomegalovirus is a double-stranded DNA virus belonging to the Herpesviridae family. The infection is asymptomatic when it happens in an immunocompetent patient but symptomatic in the immunosuppressed patient [1].

The highest risk of morbidity and mortality occurs in children with primary immunodeficiencies, above all, in severe combined immunodeficiency [2]. Cutaneous manifestations due to cytomegalovirus are rare and they are the result of its dissemination (viremia). They are characterized by polymorphous skin lesions (macules, papules, hives, nodules, erosions) and the presence of oral ulcer is associated with severity and high mortality [3,4].

Case Report

We report an 8-year-old male patient with the following antecedents: first pregnancy product from a mother with mental retardation, dystocic delivery, incomplete vaccinations, chronic malnutrition and a history of two previous hospitalizations due to pneumonia and media otitis. This patient had a two-month disease evolution, characterized by ulcers in the oral cavity, hypoxemia and general discomfort; these lesions increase in number and size and become bleeding, alongside he presents fever and severe respiratory distress, for which he is admitted in an emergency and transferred to the intensive care unit, due to this general condition.

The physical examination revealed necrotic ulcers with bleeding, hematic crusts involving the lips, gums, palate and cheeks (Fig. 1). Erosive papules and plaques appear covered by hematic crust on the cheeks and neck after a week (Fig. 2 and 3). Alongside, hepatomegaly and acral edema are shown. Laboratory tests highlight pancytopenia: Hemoglobin: 6.8 g/dL, platelets: 1000/ mm³, leukocytes: 4320/ mm³ and lymphocytes: 1020 (Normal values:1500-8000); altered coagulation profile: prothrombin time: 16.1", INR: 1.4, fibrinogen: 98.5 mg/dl, D-Dimer: 1.86; C-reactive protein : 5.3 mg/dl, urea: 50 mg/dl (Normal values:10-38), glutamic oxaloacetic transaminases: 90 U/L (Normal values: 0-47), glutamic pyruvic transaminases: 82 U/L (Normal values: 0-39), total proteins: 4.3 g/dl (Normal values:6-8.3), albumin: 2.8 g/dl (Normal values:3.2-5.2), lactic dehydrogenase: 1648 U/L (Normal values:230-460), ferritin: 4721 ng/ml (Normal values: 3.7-183); Immunoglobulin M and G for Herpesvirus: non-reactive; HIV-ELISA TEST and VDRL: non-reactive; Immunoglobulin M: 3 mg/dl (Normal values:48-207), the rest of immunoglobulins in normal ranges, PPD: 0 mm; Direct BK in sputum, gastric and tracheal aspirates negatives, serum galactomannan: 0.959 (positive) and viral load for cytomegalovirus: 439541 copy ADN CMV/ml (positive).

A skin biopsy of an oral ulcer is performed. Multiple fragments of fibrinoleukocyte tissue, granulation tissue with mild infiltrate composed of neutrophils are found, lymphocytes and plasma cells, in the endothelium of some vessels cells with basophilic cytoplasm and hypertrophic nucleus are observed. The chromatin is vacuolated and the prominent nucleolus has a peripheral halo; at the bottom, hemosiderin deposits are observed between the vessels (Fig. 4). Histochemistry: methanamine silver from Grocott Gomori and Periodic Acid-Schiff were negative. Immunohistochemistry: Cytomegalovirus positive in endothelial cells with a hypertrophic nucleus; markers CD3, CD68 and CD31 positive; Epstein Barr virus negative.

Due to previous respiratory infections and severity of the skin condition, a genetic panel was performed and an uncertain and heterozygous meaning was found for STAT 3, a gene related to early-onset multisystemic autoimmune disease.

Ganciclovir was given (12 mg/kg/day) with a favorable clinical and laboratory response (Fig. 5, 6).

Figure 1: Admission physical examination: presence of necrotic ulcers with hemorrhagic and bleeding crusts on the oral mucosa.

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Figure 2: Unfavorable evolution of necrotic ulcers on oral mucosa and erosive plaques covered by hematic crusts on cheeks and neck.

Figure 3: Necrotic ulcers, at third week of evolution, progressing in extension involving oral mucosa, cheeks and neck.

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Figure 4: Histopathologic findings of oral ulcer: mild infiltrate composed of neutrophils, lymphocytes and plasma cells found in endothelium, cells with basophilic cytoplasm, hypertrophic nucleus and prominent nucleolus which has a peripheral halo.

Figure 5: Patient after a 3 week-treatment of ganciclovir with decrease of ulcerative and erosive lesions.

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Figure 6: Patient after an 8 week-treatment of ganciclovir, there is resolution of lesions and the presence of only residual post-inflammatory spots.

Discussion

Cytomegalovirus invades various cells and the infection is asymptomatic in immunocompetent patients; but it is symptomatic in congenital, premature and immunosuppressed cases (patients with human immunodeficiency virus, transplanted, immunodeficiencies and with immunosuppressive therapy) [1].

Immunosuppressed patients have a higher risk of primary infection and reactivation of latent virus; presenting as cytomegalovirus syndrome (association of viremia with fever, malaise, leukopenia, thrombocytopenia, atypical lymphocytosis or elevated liver enzymes, in the absence of another cause) or invasive tissue disease (such as pneumonitis, colitis, hepatitis, retinitis and another determined by virus detection in tissue) [1,2]. In immunosuppressed pediatric patients, about 85% of the morbidity and mortality occurs in those with primary immunodeficiency's, making the treatment of active infection more complicated, with a high risk of resistance to antiviral therapy [2].

Cytomegalovirus skin manifestations could evolve in various forms, from morbilliform or scarlatiniform exanthema to papulopustular or papule-crusted lesions. Further, we could see urticarial, vesicular-ampullary, nodular, warty and ulcerative lesions, including oral ulcers [3,4].

These ulcerative lesions could result from an infection disseminated by hematogenous route, reactivation within endothelial cells, or autoinoculation through urine, feces, or saliva [4,5]. Ulcers are painful, persistent, perforated without erythema, of various sizes, with the palate and gums being the two most frequently affected sites; however, other mucosal areas may be affected, which is why they have been associated with ulcers of the esophagus, gastrointestinal tract, anus and vagina [4,5].

In the histopathological study, cytomegalic cells with inclusions in the vascular endothelium are found [6]. The pathogenic mechanism suggested that cytomegalovirus viremia could damage the endothelium or leaving it intact. Nevertheless, it affects the endothelium could progress to vasculitis, which results in infarction and ulceration [6].

This case of severe oral ulcers is presented because it is a rare and infrequent cutaneous manifestation of a viral infection in pediatric age, to date not described in children, both immunocompetent and immunosuppressed. At the same time, we report favorable responses to the treatment of the disease in children, both immunocompetent and immunosuppressed. A favorable response to treatment with Ganciclovir is also reported.

Conclusion

Oral ulcers caused by Cytomegalovirus infection, even in a pediatric patient with immunosuppression, are unusual and probably due to hematogenous dissemination of the virus. So the diagnostic of ulcer etiology could be a challenge and we need to correlate clinical, serological, immunopathological and genetic data. The treatment for severe cases is the use of Ganciclovir, as it was administered in our patient, showing clinical and laboratory improvement.

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