CASE REPORT

Report a possible correlation between necrotizing ulcerative gingivitis and mononucleosis

Reporte de una posible correlación entre la gingivitis ulceronecrotizante y la mononucleosis

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ABSTRACT

Necrotizing ulcerative gingivitis is a relatively uncommon periodontal disease, characterized by ulceration, necrosis, pain and gingival bleeding. Factors often related to its occurrence include stress and systemic viral infections, such as those caused by cytomegalovirus and Epstein-Barr virus type 1, the latter being also considered the causative agent of infectious mononucleosis. This article aims to describe a clinical case of a female patient who presented with necrotizing ulcerative gingivitis associated with a clinical picture of infectious mononucleosis, as well as to review the literature concerning a possible correlation between these pathologies. This patient presented to our health care facility with necrotizing ulcerative gingivitis accompanied by lymphadenopathy, fever and prostration, after laboratory tests, Epstein-Barr virus type 1 infection was confirmed, as well as the co-occurrence of pathologies: necrotizing ulcerative gingivitis and infectious mononucleosis. Symptom remission in both disorders also occurred concomitantly, after instruction in plaque control measures and palliative medication for control of systemic symptoms. Therefore, although there is no scientific validation of an association between these two pathologies, it is imperative that all diagnostic alternatives be considered and investigated, in order to establish the therapeutic approach most appropriate to the patient.

Key words: gingivitis, necrotizing ulcerative, infectious mononucleosis, clinical pathology.

RESUMEN

La gingivitis ulcerativa necrótica es una enfermedad periodontal no común caracterizada por ulceración, necrosis, dolor y sangrado gingival. Los factores a menudo relacionados con su ocurrencia incluyen el estrés y las infecciones virales sistémicas como aquellas causadas por *Cytomegalovirus* y el virus *Epstein-Barr* tipo 1, donde este último es el agente causal de la mononuclerosis infecciosa. El objetivo de este trabajo fue describir el caso clínico de una mujer con gingivitis ulcerativa necrótica asociada a un cuadro clínico de mononucleosis infecciosa, así como hacer una revisión de la literatura concerniente a una posible correlación entre estas enfermedades. Esta paciente se presentó con una gingivitis ulcerativa necrótica acompañada de linfadenopatía, fiebre y postración después de las pruebas de laboratorio, donde se confirmó una infección por *Epstein-Barr* tipo 1 así como la ocurrencia conjunta de gingivitis ulcerativa necrótica y mononucleosis infecciosa. También se produjo una remisión concomitante de los síntomas en ambos trastornos después de la instrucción en medidas para el control de placas y una medicación paliativa para el control de los síntomas sistémicos. Por lo tanto, aunque no existió una validación científica de una asociación entre estas dos entidades, es imperativo que se consideren e investiguen todas las alternativas diagnósticas para establecer el enfoque terapéutico más apropiado para el paciente.

Palabras clave: gingivitis ulcerativa necrótica, mononucleosis infecciosa, patología clínica.

INTRODUCTION

Necrotizing ulcerative gingivitis (NUG) is a relatively uncommon periodontal disease, characterized by ulceration, necrosis, pain and gingival bleeding.[1] Infection often occurs in the presence of emotional stress in young people. In addition to stress, other factors have been associated with the increased prevalence of NUG, such as smoking, gingival trauma, nutritional status, poor oral hygiene, high alcohol consumption and systemic viral infections, mainly by cytomegalovirus (CMV) and human immunodeficiency virus (HIV).[2]

Eight herpesvirus types have been identified and associated with oral lesions. Recent studies have reported the involvement of Epstein-Barr virus type 1 (EBV-1) and CMV in the of periodontal disease in humans.[3-7] *Saygun*[8] *and Sunde*[9] shows that periodontal human cytomegalovirus and Epstein-Barr virus are associated with major periodontopathic bacteria and with the severity of periodontal disease.

Infectious mononucleosis is a benign disease caused by EBV infection, being spread mostly by oral contact with exchange of saliva. The most common symptoms are high fever, discomfort, fatigue, and at times, mild hepatitis and lymphadenopathy. Infection is controlled within a few days, but the virus remains latent in some infected B lymphocytes throughout an individual's life course. Viral infection increases the multiplication rates of lymphocytes and reduces apoptotic activity, due to pro-growth and anti-apoptosis proteins of the virus genome. The result is a characteristic lymphocytosis increase in the number of lymphocytes easily detected during acute episodes of the disease.[10] This article aims to describe a clinical case of a female patient who presented with NUG associated with a clinical picture of infectious mononucleosis, as well as to review the literature concerning a possible correlation between these pathologies.

CLINICAL CASE

R.N.S. a 10 year old girl, referred to the oral pathology service of Universidade Federal do Rio Grande do Sul by her dentist, presented with approximately 10 days of prostration, ulceration of the oral mucosa and generalized gingivitis. The child had a history of recurrent anemia, treated by diet control and tonsillitis about one month previously, with use of amoxicillin 500 mg for 10 days. The patient had a chief complaint of swollen gums, itching and edematous swelling of the lips and face, accompanied by fever and prostration. Prior treatment included use of paracetamol, application of hexamidine (hexomedine® spray) to oral lesions and mouth rinses with mallow tea, following her dentist's recommendations.

Physical examination revealed bleeding, reddened, ulcerated plaque-like lesions, extending lengthwise along the gingiva, both in the upper and lower gums. There was excessive biofilm accumulation on tooth surfaces, presence of aphthous lesions extending along the gingiva and palate, lips were dry and the tongue was coated (Fig. 1). There was evidence of submandibular, cervical, axillary and inguinal lymphadenopathy on palpation.

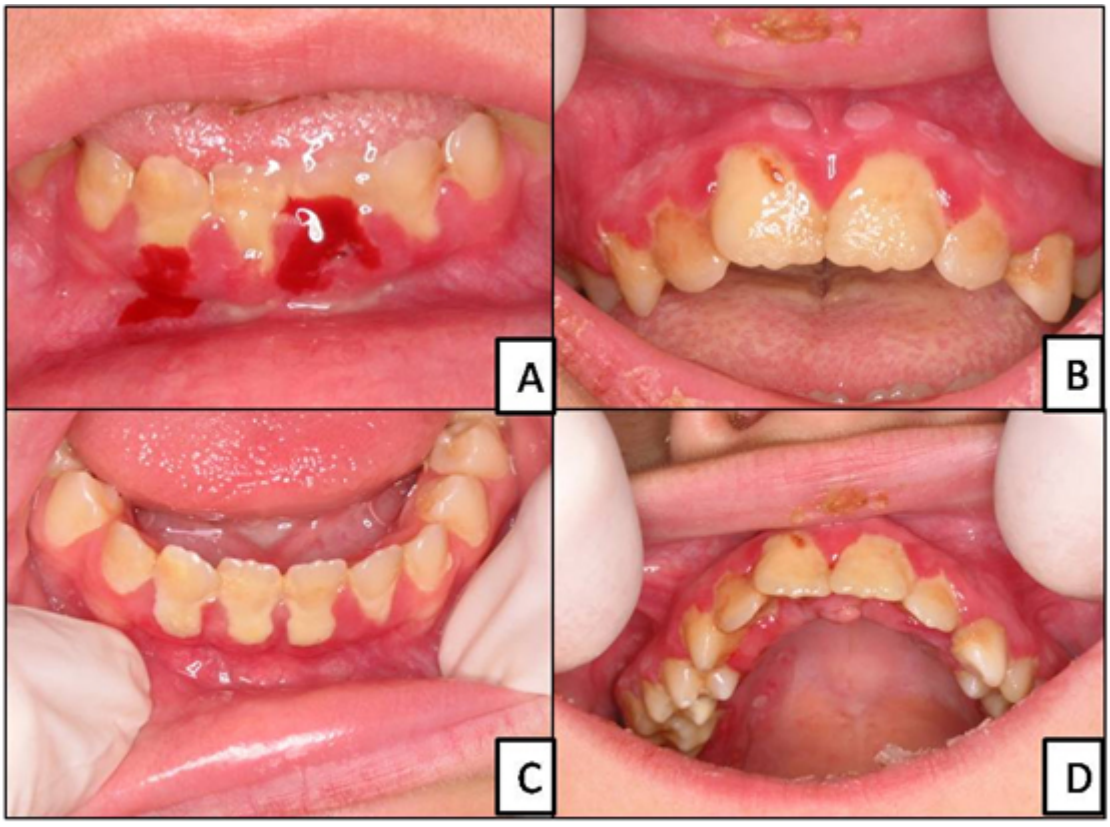

Fig. 1. A. Edematous, reddened and bleeding lower gum. **B.** Presence of aphthae, dry lips and tongue coated. **C.** Excessive plaque accumulation on tooth surfaces and plaque-like lesions on the marginal gingiva. **D.** Presence of aphthous lesions extending along the gingiva and palate. Dry lips.

The patient received a clinical diagnosis of NUG, was prescribed metronidazole 250 mg at 8-hour intervals for 7 days and a lip moisturizer and was then referred to a pediatrician. A complete blood count was requested, including platelet count, fasting glucose levels, anti-HIV and anti-EBV testing, erythrocyte sedimentation rate (ESR) test and the monospot test. The return appointment was scheduled one week later.

At the second appointment, the patient showed symptom resolution and improvement in clinical status. Although the erythema and edema decreased, the patient still had some difficulty in maintaining proper oral hygiene. Dental plaque was removed and the patient received further oral hygiene instructions.

Ten days later, the patient returned with the results of the requested tests. The anti-EBV test showed IgG and IgM reagents, suggesting infectious mononucleosis. Periodontal health had improved and the patient was able to maintain adequate oral hygiene and return to a normal diet (Fig. 2).

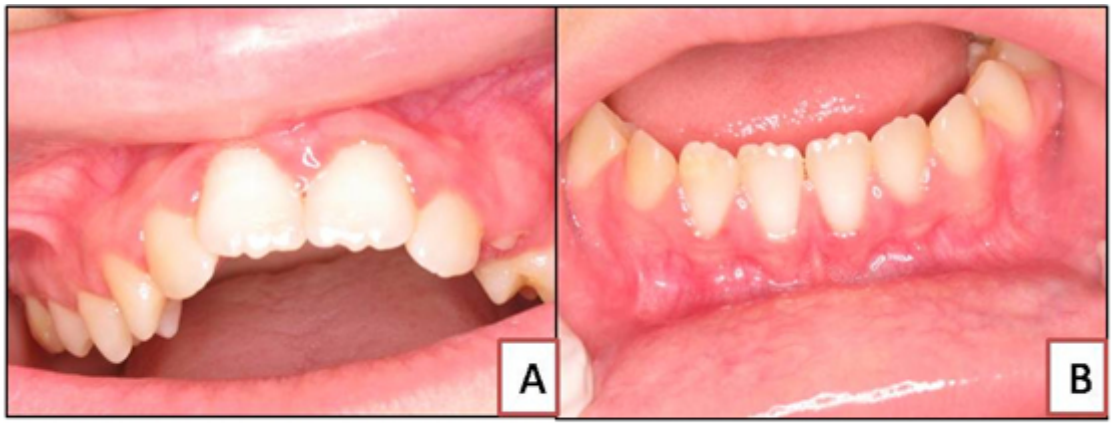

Fig. 2. A. Gingiva and lower lip mucosa in good health. **B.** Absence of biofilm accumulation and clinically healthy gingiva.

DISCUSSION

This article report the case of a patient who presented with two concomitant disorders: mononucleosis and NUG. The fundamental question underlying this case is the possible association between these two pathologies and a possible co-occurrence of the same etiologic agent.

The first case report that attempted to show a correlation between NUG and mononucleosis was described by *Cassingham and others*.[11] In that study, the authors evaluated the possibility that the signs and symptoms of NUG may be part of infectious mononucleosis. For this purpose, they conducted a study with 33 patients with a diagnosis of NUG, who underwent examination of cervical lymph nodes, body temperature, petechiae on the palate and pharyngeal ulceration, in addition to blood and serologic tests. At the end of the study, none of the patients was diagnosed with mononucleosis, leading the authors to conclude that both pathologies show similar signs and symptoms, but with no correlation between both conditions. Thus, their co-occurrence in the same patient is likely to be the result of a similarity of predisposing factors.

However, no other articles approaching these conditions together could be found in the literature. A literature search returned only speculations on the herpesvirus family as a potential etiologic factor in periodontal diseases.[3,12] Viruses of the herpesvirus family are characterized by a capacity to actively infect target cells, remaining latent in the body throughout the host's life course. Among the six main species of human herpesvirus, was find cytomegalovirus and Epstein-Barr virus, both being associated with infectious mononucleosis.[12]

It is well known that herpesviruses are opportunistic viruses, which typically occur in immunosuppressed patients. Immunosuppressive situations may result from emotional stress, trauma, immunosuppressive therapy or even from pathologies that render the patient immunodeficient.

Sabiston Jr[13] proposed a possible viral etiology of NUG, pointing out that symptoms such as fatigue, depression, lymphadenopathy, myalgia, fever, among others, occur in both NUG patients and cases of CMV and EBV infection. *Contreras and Slots*[3] reviewed the literature aiming to describe an association between herpesvirus and periodontal disease and to discuss the possible mechanism by which herpesviruses may contribute to periodontal disease. According to the authors, herpesviruses may exert their periodontopathogenic potential by five distinct mechanisms, acting alone or in combination. *Botero, Contreras and Parra*[14] concluded that altered expression of mRNA for collagens and metalloproteinases in human cytomegalovirus-infected gingival fibroblasts should be considered as possible modifying mechanisms in periodontitis-infected sites.

According to *Porter*,[15] several DNA virus infections can give rise to periodontal manifestations, which might vary in severity and be accompanied or not by other systemic or oral manifestations. Some of these infections occur preferably in susceptible patients, such as immunosuppressed patients. These viruses include EBV, which is associated with infectious mononucleosis and whose symptoms include gingival ulceration and pericoronitis and CMV, which has been related to reports of NUG.

Based on evidence from the literature, the true relationship between NUG and mononucleosis remains unclear, but it was able to state that both disorders affect the same group of patients, with possible concomitant clinical manifestations, showing direct or indirect viral etiology.

In conclusion both mononucleosis and NUG are opportunistic diseases that affect immunocompromised patients. There is solid evidence for the biological plausibility of a correlation between both disorders. In the present article, was described the co-occurrence of both diseases in a patient, whose symptom resolution also occurred concomitantly in both pathologies. However, since mononucleosis has a short-term clinical course, the physician might not routinely investigate possible viral etiologic factors that could validate this diagnosis. Therefore, in order to make an accurate diagnosis and establish an effective therapeutic approach was needed to investigate in depth the etiology of the diseases and a possible interaction between several signs and symptoms presented by the patient.

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