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Case Report

Feline chronic gingivostomatitis in a Persian cat

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ABSTRACT

A 4-year-old castrated male Persian cat with three years history of inflammatory and ulcerative lesions in the gingiva and periodontal areas of the right up jaw was referred to a veterinary clinic in Isfahan city of Iran. The clinical signs included gingival ulceration, oral pain, inappetence, ptyalism, halitosis, and chronic loss of weight. The condition was diagnosed clinically as Feline Chronic Gingivostomatitis. Feline Chronic Gingivostomatitis is an immune-mediated inflammatory condition and a painful, debilitating disease of cats. For confirmation of diagnosis, the lesions were sampled for histopathologic examination. Histopathologic examination revealed a chronic inflammatory reaction with infiltration of plasma cells and Lymphocytes predominantly and variable numbers of neutrophils and macrophages. The presence of immune cells in the lesions was followed up by immunohistochemistry for CD3, CD79a, and IgG. The most dominant cells in the lesions were $CD79a^+$ and IgG^+ plasma cells. The $CD3^+$ cells incidence concerning the severity of the lesion was high as well.

تورم لثه و دهان مزمن گربه ای در یک گربه پرشین

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چکیده

یک گربه پرشین نر اخته چهار ساله با تاریخچه ۳ سال ضایعات التهابی و اولسراتیو در لثه و نواحی اطراف دندانی در سمت راست فک بالا به یک کلینیک دامپزشکی در شهر اصفهان ارجاع داده شد. نشانه های بالینی شامل زخم لثه، درد دهانی، بی اشتهایی، ریزش بزاق، بوی بد دهان و کاهش وزن مزمن بودند. بیماری از نظر بالینی تورم لثه و دهان مزمن گربه ای تشخیص داده شد. تورم لثه و دهان مزمن گربه ای یک بیماری التهابی با واسطه ایمنی، دردناک و تحلیل برنده گربه ها است. برای تأئید تشخیص، از ضایعات برای بررسی هیستوپاتولوژیک نمونه گیری گردید. بررسی هیستوپاتولوژیک یک واکنش التهابی مزمن با نفوذ پلاسماسل ها و لنفوسیت ها بطور غالب و تعداد متغییری از نوتروفیل ها و ماکروفاژها را آشکار نمود. حضور سلول های ایمنی در ضایعات بوسیله ایمونوهیستوشیمی برای CD3، CD79a و IgG دنبال شد. بیشترین سلول ها در ضایعات پلاسماسل های $CD79a^+$ و IgG^+ بودند. رخداد سلول های $CD3^+$ با توجه به شدت ضایعات نیز، بالا بود. این گزارش نخستین گزارش مستند از یک گربه مبتلا به تورم لثه و دهان مزمن گربه ای در ایران است.

واژه های کلیدی: تورم دهان و لثه، هیستوپاتولوژی، ایمونوهیستوشیمی، گربه

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INTRODUCTION

Feline Chronic Gingivostomatitis (FCGS) is an immune-mediated inflammatory condition and a painful, debilitating disease of cats, which is characterized by severe inflammatory, ulcerative and proliferative lesions typically affecting gingival and non-gingival mucosa such as buccal and glossoplatine mucosa lasting for months and years [1, 2, 3]. The etiopathogenesis of disease is not well understood but it has been proposed that viral and bacterial antigens and modifications in the innate immune response may play important role in the pathogenesis of the disease [3]. The prevalence rate of the condition is estimated 0.7% to 12.0% among cats [4]. Thirty percent of affected cats are refractory to the current treatment procedures [1]. FCGS is considered an animal model for researching the immune-based oral mucosal inflammatory diseases of human beings [5]. Therapeutic methods for FCGS condition generally categorized as medical treatment (including traditional immunosuppression by corticosteroids or cyclosporine) and surgical treatment involves the extraction of premolar and molar teeth or full dentition [4, 5]. Approximately 70% of cats with FCGS responded to the present standard treatment which is full or near-full tooth extraction and about 30% of affected cats did not respond to the tooth extraction which is called refractory FCGS [5].

CASE PRESENTATION

A 4-year-old castrated male Persian cat weighing 2.5 kg and a 3-year history of oral pain, inflammatory and ulcerative lesions in the large part of the gingiva and periodontal areas of right up jaw (Figure 1) was referred to a veterinary clinic in Isfahan city, Iran. The client reported inappetence, anorexia, ptyalism, halitosis, and chronic loss of weight on referral. Based on the clinical signs, a working diagnosis of feline chronic gingivostomatitis (FCGS) but for confirmation of diagnosis was made. To confirm the diagnosis, the samples were taken from the affected area under general anesthesia for histopathologic examination. Unfortunately, failure to respond to standard and supportive treatment including extraction of teeth in the affected area in this case eventually led to euthanasia of the animal.

Histopathology and Immunohistochemistry evaluation

Tissue samples of the oral lesions were fixed in 10% buffered formalin and embedded in paraffin. Tissue sections were cut at 5 μm and stained with H&E (Harris hematoxylin and Eosin Y; Fisher Scientific, Pittsburg, PA) to characterize the inflammatory cells. Immunohistochemistry (IHC) was performed on formalin-fixed sections of the affected tissues using a panel of antibodies to CD3 (Mouse anti-human CD3 monoclonal antibody, Biocare Medical, Pacheco, CA, USA) and, CD79a (Mouse anti-human CD79a monoclonal antibody, Abcore, Ramona, CA, USA) [3]. For immunohistochemical examination, unstained sections were stained with immunohistochemical markers for CD3 and CD79a. All samples were sectioned at 4μm and processed for IHC labeling. In brief, for CD3 and Cd79a, the slides were deparaffinized and underwent antigen retrieval, endogenous peroxidase blocking, and power block. Next, they were incubated with the primary anti- CD3 and anti-CD79a antibodies. This incubation was followed by an incubation with the respective secondary antibodies: biotinylated anti- mouse & rabbit

for CD3 and CD79a (PolyVue plus Enhance (DBS), Ca, USA). Then they were incubated with streptavidin and horseradish peroxidase, followed by chromogen development using 3, 30-diaminobenzidine (DAB) and hematoxylin counterstaining. The IHC slides were evaluated by using light microscopy for the determination of immunophenotyping and the distribution of cells positive for CD3, and CD79a. Histologic examination of the oral

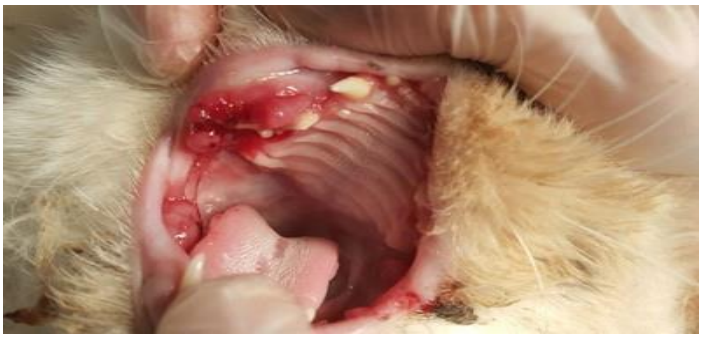

Figure 1. A Persian cat with inflammatory and ulcerative lesions in the gingiva and periodontal areas of the right up jaw.

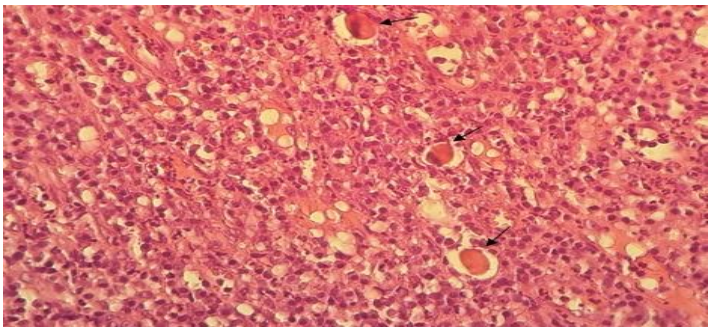

Figure 2. In the histopathologic examination, a mixed population of inflammatory cells were observed but plasma cells and lymphocytes were the dominant cells. Also, numerous Mott cells were observed containing immunoglobulin aggregates called Russell Bodies (arrows) (H&E, 400×).

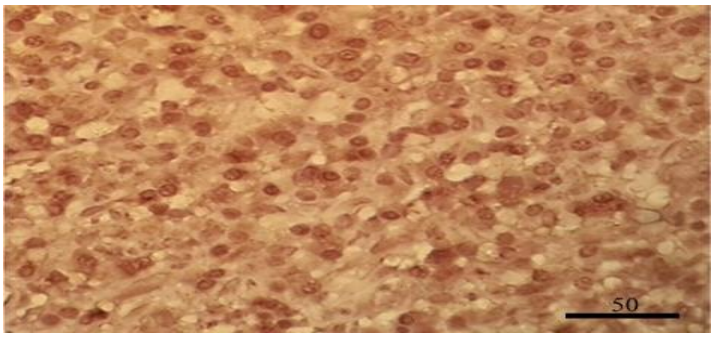

Figure 3. CD3. Some of the cells in the lesions were $CD3^+$ T-lymphocytes, which were scattered in the different parts of the lesion. IHC. Bar= 50 µm.

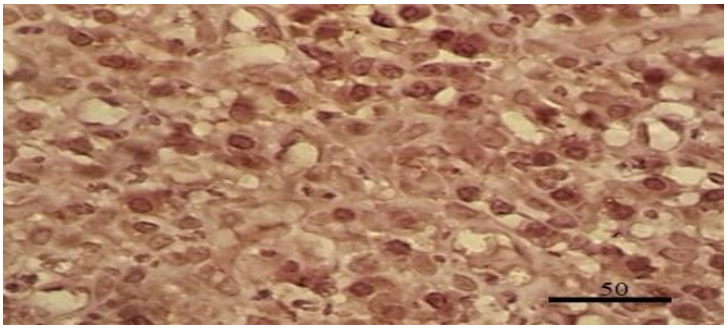

Figure 4. CD79a. A large number of the cells in the lesion were plasma cells containing intracytoplasmic CD79a protein. IHC. Bar= 50 µm.

tissues revealed a chronic inflammatory reaction with dominated infiltration of plasma cells and lymphocytes in the lamina propria and submucosa. Plasma cells occasionally contained Russell bodies (Mott cells). There were also a few neutrophils and macrophages scattered among plasma cells (Fig 2). On IHC, the inflammatory cells were positive for CD3 and CD79a (Figures 3 and 4). Based on the histopathological and IHC findings, the diagnosis of FCGS was made.

DISCUSSION

Feline chronic gingivostomatitis (FCGS) or feline chronic lymphocytic plasmacytic stomatitis/ gingivitis is a debilitating disease in cats. This condition is characterized by severe painful ulcerative and proliferative lesions in oral mucosal including gingival and non-gingival tissues, and palatoglossal arch which lasts months to years and is sometimes refractory to treatment [2]. It is estimated that FCGS affects 0.7% - 12% of the cat population [4]. Clinical signs include oral pain, inappetence, anorexia, weight loss, ptyalism, halitosis, and reduced grooming [6]. Several studies have revealed multifactorial etiology of FCGS, such as infection with *feline immunodeficiency virus (FIV), feline leukemia virus (FeLV), feline calicivirus (FCV), feline herpesvirus 1 (FHV-1), coronavirus*, *Haemobartonella henselae*, *Bergeyella zoohelcum*, dental diseases, breed predisposition, environmental stress, hypersensitivity to plaque bacteria and food allergies [7,8]. However, the role importance of these factors in the etiopathogenesis of FCGS is obscure [3]. The pathogenesis of FCGS is poorly understood but it is accepted that the disease results from an inappropriate response of the immune system to chronic oral antigenic stimulation [9]. There is a weak relationship between some of the infectious agents such as *FCV, FHV-1, FeLV, FIV, Bartonella* species, and FCGS, because these agents not only have been isolated from FCGS-affected cats but also healthy animals [10]. However, an immunologic basis for FCGS was suggested by altered cytokine profiles in the mucosal lesions [11]. As an immune-mediated inflammatory condition, it has been shown that oral mucosal tissues from cats with FCGS have high tissue infiltration of B cells and that T cells include both CD4+ and CD8+ lymphocytes [12]. The diagnosis of FCGS is typically based on clinical signs and histopathological examination of oral lesions, which represents an infiltration of plasma cells and lymphocytes in the mucosa and submucosa [10]. In the histopathologic examination of the lesions in our case, many Mott cells were observed. Mott cells are abnormal plasma cells containing immunoglobulin aggregates termed Russell bodies, which are found in some forms of myeloma, inflammatory diseases, and autoimmune disorders [13]. The histopathologic changes in the lesions of FCGS-affected cats show a chronic inflammatory response that is demonstrated by infiltration of plasma cells, lymphocytes, mast cells, and variable numbers of macrophages and granulocytes [14, 15]. Investigations to characterize the phenotype of immune cells in the lesions of FCGS-affected cats have been rarely performed [16]. In our case, we employed three major markers including CD3, CD79a, and IgG. In our case, the most population of cells in the lesions were $CD79a^+$ plasma cells. It has been shown that IgG^+ or $CD79a^+$ plasma cells are prominent in severe lesions of FCGS-affected cats [3]. CD3 as a T-cell lineage marker was another marker, which followed in the case. $CD3^+$ T-cells population in our case was fewer in comparison with IgG^+ and $CD79a^+$ plasma cells population in the

lesions. A large population of $CD3^+$ T-cells infiltration was reported in the lamina propria of the lesions from cases with FCGS [3]. This infiltration is also important in the immunopathogenesis of the disease [14]. The response to FCV-derived antigens may have a significant role in the formation of the T-cell population in the mucosal lesions of FCGS-affected cats [17]. The FCGS is a useful animal model of refractory oral mucosal inflammatory diseases in human beings and the effector T and B cells have a consistent tissue involvement in these diseases [6]. Therefore, more investigations are needed to determine precise phenotype cell population in these lesions. to the best of researchers' knowledge, this is the first report of FCGS in a Persian cat in Iran. Histopathologic examination of the affected tissues in a combination of the clinical signs is important for the diagnosis of FCGS. Though this condition has been previously reported in cats but a panel of markers, using IHC has been rarely employed to confirm the diagnosis. CD3 as a T-cell lineage marker and CD79a as a plasma cell lineage marker are significant in the demonstration of immune cell presence in the feline gingival lesions with immune-based pathogenesis. This report shows CD3, CD79a, and IgG as useful markers in severe FCGS cases. Because feline chronic gingivostomatitis in cats could be used as an animal model of refractory oral mucosal inflammatory diseases in humans; therefore, the results of this study can help to characterize possible pathogenesis and precise phenotype cell populations involved in these lesions.

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ETHICS

Approved.

CONFLICT OF INTEREST

None declared.

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