CASE REPORT

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A RARE CASE OF PYODERMA GANGRENOSUM WITH COMPLETE SOFT PALATE DESTRUCTION

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Abstract

We present the case of a 24 year old male who was admitted to Sf. Maria Clinical Hospital's Internal Medicine and Rheumatology Department having an impressive soft palate destruction and necrotic ulcers of the posterior oropharynx wall and left palatine tonsil, as well as a gigantic skin ulcer on the left calf. His disease started in 2010, at age 17, with an apfhtous ulceration on his left tonsil and evolved with multiple ulcerations: firstly, in the oral cavity and in time, on skin (face, vermillion, scalp, upper and lower limbs) with bacterial colonisation, and also aseptic arthritis of his both knees. Throughout the past 7 years he was evaluated in many departments and clinics and several diagnoses were raised into question, such as amigdalitis, tonsil tumour, lymphoma, Wegener's disease, Pyoderma Gangrenosum, PAPA, incomplete SAPHO, Crohn's disease, Behcet's disease. Despite the fact that he received multiple therapies, including cDMARDs and bDMARDs, the mucosal and skin lesions had a good response only to corticosteroid treatment and flaired up at the attempt of stoping it.

Keywords: soft palate destruction, skin ulcer, Pyoderma gangrenosum

INTRODUCTION

Pyoderma gangrenosum is a skin condition of a not fully understood origin manifested as a sterile neutrophilic infiltrate. It is often associated with systemic diseases in more that 50% of cases (1,2) and is diagnosed by excluding other conditions that could cause similar skin lesions, such as vasculites, infections, malignancy and trauma, due to lack of histopathological and laboratory diagnostic criteria (3). It is commonly characterised by pathergy, meaning that any minor trauma or injury can cause a new ulceration. The clinical presentation of the disease can take several forms, the most common one being the classic Pyoderma gangrenosum, manifested with a deep, painful ulceration, most frequently on the lower limbs that can leave a scar. Besides the skin involvement, Pyoderma gangrenosum can affect other organ systems, like the lungs, this site being the most common extracutaneous manifestation (4) and also the heart, the central nervous system, the gastrointestinal tract, the eyes (5,6), the liver, the spleen, the bones and the lymph nodes. The treatment for Pyoderma gangrenosum includes topical and systemic cortosteroids (7), immunosuppressives like cyclosporine (8,9,10), mycophenolate mofetil (11-13), azathioprine (14), dapsone, tacrolimus, cyclophosphamide, chlorambucil (15), thalidomide and also TNF-alpha inhibitors, such as infliximab, adalimumab and etanercept (16).

CASE PRESENTATION

We present the case of a 24 year old male who was admitted to Sf. Maria Clinical Hospital's Internal Medicine and Rheumatology Department for an impressive soft palate destruction and necrotic ulcers of the posterior oropharynx wall and left palatine tonsil causing mild sore throat and dysphagia, as well as a gigantic skin ulcer on the left calf in course of healing and multiple scars on the lips, cheeks, scalp, both upper and lower limbs.

His disease started at the age of 17 years old, in 2010, with an aphtous ulceration on the left tonsil

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that extended progressively through a 7 year period and evolved with tissue necrosis leading to complete destruction of the soft palate and ulcero-necrotic lesions of the posterior oropharynx wall and tonsils. The lesion was first interpreted as acute amigdalitis and treated with antibiotics. After trying different antibiotic schemes with no improvement whatsoever, the patient was exhaustivelyinvestigated in several departments and clinics. There were performed tests for various infections, with negative results (HIV, CMV, EBV, HSV, HBV, HCV, TPHA, Toxoplasmosis); tests for autoimmune diseases, with an emphasis on Wegener's disease, all negative (p-ANCA, c-ANCA, ANA, AMA, ASMA) and also several histopathological analyses of a spontaneously detached tonsil fragment were performed, but with no specific result (no granulomatous inflammation foci, nor suggestive elements for lymphoma). Thus, there were exluded infectious, autoimmune and malignan t diseases. Throughout this period of time, the patient received antibiotic and antifungal treatment and decreasing doses of corticosteroids with good response to high and medium doses. One year and 3 months after the onset of the disease, while being corticosteroid free, the oral lesions got worse and also the first skin lesions appeared on the right upper limb, at first as a papulo-pustular lesion and then evolving to a painful skin ulcer. The pacient was then referred to a foreign clinic where more specific tests for Wegener's disease unavailable in our country were done (NBT – nitroblue tetrazolium, DHR – dihydrorhodamine) and came out negative. There were also performed immunity investigations that revealed low IgG and IgA and also slightly low naive T cells and B cells. While Wegener's disease being excluded, the suspicion of Behcet's disease was raised although the HLA B51 gene was absent.

Three months later, after the skin and oral lesions got worse, by raising in number and extension, the patient was readmitted to the same clinic; a skin lesion biopsy was performed and the histopathological findings showed necrotizing inflammation and rich neutrophil and granulocite infiltrate. A colonoscopy was also performed and showed ulcerative lesions in the terminal ileum and colon but with histological unspecific inflammation. Thus, the diagnoses of Pyoderma gangrenosum and Crohn's disease were put into question and the patient received corticosteroids and biological treatment with infliximab (after excluding viral, bacterial infections once again). After returning home, he also received IVIg therapy and a 2 year remission period followed (no new lesions, no sore throat, no dysphagia). After this 2 year period the patient developed aseptic femoral head necrosis and stopped the corticotherapy, thereby, the lesions worsened, got infected, and he was forced to also stop the biological treatment. From this point the disease only got worse, the patient also developing aseptic knee arthritis, and multiple other lesions on the scalp, cheeks, lips, upper and lower limbs. During the course of the disease, multiple immunosuppressive therapy schemes were tried but without success (metothrexate, cyclosporine, azathioprine, sulfasalazine, anakinra) and 2 other biological molecules that caused exacerbation of the disease (etanercept, adalimumab). The only therapy that controlled the disease so far was the corticotherapy and maybe, the IVIg therapy. In 2017 he was admitted to another foreign clinic with an impressive necrotising lesion on the left calf that affected all the skin layers, the fascia and partially the muscles, reaching to the tendons, as well as soft palate destruction with necrotic ulcers of the oropharynx. During hospitalization he received antibiotic and antifugal therapy, high dose corticotherapy, biological treatment with infliximab and appropriate care of the wounds. Another superior and inferior digestive endoscopy were performed but didn't find any Crohn's specific le-

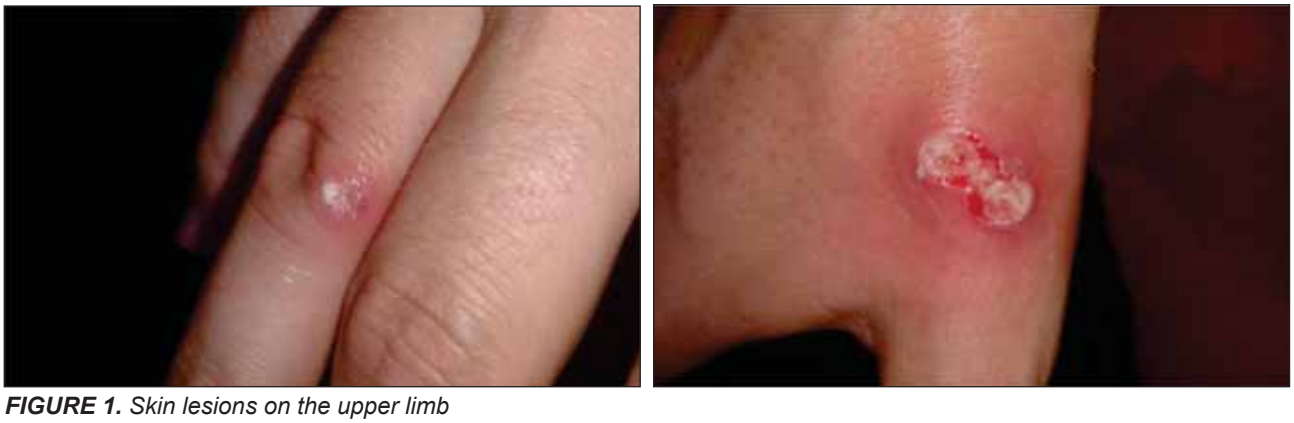

FIGURE 1. *Skin lesions on the upper limb*

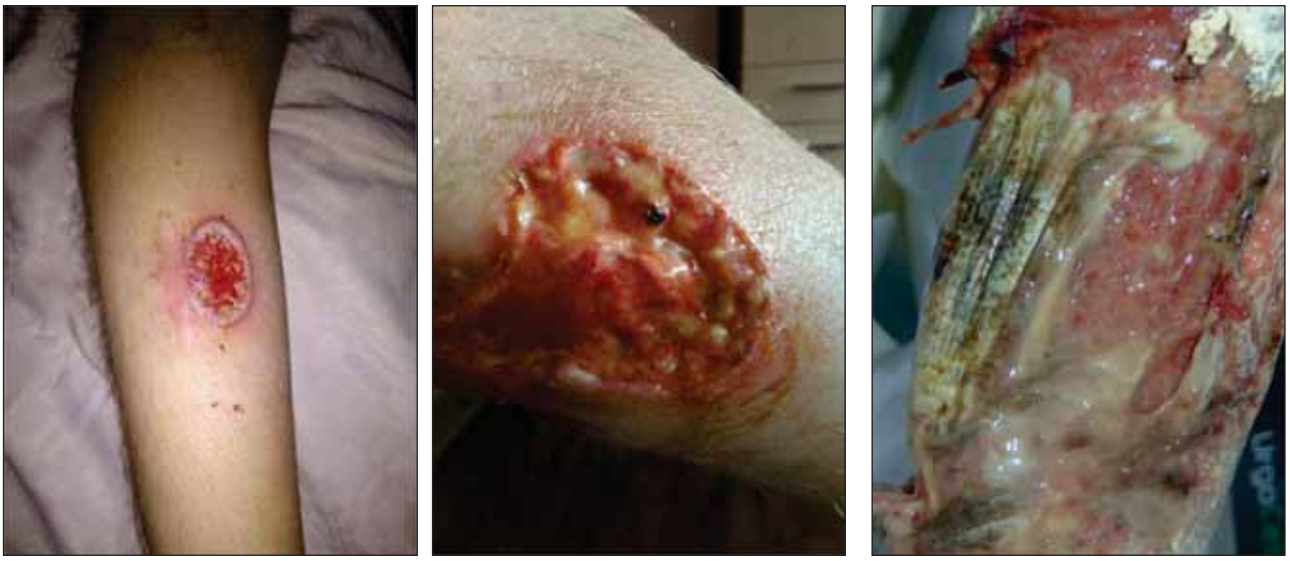

FIGURE 2. *The evolution of the left calf skin lesion during a 4 month period*

sions; therefore a genetic test for Crohn's was performed and came out negative. He was diagnosed with Behcet's disease due to having enough clinical elements in favour of (positive pathergy test, recurrent oral ulcers, one genital ulcer, papulo-pustular skin lesions, post catheter jugular vein thrombosis) and was let out with a decreasing dose of prednisolone.

One month before admitting to our department, the patient restarted taking high dose corticotherapy because of a new episode of oral ulcers, important biological inflammatory syndrome, high leukocytosis and neutrophilia.

At presentation in Sf. Maria Clinical Hospital's Internal Medicine and Rheumatology Department, the patient had an impressive soft palate destruction and necrotic ulcers of the posterior oropharynx wall and left palatine tonsil, with mild dysphagia and sore throat, as well as a gigantic skin ulcer on the left calf in course of healing and multiple scars on the lips, cheeks, scalp, both upper and lower limbs. The blood analyses showed no sign of inflammation and the cultures taken from the oral and skin lesion were sterile. The biopsy taken from the oral ulcer revealed the presence of a dense, perivascular inflammatory infiltrate rich in polymorphonuclear cells and a zone of ulcered scuamous epitelium bordered by a chronic lympho-plasmocytic infiltrate.

DISCUSSIONS

Given this impressive clinical presentation and disease history, we were confronted by the difficult situation of making a differential diagnosis and reaching to the correct positive one. The main two diagnoses standing up of all those raised into question through all the 7 years of exhaustive investigations were Behcet disease and Pyoderma gangrenosum.

The elements in favour for Behcet disease were the recurrent oral aphtous ulcers, the skin lesions that firstly occured as pustules, one genital ulcer-

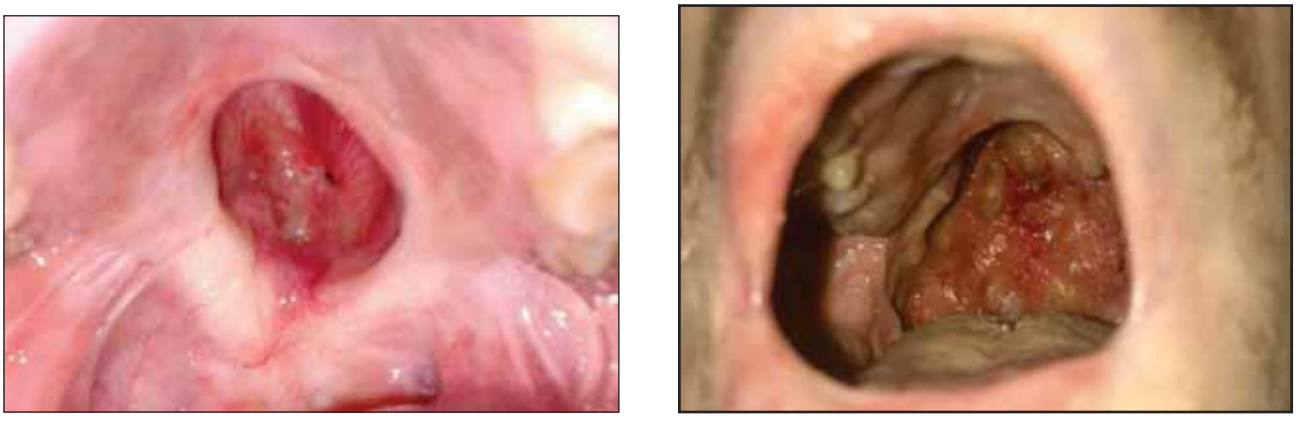

FIGURE 3. *Evolution of the oral ulcers with complete soft palate destruction*

ative lesion, the presence of pathergy, the knee aseptic arthritis, knowing that this extraoral involvement occurs in almost 60% of cases, the gastrointestinal involvement (ileum and colon lesions present at one point in the evolution of the disease) known to occur in 3 to 16% of patients with Behcet disease (17). On the other hand, our patient had no history of eye involvement, was HLA B51 antigen free and the important tissue damage of the lesions was untypical for Behcet disease. There were no cases of such impressive oral tissue destruction in patients with Behcet's mentioned in the specialty literature.

This type of agressive evolution with extended tissue damage is more typical for Pyoderma gangrenosum. Even though our patient's first lesions occured in the oral sphere and it took one year and 3 months for the skin lesions to appear, the histopathologycal findings of the oral lesions and going through the specialty literature for cases alike helped us solve the puzzle. It is known that besides the skin involvement, Pyoderma gangrenosum can affect other organ systems, like the lungs, the heart, the central nervous system, the gastrointestinal tract, the eyes (5,6), the liver, the spleen, the bones and the lymph nodes. Although the oral lesions aren't mentioned as one of the extracutaneous involvements in Pyoderma gangrenosum, there are a few case reports and a meta analysis of oral lesions in patients dignosed with with this disease.

A systematic review published by Caroline Bissonnette, Adel Kauzman and Gisele N. Mainville in Head Neck Pathol. Dec. 2017 showed important features as well as clinical and epidemiological data from 20 cases of intraoral Pyoderma gangrenosum. This article revealed that men were affected more frequently than women (13 cases out of 20); in 4 cases out of 20 (20%) the oral lesions occured in absence of concomitant cutaneous involvement; the most frequently affected sites were the tongue, bucal mucosa and soft palate (23 out of 34 reported oral lesions); the lesions had a rapid onset and evolution causing pain, dysphagia, sore throat and difficulty in movement. It also reported that biopsies often showed extensive ulceration bordered by an overlying fibrinopurulent membrane with heavy neutrophilic infiltration or mixed inflammatory cell infiltrate comprised of polymorphonuclear neutrophils, lymphocytes, histiocytes and plasma cells and also granulation tissue in cases of chornic inflammation (18).

CONCLUSIONS

Pyoderma gangrenosum is a rare skin condition characterised by the presence of a sterile neutrophilic infiltrate. Because of lack of laboratory and histopathologycal, the diagnosis is established by clinical features and by excluding other diseases that can cause similar lesions such as vasculitis, infections, malignancy and trauma. Although it is often associated with an underlying systemic illness in more that 50% of cases (1,2), Pyoderma gangrenosum can be a lone standing disease. Besides affecting other organ systems, like the lungs, the heart, the central nervous system, the gastrointestinal tract, the eyes (5,6), the liver, the spleen, the bones and the lymph nodes, we learned that it can also affect the oral mucosa in very rare cases. That is why it is important to think of Pyoderma gangrenosum as a possible diagnosis in a patient with recurrent, agressive oral ulcers, especially in one with an underlying systemic disease and associated skin ulcers.

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