

## PYODERMA GANGRENOSUM IN A PATIENT WITH PRIMARY SJÖGREN'S SYNDROME – CASE REPORT

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**Abstract:** *We will present the case study of a 61 years old Caucasian female patient who required a dermatological consult for two well defined painful ulcerations on her right leg, with overhanging borders, a geographical erythematous-purplish outline and a surface covered with adherent necrotic deposits. Ten years prior she was diagnosed with Sjögren's syndrome. After skin biopsy, pyoderma gangrenosum diagnostic was established, a rare finding in a Sjögren's syndrome patient. Systemic corticotherapy and chemical debridement of the lesions proved a successful treatment method.*

**Key words:** *Sjögren's syndrome, skin ulcers, pyoderma gangrenosum.*

### 1. Introduction

The inflammation of the exocrine glands (lacrimar, salivary, sweat), autoimmune mediated, gives rise to the clinical manifestations that define the Sjögren's syndrome, described in 1933 by the one it was named after [1]. It is more common in women (F/M=9/1) between 40-60 years old [6], [5]. It is characterised by a cyclic polymorphism, especially xerostomia and dry keratoconjunctivitis [6]. The secondary Sjögren's syndrome presents with an associated connective tissue disease [6]. The diagnosis is sustained by clinical signs and the presence of anti-Ro/SSA

antibodies. The histopathological modifications of the exocrine glands shows a lymphoplasmacytic infiltrate, collagen fibers proliferation and fibrosis, glandular tissue atrophy [6], [18].

We emphasize that a histopathological examination without the diagnostic elements does not exclude the presence of the disease [5], [18].

The cutaneous manifestations are found in 50% of the patients and are represented by: xeroderma (the most common manifestation), vitiligo, angular cheilitis, amyloidosis, alopecia areata or diffuse alopecia, Sweet's syndrome, Behcet's syndrome, dermatitis herpetiformis,

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sarcoidosis, Darier's disease, cutaneous vasculitides, pyoderma gangrenosum and pyoderma gangrenosum-like ulcerations [6]. Cutaneous vasculitides appear in 16% of the Sjögren's syndrome patients. Among those, 95% present damage of the small caliber vessels (leukocytoclastic vasculitis). In only 5% of the cases the damage occurs in the medium caliber vessels (necrotizing vasculitis) [22]. The medium caliber vessels damage is clinically translated as livedo reticularis, retiform purpura, ulcerations, subcutaneous nodules, digital necrosis. The entity in which medium caliber vessels damage is found is represented by panarteritis nodosa. In cryoglobulinemic vasculitis, Wegener's granulomatosis and certain secondary vasculitides (infections, neoplasms, connective tissue disease) there is damage of the small and medium caliber vessels [3].

## 2. Clinical case

We present the case of a 61 years old female patient, caucasian, who required a dermatological consultation for two intensely painful ulcerations on her right shin, one located to the internal supramalleolar area and the other to the lateral middle third of the shin. The lesions presented irregular, overhanging and erythematous-purplish borders and a surface covered with adherent necrotic deposits (Fig. 1 and 2). The lesions started three weeks prior as papulo-pustules that transformed into ulcerations with centrifugal expansion. The patient also presented xerophthalmia, xerostomia, cutaneous xerosis and right angular cheilitis.

From her personal medical history we noted that the patient was suffering from

Sjögren's syndrome, clinically, immunologically and histopathologically documented 10 years prior to this admission, the disease being therapeutically controlled with 20 mg/day Azathioprine and 5 mg/day Prednisone. The patient stopped the treatment 2 months prior to this admission. The laboratory tests revealed: anti-Ro and antinuclear positive antibodies, high ESR, LDH, CPK in normal limits, absent cryoglobulins. The bacteriological culture from the secretion of the ulcers was sterile. A cutaneous biopsy was performed from the overhanging border of one of the ulcerations. The haematoxylin and eosin stained histopathological examination presented a mixed inflammatory infiltrate, with the predominance of neutrophils. We established the diagnosis of pyoderma gangrenosum on the background of a primary Sjögren's syndrome. We administered systemic corticosteroids, pain relievers, topical corticosteroids and hydroactive dressings. The evolution was favourable, with stagnation of the expansion of the ulcerations, with a decrease in the necrotic deposits and the local pain, as well as a slight reduction in the size of the ulcerations.

## 3. Discussions

We considered the following clinical diagnosis: pyoderma gangrenosum, necrotizing vasculitis, panarteritis nodosa, pyoderma gangrenosum-like ulcerations.

Pyoderma gangrenosum (PG) represents a dermatosis with polymorphic clinical manifestations and overhanging erythematous-purplish borders. It has a fast expansion (a few weeks) and in most cases it develops from a papulo-pustule [3].



Fig.1. *Internal supramalleolar ulcer*



Fig.2. *Lateral middle shin ulcer*

The histopathological examination, that has to be from the border of the ulceration, is more often non-specific. In the onset lesions there is a neutrophilic or lymphocyte infiltrate, predominantly perifollicular. In the established ulceration there is spongiosis in the epidermis, mixed infiltrate (neutrophilic and lymphocyte) in the dermis and adipose tissue. To these it is often added focal vasculitis phenomena, but without the presence of fibrinoid necrosis, a key element in the histopathological diagnosis of a vasculitis [9]. The PG diagnosis is sustained on clinical signs and the histopathological examination that has a role in excluding a vasculitis. In the peri-ulcerative area the lymphocytes predominate giving the appearance of a lymphocytic vasculitis. The borders of the ulceration are characterised by a mixed infiltrate (neutrophilic and lymphocyte)

with predominance of the neutrophils. In the center of the ulceration the neutrophilic infiltrate is abundant with formation of abscesses [26]. In conclusion, the neutrophilic infiltrate decreases from the center of the ulceration to the peri-ulcerative area, as opposed to the lymphocytic infiltrate. This nonspecific histopathological aspect, different according to the analysed ulcerative area, led to the term of pyoderma gangrenosum-like, representing ulcerations with evocative clinical aspect, but with the histopathological equivalent of a poor neutrophilic infiltrate.

Ravic-Nikolic et al. described the first case of Sjögren's syndrome associated with pyoderma gangrenosum in 2009 [23]. Later on, in 2013 Yi-Hsuan Tsai described a new case [25]. In March 2014, ML Anderson described in a primary Sjögren's syndrome patient the appearance of some

painful ulcerations that he diagnosed as pyoderma gangrenosum [2].

The PG type lesions appeared 2 months after the cessation of the background Sjögren's syndrome therapy, which brings up the implications of the background therapy cessation as a contributing factor to the genesis of the PG type lesions in Sjögren's syndrome patients.

A particularity of the presented case is the unilateral localisation of the both ulcerations of the right leg.

Pyoderma gangrenosum-like (PG-like) ulcerations are cited as clinical manifestations especially in antiphospholipid syndrome [24], [12]. Other causes are represented by drugs (anticoagulants, sunitinib, hydralazine), chronic hepatitis C, mycosis fungoides [21], [1], [19], [15], [8].

Chams-Davatchi et al described the presence of pyoderma gangrenosum-like ulcerations in two patients with Behcet's syndrome, where the only effective therapy was cyclosporine [7]. Joshi and Mamta reported an effective treatment with dapsone for genital and oral ulcerations that during their evolution acquired the aspect of pyoderma gangrenosum in a patient with the same condition [13].

Namazi and Kerchner reported in 2008 the case of a female patient that presented painful PG-like ulcerations on her feet in association with type II cryoglobulins and no histopathological signs of vasculitis. [17]. Gail et al described in 2012 the case of a female patient with Sjögren's syndrome and rheumatoid arthritis that developed a painful ulceration on the right internal malleolus that clinically pleaded for pyoderma gangrenosum and histopathologically lacked the neutrophilic infiltrate [14].

Necrotizing vasculitis is characterised by segmental inflammation of the medium caliber vessels. A frequent clinical manifestation corresponding to this type

vessel damage is represented by the cutaneous ulceration. The substrate is represented by the deposition of immune complexes in the walls with attraction of neutrophils, these cells being responsible for the release of lysosomal enzymes that destroy the vascular tissue [26]. The location of choice for these lesions is the leg and the involvement is usually symmetrical. We can find tangible purpuric lesions that ulcerate, leaving behind atrophic scars. These lesions can be accompanied by livedo reticularis, subcutaneous nodules, retiform purpura [3], [26]. Brito-Zeron P et al, in a retrospective study performed on 250 patients with primary Sjögren's syndrome, found the presence of vasculitis as one of the main factors for an unfavorable prognosis along with hypocomplementenemia, the presence of cryoglobulinemia in the moment of the diagnosis, as well as the severe damage of the parotid gland (evaluated with scintigraphy) [4].

Polyarteritis nodosa represents a necrotic vasculitis of the medium caliber vessels, with cutaneous and systemic involvement and an acute or subacute evolution. It is more common in men (M/F=3/1). Among the patients, 80% of them have general manifestations (fever, myalgia and arthralgia). The cutaneous involvement, present in 35% of the cases, is represented by dermal and hypodermal nodules on the vascular trajectories, suffusions and necrotic ulcerations with slow evolution and a difficult healing. A form with only cutaneous involvement, found in 10% of the cases is met especially in children, being correlated with streptococcal infections [5], [3]. There were described 3 cases of polyarteritis nodosa in patients with primary Sjögren's syndrome [16], [10], [11] and a simultaneous onset of the Sjögren's syndrome manifestations with the polyarteritis nodosa (overlap

syndrome). Prajs K et al. cited in 2012 the fourth case of an overlap syndrome of polyarteritis nodosa with Sjögren's syndrome [20].

The treatment of the ulcerations occurring in Sjögren's syndrome patients includes in the first place the control of the underlying disease. This objective is attained through the use of high doses of corticosteroids with a gradual decrease from the moment the clinical remission is achieved. Local therapy focuses on the chemical debridement of the ulcerations.

#### 4. Conclusions

Sjögren's syndrome patients can develop, rarely, cutaneous lesions of pyoderma gangrenosum type that respond to systemic corticosteroids and chemical debridement of the lesions.

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