Pyoderma gangrenoum secondary to infection by hepatitis C virus. A case report

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Background
Pyoderma gangrenosum is a rare, inflammatory skin disease where painful pustules or nodules become ulcers that progressively grow often associated with systemic disease. The diagnosis is made clinically after excluding other similar skin disorders. We present an interesting case report. At present, the diagnosis and treatment of pathologies associated with pyoderma gangrenosum varies due to the lack of specific histological and clinical findings, which supports the which supports a multidisciplinary approach to this pathology.

Keywords: Pyoderma gangrenosum.

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Pyoderma gangrenosum (PG) is a chronic, uncommon and relapsing neutrophilic dermatosis that presents as an inflammatory and ulcerative disorder of the skin, with variable laboratory and histopathological characteristics, which requires that the diagnosis has a correlation between the clinic and the pathological anatomy. More than half of the patients who develop this condition have an associated underlying systemic disease; inflammatory bowel disease, hematologic disorders, and rheumatoid arthritis account for the majority of cases.[1] Although the association of pyoderma gangrenosum and chronic liver disease is frequently reported, its relationship with viral hepatitis is less frequently described, specifically with the hepatitis C virus (HCV), with few cases of pyoderma gangrenosum and hepatitis C virus.[2]

Case report

This is a 59-year-old female with a 10-year history of trigeminal neuralgia, liver cirrhosis secondary to hepatitis C virus infection, diagnosed and treated in 2020 with sofosbuvir-velpatasvir for 3 months with the last negative charge in 2022. He began with symptoms on July 15, 2021 with pain in both lower limbs, edema, pain that increases with walking and progressive standing that causes claudication, impaired walking.

She persisted with dermatosis with papules and nodules that progressed to persist with a chronic ulcer with a violaceous border and intense pain until 2022. Treatment was started with systemic steroid prednisone 50 mg and topical mupirocin. She presented episodes of improvement of the lesions but continued with intense pain and a quantified fever of 39ºC, nocturnal diaphoresis and the appearance of new lesions in the area (Figure 1). It is evaluated by hematology in the protocol for vasculitis with eosinophilia to consider Wegener's granulomatosis.

Antibodies are taken reporting negative Anti Smith 0.10 U/ml, Anti RNP not detected (0.36), Anti double stranded DNA negative 0.05 U/ml, Complement C4 21.9 mg/dL, Complement C3 97.9 mg/dL, Anti SSA/RO negative 2.5 U/ml, Anti SSB/LA negative 0.40, C-ANCA negative 0.5 AU/ml, P-ANCA negative 7.1 AU/ml, ANA with staining pattern 1:40 fine speckle staining, Protein electrophoresis: Total protein: 7.5 g /dL, Albumin: 3.7 g/dL, Alpha fraction: 1 0.20 g/dL, Alpha 2 fraction: 0.70 g/dL, Beta fraction: 0.8 g/dL, Gamma fraction: 2.10 g/dL, ruling out IgG4 disease since There is no clonality in the protein electrophoresis, with negative studies for systemic lupus erythematosus and negative antibodies for the detection of vasculitis, so methotrexate 10 mg weekly is added and it is decided to continue with systemic steroid.

A biopsy was taken and a report was collected with leukocytoclastic vasculitis plus eosinophilic infiltrate in the lesion, panniculitis and vasculitis (Figure 2). The dermatosis found on the right leg consisting of a hyperchromic macula presented improvement with methotrexate 7.5 mg and

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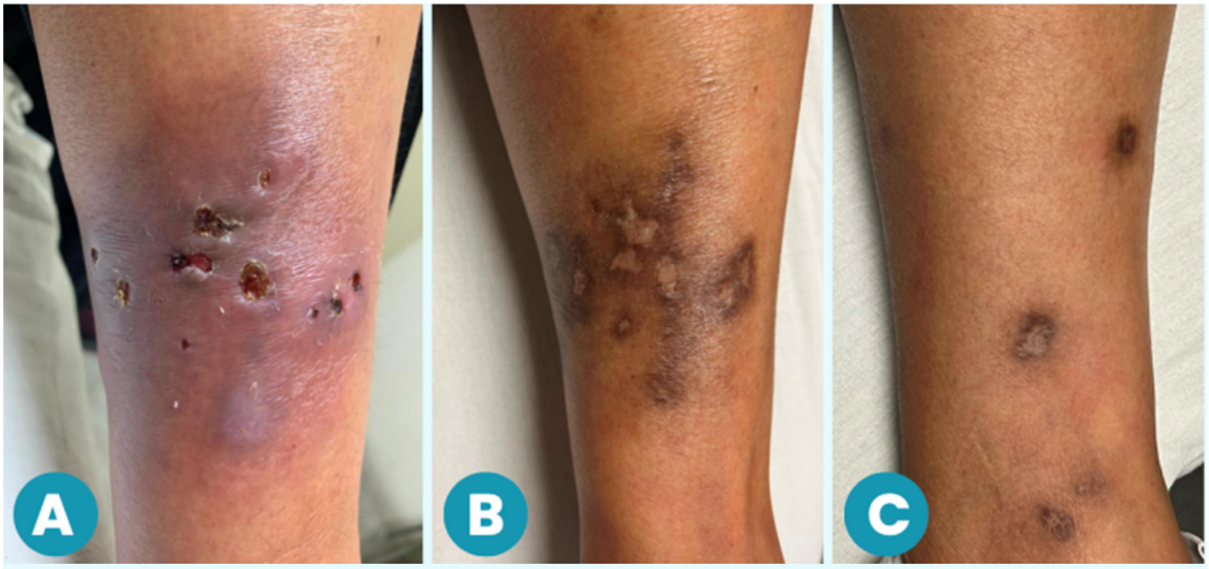

Figure 1. A) Dermatosis affecting the right tibia made up of nodules and chronic ulcers. B and C) Dermatosis constituted by hyperchromic macula

prednisone 10 mg, suspending methotrexate in November 2022 with progressive weaning from the corticosteroid due to clinical improvement. He continues to be monitored by the dermatology service and the hepatitis clinic.

Discussion

Pyoderma gangrenosum is a rare chronic, recurring cutaneous ulcerative condition with a particular morphologic appearance. Systemic illness is commonly accompanied with neutrophilic dermatosis. There are four major clinical manifestations of granulomatous disease: ulcerative, bullous, pustular, and superficial granulomatous. A pustule on an erythematous or violaceous base, an erythematous nodule, or a bulla are common first lesions. The typical lesion is an ulcer with a necrotic undermined border, with a purulent or vegetative foundation[3].

The incidence of pyoderma gangrenosum is unknown, however it is thought to be 3-10 patients per million people per year, occurring at any age but most usually between the ages of 20 and 50, with a small female predominance [4,5].

PG is considered an exclusion diagnosis, with the greatest issue being the clinician's ability to rule out other causes of necrotic ulcers. Because laboratory and histopathologic data often differ, clinicopathologic correlation is required for diagnosis. Histologically, it is defined as a neutrophilic dermatosis with dermal inflammatory neutrophil infiltrates but no evidence of main vasculitis. The clinical and histological findings of PG, on the other hand, are vague and can resemble a variety of illnesses. As a result, additional causes of cutaneous ulcerations must be ruled out, as roughly 50% of PG cases are associated with systemic disorders. There have been over 500 case studies of PG reported to date; it is most usually related with inflammatory bowel illness, arthritis, and hematologic diseases [6,7]. Wegener's granulomatosis must be ruled out as the primary differential diagnosis of PG, in addition to bacterial, fungal, and small vessel vasculitis and malignant illnesses including cutaneous lymphoma, which was the situation with our patient. Only a few cases of PG and HCV have been documented in the medical literature, despite the frequent reporting of the link between PG and chronic liver disease.

Although rare, Pyoderma gangrenosum has been identified as one of the extrahepatic cutaneous symptoms of chronic hepatitis C infection, with only a few instances described to date [8]. Patients who have both PG and HCV are more likely to be female (1:5 men), with an average age of onset of 48 years. 60% of patients have multiple ulcers, which are typically found on one leg (70%) or both (20%). In biopsies, 33% of ulcerative cases show a neutrophilic infiltration, while 38% show vasculitis without neutrophils. Steroids (55%), interferon (33%), antiretrovirals (33%), cyclosporine (11%), and other immunomodulators (25% dapsone, 11% thalidomide, and 25% other antibiotics) are among the treatments available. However, immunosuppression of some kind is ultimately used to treat the majority of patients [9,10]. Systemic therapy is preferred as the first line of treatment for small lesions resistant to local treatment as well as large and fast progressing lesions. The underlying condition and any potential adverse effects must be taken into account when choosing an agent [11]. The cornerstone of PG treatment is systemic immunosuppressants. Nevertheless, extended therapy is linked to important adverse effects. Long-term systemic glucocorticoid medication has the potential to cause iatrogenic Cushing's syndrome and put the patient at risk for wound infection [12].

A common immunomodulating medication for the treatment of chronic inflammatory skin conditions is methotrexate (MTX). It works by increasing the

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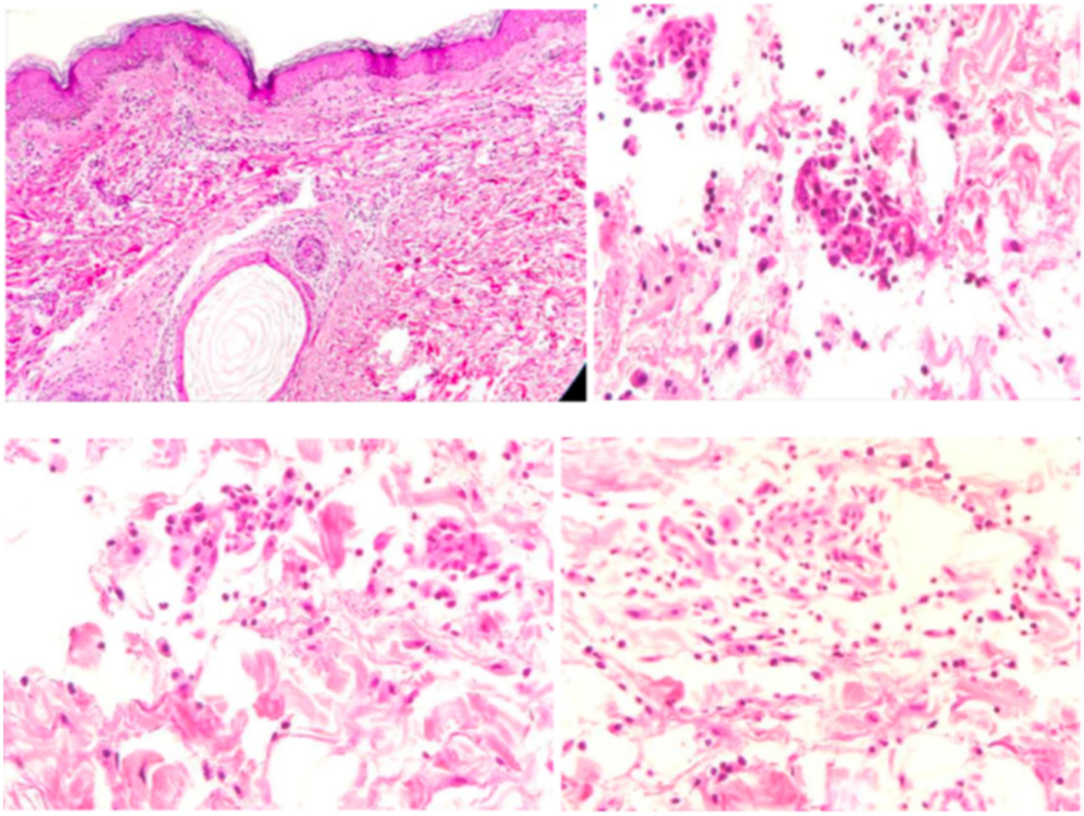

Figure 2. Biopsy microscopic description: epidermis with thin stratum corneum, spongiosis, perivascular and pericytic lymphocytic infiltrate, macrophages, multinucleated giant cells, lichenoid pattern. Edema. Dilated hair ducts and perivascular lymphocytic infiltrate. Hyperplasia of the nerve fillets. Eosinophils in the stroma. Numerous perivascular eosinophils. Liquefactive necrosis. There is a pustular lesion in the deep tissue. Vasculitis.

release of adenosine, which inhibits a number of immune and inflammatory responses, by uncoupling nitric oxide synthase, which makes T cells more susceptible to apoptosis, and by increasing the expression of the long intergenic non-coding RNA p21, which in turn affects a number of immune and inflammatory signaling pathways[13,14].

According to some theories, the chronic HCV disorder is characterized by receptiveness between intrinsic and viral antigens, which may trigger immune responses, enhanced B-lymphocyte stimulation by virus particles leading to B cell expansion, autoantibody production along with circulating immune complexes, and neutrophil dysregulation, which may cause lesions similar to pyoderma gangrenosum [15]. Given that methotrexate has been demonstrated to reduce neutrophil migration and chemotaxis, pyoderma gangrenosum treatment may benefit from its use. Furthermore, individuals with severe PG may benefit from using MTX as a rescue medication.

Conclusion

Due to the lack of a definitive test, pyoderma gangrenosum is a commonly missed diagnosis. The most common misdiagnoses are soft tissue infections, vascular diseases, cutaneous lymphomas, or vasculitis. Etiological investigation of the condition is vital, leading to early diagnosis and timely treatment of the underlying disease.

Conflicts of interests

There was no conflict of interest during the study, and it was not funded by any organization.

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