

Necrotic ulcers during pregnancy: What is your diagnosis?

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A 27-year-old female patient, 24 weeks pregnant, is being monitored for gestational diabetes. Her medical history includes a miscarriage in the first trimester three years ago.

She was admitted to our department for the management of painful diffuse purpuric and necrotic lesions that have been evolving for the past 3 weeks before the consultation, without any other associated signs.

The clinical examination revealed a patient in good general condition. The skin examination identified a well-defined, painful, necrotizing ulcerative plaques on the posterior of both legs (Fig. 1). The remainder of the dermatological examination revealed purpuric plaques on the legs, thighs, abdomen, and both arms. The remainder of the clinical examination, including the obstetrical assessment, did not show any specific abnormalities.

WHAT IS YOUR DIAGNOSIS?

The histology of the lesions suggested leukocytoclastic vasculitis, characterized by a chronic inflammatory infiltrate consisting of lymphoplasmacytes and predominantly perivascular neutrophils. Leukocytoclasia and fibrinoid necrosis were observed.

Direct immunofluorescence revealed weakly positive C3 along the vascular walls.

In the laboratory findings, the complete blood count revealed a white blood cell count of 11,570,

with neutrophils at 9,025 and lymphocytes at 1,736. Hemoglobin level was measured at 11.2, and platelet count at 110,000. Renal function tests, 24-hour urine protein analysis, and liver function tests were all within normal limits. Serological tests for HIV, hepatitis B and C were normal. Immunological evaluation showed no abnormalities, with negative results for anti-nuclear antibodies, anti-neutrophil cytoplasmic antibodies, complement C3 and C4 levels, cryoglobulinemia, circulating anticoagulant, anti-beta 2 glycoprotein antibodies, and anti-cardiolipin antibodies. Venous Doppler ultrasound of both lower extremities did not reveal any signs of venous or arterial thrombosis.

The treatment was intravenous methylprednisolone bolus for 5 days, followed by oral corticosteroid therapy with prednisone at a dose of 0.5mg/kg/day. Local care for the necrotic lesion's hydrocolloid dressings.

The progression was marked by a very favorable clinical outcome, with the healing of necrotic lesions and no appearance of additional vasculitis lesions.

The patient delivered at full term without complications, experienced a normal postpartum period, and the newborn demonstrated good psychomotor development.

DISCUSSION

Cutaneous ulcers during pregnancy are uncommon but may arise from a range of underlying etiologies [1]. Although specific prevalence data are

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Figure 1: (a-c) Necrotizing ulcerative plaques of both legs.

scarce, pregnancy-related physiological changes, such as increased venous pressure and hormonal modulation, predispose to conditions like chronic venous insufficiency (CVI), which can culminate in ulcer formation [2]. Pyoderma gangrenosum, a rare neutrophilic dermatosis often triggered by minor trauma, has been occasionally reported during pregnancy. Infectious agents, including herpes simplex virus (HSV) and leishmaniasis is recognized causes of mucocutaneous ulcers in pregnant women. Systemic vasculitides also contribute to cutaneous ulcers during pregnancy by inducing vascular inflammation and thrombosis [3,4].

The scarcity of reported pregnancies during vasculitides can be attributed to their rarity, historically high mortality rates until recent years, and the use of immunosuppressants, which are contraindicated during pregnancy and may potentially lead to infertility. Additionally, the disease itself may contribute to a decrease in fertility in some cases [1].

More than a thousand pregnancies have been documented in patients with systemic vasculitides, primarily through case reports and small observational series. To our awareness, the sole prospective observational study on vasculitis and pregnancy originates from the Vasculitis Pregnancy Registry (VPreg), which is part of the Vasculitis Patient-Powered Research Network (VPPRN) [5].

Several cases of vasculitides, notably Granulomatosis with Polyangiitis (GPA) [6-9], rheumatoid purpura, microscopic polyangiitis [10,11], Churg-Strauss syndrome [12], or polyarteritis nodosa [13] have emerged and been diagnosed during pregnancy or in the postpartum period with fewer than ten cases reported for each of these conditions [14]. Other vasculitides have been revealed during pregnancy, but these cases are much rarer [15,16]. In the case of our patient, the etiology of leukocytoclastic vasculitis has not been identified.

In recent years, advancements in identifying primary vasculitides and expanding treatment choices have

resulted in improved survival rates and enhanced quality of life for patients. Consequently, pregnancy in women with vasculitis has become a more common occurrence or consideration. The outcomes of most pregnancies reported in patients monitored for vasculitis are typically very positive for both the mother and the child, provided that the pregnancy is planned, the vasculitis is in sustained remission, and there is regular specialized and multidisciplinary follow-up [17].

The treatments for vasculitides that do not pose a problem during pregnancy are primarily limited to corticosteroids, intravenous immunoglobulins (IV Ig), azathioprine, and for limited cutaneous forms or Behçet's disease, hydroxychloroquine, tacrolimus and colchicine [18]. However, cyclophosphamide remains the most effective medication for severe forms of the disease. Its use is particularly challenging and theoretically contraindicated during the first trimester and early second trimester [1]. The risk for the mother and the pregnancy from severe, progressive vasculitis that is inadequately and/or too late controlled may, however, be much greater than that associated with cyclophosphamide prescription during pregnancy. Intravenous administration is preferred for cyclophosphamide, as it is comparably effective to oral administration, with lower cumulative doses required for achieving remission and thus associated with fewer side effects [19,20]. Concerns have been raised regarding congenital anomalies associated with the use of biologics, with reports indicating an increased risk of 30% [17]. However, a meta-analysis, which primarily focused on tumor necrosis factor (TNF) inhibitors or anti-B cell (rituximab) therapies and included only one study with vasculitis patients (Behçet's disease), found that this association became insignificant when adjusted for disease activity. The analysis also showed similar results for pre-term deliveries. Although there was a 68% increase in the risk of low birth weight (LBW) babies with biologic exposure, there was no elevated risk of serious neonatal infections during their first year of life [21].

Limited data exist regarding pregnancies in the context of systemic vasculitides. Published cases of vasculitis occurring during pregnancy are scarce, suggesting a minimal role of pregnancy in triggering or exacerbating these conditions. The outcomes of most reported pregnancies in patients with vasculitis are generally favorable for both the mother and the child.

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

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