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CASE AND RESEARCH LETTERS

Pemphigoid Gestationis: Therapeutic Response to Pre- and Postpartum Immunoglobulin Therapy[☆]

Penfigoide gestacional. Respuesta terapéutica a inmunoglobulinas pre y postparto

To the Editor:

Pemphigoid gestationis or herpes gestationis is a subepidermal blistering disease that occurs in women in the second or third trimesters of pregnancy or even during puerperium. It is a rare skin disease whose incidence has been estimated at around 1 case in every 40 000 to 60 000 pregnancies. It is more common in patients with HLA DR3 and DR4 haplotypes.¹ Although most cases respond well to oral corticosteroids, some can be resistant to this and other treatments. We report a case in which we successfully applied intravenous immunoglobulin treatment.

A 25-year-old, primiparous woman with hypertension on treatment with enalapril, presented in the second trimester of pregnancy, at 22 weeks, with a rash of intensely pruritic plaques that started in the periumbilical region and subsequently appeared on the anterior aspect of both wrists and extensor surfaces of the lower limbs. Laboratory and serological tests (hepatitis B and C viruses, cytomegalovirus, and Epstein-Barr virus) showed no abnormalities except for mild eosinophilia. Tense blisters developed on several of the lesions (Fig. 1A). Histology revealed edema with an infiltrate formed of lymphocytes and abundant eosinophils (Fig. 2A), and direct immunofluorescence showed linear deposits of C3 at the dermoepidermal junction (Fig. 2B). Pemphigoid gestationis was diagnosed and treatment was initiated with prednisone (30 mg/d). The dose was increased to 60 mg/day and subsequently to 75 mg/d due to the lack of response on weekly follow-up.

In the final month of pregnancy intravenous immunoglobulin was administered at a dose of 500 mg/kg/d for 5 days. We succeeded in reducing the dose of prednisone to 30 mg/kg/d (reducing 5 mg/wk until that dose was reached) with no worsening of symptoms.

At 15 days after delivery, the dose of prednisone was dropped to 15 mg/d. In agreement with the gynecology department of our hospital, a new course of intravenous immunoglobulin was initiated at the same dose in order to prevent a probable resurgence of the condition, given the poor response. At 18 weeks after delivery, prednisone was suspended with no recurrence of lesions in the following 6 months (Fig. 1B). Follow-up laboratory tests and blood pressure values showed no variation either during or after treatment.

The treatment of choice in pemphigoid gestationis is oral corticosteroids. The usual dose is around 0.5 mg/kg/d of prednisone by mouth, which rapidly improves symptoms in most cases. However, systemic corticosteroid therapy is sometimes insufficient to control the disorder, as occurred in our patient. Other treatments have been tested, including plasmapheresis, intravenous immunoglobulin, pyridoxine, ritodrine, and immunosuppressant drugs such as cyclosporin,² azathioprine, dapsone, and tacrolimus.

The use of intravenous immunoglobulin in autoimmune bullous diseases resistant to conventional treatment is increasing, since it offers a convenient alternative treatment with few side effects, most of which are mild and self-limiting. Episodes of flushing, myalgia, headaches, nausea and vomiting, tachycardia, and a slight increase in blood pressure have been reported in most cases between 30 and 60 minutes after starting infusion.³ Anaphylaxis is very rare and has mainly occurred in patients with immunoglobulin A deficiency. These adverse effects are almost always avoidable with premedication according to an established protocol at the medical day care units where the infusion is administered.⁴

The literature reports few cases of the use of intravenous immunoglobulin in pemphigoid gestationis,^{5–8} though it has been employed successfully to manage other blistering diseases such as pemphigus vulgaris, bullous pemphigoid, and acquired epidermolysis bullosa.⁸ The mechanism of action of intravenous immunoglobulin is not fully understood but it appears to act at different points in the immune cascade, including functional blockade of Fc receptors on splenic macrophages, inhibition of complement-mediated actions, and modulation of cytokine production.³

In the absence of large patient series, given the low incidence of this pathology, the dose and time of administration of immunoglobulin vary according to the author reviewed. No significant differences were detected between regimens

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Figure 1 A, Papular eruption with tense blisters on the patient's abdomen. B, Condition of the patient at 6 weeks after delivery.

of 3 or 5 days, and most authors followed existing protocols at their hospitals. We considered applying this treatment pre- and postpartum in order to control skin disease in the final stages of pregnancy and prevent a possible recurrence during the puerperium. Jolles et al³ observed that treatment with intravenous immunoglobulin in autoimmune bullous diseases is always more successful when used as adjuvant therapy (91%) rather than monotherapy (51%). Subsequently published cases of pemphigoid gestationis report therapeutic success in both situations.⁵⁻⁸

In our patient, we used intravenous immunoglobulin associated with systemic corticosteroids, owing to the difficulty of controlling the skin symptoms and taking into account that corticosteroids during pregnancy can involve risk for the fetus (growth retardation, prematurity) and for the mother (osteonecrosis, hypertension, infections, etc.). We believe that the regimen followed in our patient may be of interest in cases with an indolent clinical course and that are refractory to conventional treatment.

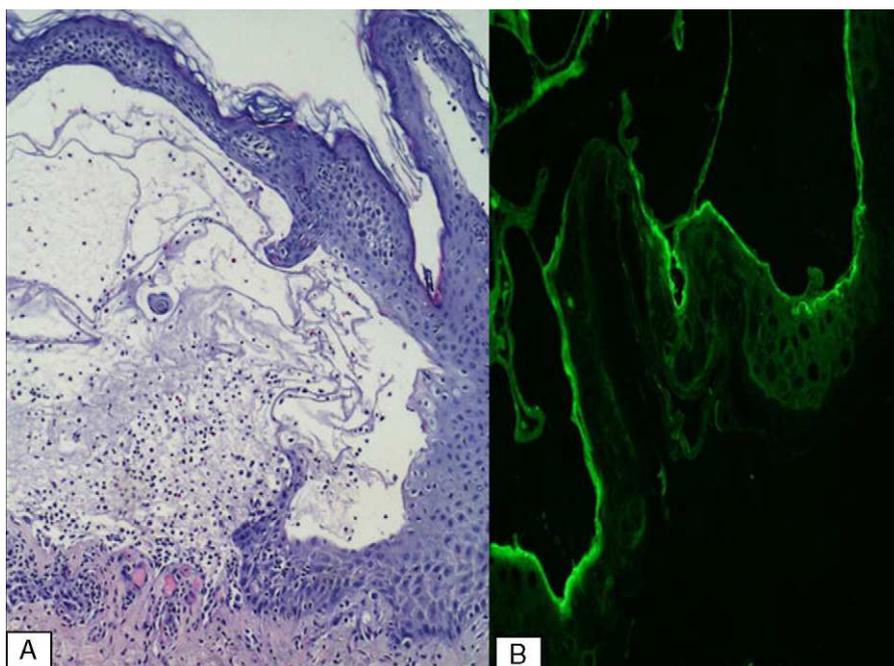


Figure 2 A, Subepidermal blister with eosinophils (hematoxylin-eosin, original magnification x10). B, Direct immunofluorescence: linear deposits of C3.

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Myeloid Sarcoma in the Area of a Skin Flap[☆]

Sarcoma mioelóide en un área de plastia

To the Editor:

Leukemia cutis, which is the infiltration of leukocytes into the skin, is rare and accounts for just 3.1% of all types of leukemia. The subtypes that most commonly affect the skin are monocytic acute myeloid leukemia (AML-M5 [French-American-British classification]) and acute myelomonocytic leukemia (AML-M4), with a respective prevalence of 33% and 13% to 18%. Myeloid sarcoma, formerly known as granulocytic sarcoma, is an extramedullary tumor composed of immature myeloid cells.¹ Although the skin is among the organs most frequently affected by myeloid sarcoma, this tumor is still a rare variant of leukemia cutis. We report the case of a patient with myeloid sarcoma in the area of a skin flap.

The patient, an 86-year-old man, had been diagnosed with myelodysplastic syndrome 2 years earlier. He had consulted for 2 basal cell carcinomas, one on the left temple and the other on the right ala nasi. Both tumors were excised. The surgical defect was repaired by direct closure in the first case and with a nasolabial fold flap in the second. A few hours after surgery, the patient presented at the emergency department with diffuse hemorrhage from both surgical wounds and a large hematoma in the area of the skin flap. Laboratory tests showed a leukocyte count of 12 200/ μ L (upper limit of normal, 10 000/ μ L; neutrophils, 31.2%; lymphocytes, 21.3%; monocytes, 43.6%); a hemoglobin level of 11.7 g/dL (lower limit of normal, 13 g/dL), a platelet count of 65 000/ μ L (lower limit

of normal, 150 000/ μ L), and a creatinine level of 1.5 mg/dL (upper limit of normal, 1.3 mg/dL). The other tests (coagulation studies, liver function tests, and lactate dehydrogenase) were normal. One month after surgery, a fast-growing asymptomatic nodule appeared in the area of the skin flap, accompanied by progressive infiltration of the lower part of the flap (which had healed perfectly) and ulceration (Fig. 1). Biopsy of the nodule and the infiltrated scar revealed a diffuse neoplastic proliferation of medium-sized, round/oval mononuclear cells with eosinophilic cytoplasm and basophilic nuclei in the dermis and adipose tissue (Fig. 2). Immunohistochemical staining showed diffuse positivity for myeloperoxidase (MPO), CD68, and CD43, and focal positivity for CD34, leading to a diagnosis of myeloid sarcoma (Fig. 3). During this time, the patient's myelodysplastic syndrome progressed to AML-M4. Palliative treatment was initiated with thioguanine, but the patient died 3 weeks later.

Myeloid sarcoma presents as one or more tumor masses composed of immature myeloid cells. While the tumors can affect any part of the body except the bone marrow, the most common sites of involvement are bone, periosteum, skin, gums, and lymph nodes. Multifocal disease is seen in less than 10% of cases. Myeloid sarcoma can precede, coincide with, or indicate recurrence of AML. It can also indicate blastic transformation of a myelodysplastic syndrome, chronic myeloid leukemia, or other myeloproliferative disorders. It is slightly more common in men than in women (male to female ratio, 1.42:1) and in advanced ages (mean age at diagnosis, 56 years). Myeloid sarcoma of the skin presents as a solitary tumor that grows in a matter of days or weeks and typically affects the face, the scalp, or the trunk. There have also been reports of multiple and even disseminated lesions.^{1–4} The literature contains approximately 20 reports of myeloid sarcoma in leukemia cutis, arising at sites of previous skin lesions or trauma, mainly at central venous catheterization sites (11 cases)⁴ and puncture sites for venous and arterial sampling and bone marrow aspiration (4 cases).⁵ There have also been isolated reports of myeloid sarcoma at sites of extravasation of chemotherapy agents,⁶ traumatic scars and excoriations,⁸ Mantoux test injection

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