Recurrent sweet's syndrome in acute myeloid leukemia successfully treated with amphotericine b

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Different types of skin manifestations can occur during the course of myelodysplastic syndromes (MDS) or acute leukemias (AML), which usually are classified as specific (dermal infiltrates by malignant cells)[1,3] or non specific (infections, vasculitis or neutrophilic dermatoses).[4,5] These latter encompass from a transient increase in permeability to necrosis with ulceration[6,7] and are histologically characterized by polymorphonuclear infiltration without evidence of malignant myeloid cells.[8,9] The therapy for these conditions is treatment of the underlying disorder, but best responses are obtained with systemic corticosteroids, sulfadrugs or immunosuppressive agents.[10] We report a case of a neutropenic patient with an AML, who presented recurrent hemorrhagic pseudovesiculated plaques on both hands, identified as a Sweet's syndrome that, after unsuccessful treatment with wide spectrum antibiotics and prednisone, responded to Amphotericine B.

A 65-year-old woman with a 18 month history of AML secondary to MDS was admitted to our hospital for fever and a painful skin lesion on her right hand. The patient was receiving hydroxyurea (HU 1 gr/day) and prednisone (20 mg/day). Physical examination showed a large, well demarcated, violaceous, pseudovesiculated, smooth-surfaced, elevated and infiltrated plaque 10 mm in diameter on the dorsum of the hand, with a purple, erythematous, regular border (Figure 1). White blood cell count was $6.5x10^9$/L with 10% polymorphonuclear cells; hemoglobin was 7.4 g/dL, platelet count was $12x10^9$/L.

The patient was immediately started on wide-spectrum antibiotics (Ceftriaxone 2 g/day, Amikacine 20 mg/kg/day) and continued HU and prednisone at the previous dosages. After 72 hours, owing to the persistence of fever and worsening of the skin lesion, Teicoplanine, 350 mg/day, and Meropenem, 3 g/day, were added. Repeated cultures from blood and cutaneous lesion were negative for viral, bacterial and fungal infections. No improvement was obtained, and the cutaneous lesion progressed to a bullous hemorrhage slowly enlarging on the whole hand, with new lesions arising on both arms. A skin biopsy was performed which showed a dermal infiltrate of mature neutrophils -despite severe granulocytopenia- without immature myeloid cells; these findings led to diagnose a Sweet's syndrome. On the 10^{th} day, owing to patient's clinical conditions deterioration, we empirically started on systemic Amphotericine B, 50 mg/day. Fever soon disappeared and cutaneous lesions progressively subsided in the following 3 weeks, by forming progressively enlarging cutaneous ulceration with raised, tender, undetermined border, and necrosis. After 5 weeks, residual hyper pigmentation in the absence of scarring was seen at the site of the lesions (Figure 2).

One month later, two new cutaneous lesions, consisting of painful, tender, hemorrhagic, pseudovesicular plaques, appeared on the forefinger of the left hand (Figure 3), the lower lip and inside the mouth, with recurrence of fever.

Following unsuccessful treatment with wide spectrum antibiotics and prednisone, we administered again Amphotericine B at the dosage of 50 mg/day for 15 days. Fever rapidly remitted and the lesions gradually ulcerated in the center and after 4 weeks completely resolved, with residual hyper pigmentation in the absence of scarring.

Figure 1. Large, edematous, well demarcated, violaceous, pseudovesiculated at diagnosis.

Figure 2. Residual hyperpigmentation after 5 weeks, post-therapy with Amphotericine B.

Figure 3. Two new cutaneous lesions appeared on the forefinger of the left hand after one months.

Presently, the patient is alive and in stable hematological disease condition, after 6 months from the second dermatosis episode.

Sweet's syndrome is the most commonly observed vasculitis in MDS or secondary AML1-3; it may present atypically, as it can lack some of the characteristics (i.e. initial fever or leukocytosis) which have been included in the diagnostic criteria as proposed by Su and Liu.[8]

Most patients with these dermatoses respond to oral steroids alone.[1-3] In our case, fever in the presence of severe neutropenia, led us to promptly initiate empiric treatment with wide-spectrum antibiotics; however persistence of fever in the absence of microbiological positivities and deterioration of skin lesions, induced to empiri-

cally start on systemic antifungal treatment, which allowed skin lesions resolution.

So far, Amphotericine B has never been reported as second-line therapy for treatment of a Sweet's -like syndrome. Dapsone and other agents such as colchicine, indomethacin, pentoxifylline, metronidazole, cyclosporine, potassium iodide, doxycycline, and interferon alfa are also included in anecdotal reports, as possible therapy.[10] In our case, it is possible that abnormal immune complexes, originated by exposure of dysfunctioning granulocytes and/or macrophages to the etiologic agent may have allowed inappropriate response and/or abnormal cytokine production.

Possible recurrence of Sweet's syndrome with involvement of skin and other systemic sites is suggested by present observation; furthermore, Amphotericine B should be considered a second-line drug to be attempted for this type of dermatosis in neutropenic patients with myeloid malignancies, who do not improve with systemic steroids and antibiotic therapy.

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