Transformation of a myelodysplastic syndrome to acute myeloid leukemia and concurrent necrotizing sweet syndrome

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Abstract

The Sweet's syndrome, is an inflammatory skin disorder characterized by extensive infiltration of neutrophils in the dermis with extension to the subcutis, known as acute febrile neutrophilic dermatosis. It may occur as a paraneoplastic syndrome. To our knowledge, there are currently few reports about transformation of a myelodysplastic syndrome to acute myeloid leukemia and concurrent necrotizing Sweet syndrome in the literature. Herein we describe an unusual case in a young patient with these characteristics that evolved to a fatal outcome.

Introduction

The Sweet's syndrome (SS), is an inflammatory skin disorder characterized by extensive infiltration of neutrophils in the dermis with extension to the subcutis, known as *Acute febrile neutrophilic dermatosis.*[1]

The clinical spectrum of manifestations is wide, some of the most representative characteristics are tender skin lesions, erythematous plaques, papules or nodules located in extremities, neck and head, usually accompanied by fever and neutrocytosis.[2] Some of the clinical conditions related to this syndrome include infections, autoimmune diseases, inflammatory bowel diseases, vaccines, pregnancy, certain medications, neoplasms and idiopathic.[3]

Paraneoplastic syndromes are clinical clues that neoplasms cause in places outside their primary location and that are directly associated with them or with their metastases. They may occur accompanying an established cancer or as the first sign of malignancy or its recurrence.[4]

The malignancy-associated Sweet's syndrome (MASS) can occur as a paraneoplastic syndrome in patients with solid tumors such as carcinomas of the genitourinary tract, breast, and gastrointestinal tract or related to hematologic condition including myeloproliferative, lymphoproliferative, and myelodysplastic disorders. Among the hematologic malignancies most commonly associated with Sweet's Syndrome is Acute Myeloid Leukemia (AML).[5]

Herein, we report a case of Myelodysplastic Syndrome (MS) that evolved to AML with concurrent SS as a skin paraneoplastic condition.

Case Report

A 23-years-old female patient, with a history of marijuana addiction for one year, tobacco and alcohol consumption since the age of 17, three abortions before 10 weeks of gestation, previously diagnosed in May 2012, with Human Papillomavirus (HPV) infection by cervical cytology and aplastic anemia by bone marrow aspiration (BMA). She received treatment with Antithymocyte Globulin for 2 cycles (May 2012 and April 2014) and posteriorly Cyclosporin A, with subsequent liver toxicity, changing to Mycophenolate Mofetil and Danazol, with a partial response, requiring multiple hospitalizations and transfusion support, with more than 40 units of globular packages, complicating with transfusional hemosiderosis, treated with Deferasirox. In May 2015, she presented cellulitis of the right thoracic limb, with spontaneous resolution and a secondary atrophic scar. In November 2015, she began with asthenia, adynamia and fever up to 41ºC, predominantly in the evening and a nodular lesion of 3 cm diameter in the upper inner quadrant (UIQ) of the right breast, which increased in size progressively, with very painful violaceous skin lesions, evolving to confluent blisters and later ulceration with non-purulent secretion and necrosis (Figure 1A). She was treated with Dicloxacillin, Piperacillin / Tazobactam and Carbapenemic. In the absence of improvement, stage IIIB breast cancer was suspected, so she was referred in December 2015 to a tertiary level hospital. Upon admission, it was documented the lesion in the right breast, with bleeding nipple, as well as confluent blisters and edema on the outer side of the left thigh (Figure 1B,C). The patient had a non-reactive viral

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panel for HIV, HCV, HBV. A breast skin biopsy revealed a neutrophilic inflammatory infiltrate with no evidence of vasculitis (Figure 2). Treatment with systemic steroid was started, with excellent response and remission of lesions. Imaging tests were performed, as chest x-ray and Thoracoabdominal computed tomography, finding hepatosplenomegaly, the final diagnosis was necrotizing Sweet's syndrome. A month later, a new BMA was performed, finding dysplasia of more than 50% of the cells of the erythroid and granulocytic series, as well as absent megakaryocytes, diagnosing MS. The patient persisted with transfusion support with globular packages and treatment with Mycophenolic Acid. On November 2016, the patient was hospitalized for a 2-week course consistent with fever, anemia and purpuric syndrome, low cardiac output data, syncope, and acute kidney injury. BMA congruent for AML with absent megakaryocytes, 7% adult neutrophils, 2% young neutrophils, 1% lymphocytes, 77% normoblasts, 13% myeloid blasts and 58% myeloid blasts. Immunophenotyping: 32.6% HLA-DR, 29.2% CD34, 36.5% Glycophorin, 2.08% Glycophorin A/34, 28.6% CD117, 53.8% CD13, 51% CD33, 12,7% CD64, 1.9% CD7 and 31.6% CD22. Management began with anti-tumor lysis measures, hemoderivatives, and leukapheresis. Five days after admission, the patient presented respiratory failure, requiring mechanical ventilatory support, progressing to multiple organ failure culminating in death, with final diagnoses of AML subtype M2, aplastic anemia and Sweet's Syndrome.

Discussion

We described a case in a young patient with aplastic anemia that evolved to myelodysplastic syndrome and further to acute myeloid leukemia with necrotizing Sweet syndrome as a paraneoplastic expression of the latter. This hematologic disorder is the most common associated malignancy, being important to carry out the differential diagnosis since breast cancer was initially suspected.[5]

Hematologic disorders represent more than 15-20% of MASS, being AML and MS the most common.[6]

Few cases coincident with MS, AML and SS have been reported in the literature as the case of a 15-year-old girl who presented these three entities with FLT3 and NPM1 type A mutations. Risk factors for MASS in AML encompass deletion of chromosome 5 or 5q, presence of FLT3 mutations, and AML with myelodysplasia-related features. Unfortunately, our patient did not have a karyotype due to a rapid adverse clinical course.[7]

Pourmoussa and Kwan reported another case of an extremely rapid transformation from MS with concomitant SS to AML, in an elderly patient.[8] Our patient also followed that sequence with a fatal ending. Myelodysplastic Syndrome can evolve into AML, which often leads to a poor prognosis.

The outlook of SS is little known, with an incidence of 2.7 at 3 cases/100,000 in the general population.[9] The diagnosis of SS associated with MS with transformation to AML has a low incidence and it is scarcely described in the literature, but of importance in the diagnostic suspicion.

In Mexico, a recent multicenter study identified that AML presents at a younger age in comparison with developed countries, with a median age of onset of 47 years, however this patient presented AML at an earlier age.[10]

SS related to hematological neoplasia may present prior to or concomitant to the primary diagnosis, that means a paraneoplastic event, in the patient occurred concomitantly with acute myeloid leukemia, similar to that reported by Mo *et al.*[11]

Necrotizing SS or acute necrotizing neutrophilic dermatosis is an infrequent and severe variant, distinguished by aggressive skin lesions that can easily simulate and be mistaken for necrotizing soft tissue infections such as necrotizing fasciitis or pyoderma gangrenosum. It is characterized by hyperpyrexia, neutrophilia and painful skin lesions that can be single or multiple, be vesicular, pustular, bullous or ulcerative, and mainly necrosis.[12]

The term Necrotizing SS proposed in 2012 and to date only 4 cases have been reported worldwide, in which patients had concealed hematological diseases and histopathological findings with necrosis of the fascia and fat, simulating necrotizing

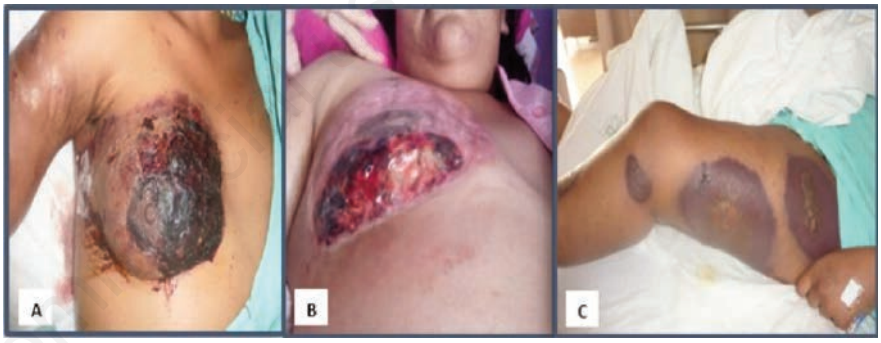

Figure 1. A) Cutaneous necrosis of the right breast. B) Erythematous violaceous plaque with undefined edges, ulcerated with perilesional edema and purpuric raised edges, central blisters, erosion and bleeding nipple; 1C. Lesions on the outer side of the left thigh characterized by confluent blisters and peripheral edema.

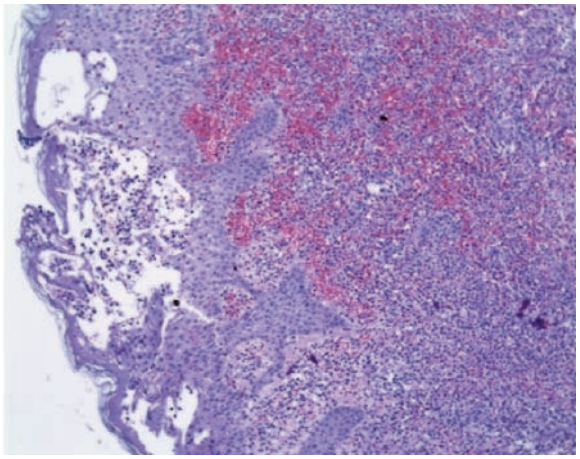

Figure 2. Superficial and deep neutrophilic dermatosis, with spongiform pustules, secondary neutrophilic vascular reaction in small vessels, and added purpuric phenomenon.

fasciitis. Previous cases were males with a median age of 57.5 years of onset, all of them with underlying hematological diseases, however the present case was in a very young woman with an aggressive clinical course.[13]

This entity may be confused with other pathologies, among the most common differential diagnoses that mimic SS are bacterial, mycobacterial, fungal, and parasitic infections. To avoid this, a biopsy should be considered to detect characteristic features consistent with SS.[5] This disease has a low incidence and is little described in the literature. Communications of fatal outcomes of Sweet's syndrome are uncommon, as it is depicted as an idiopathic chronic systemic inflammatory response syndrome or as in this case, related to malignancy with a fatal outcome in a young patient.[1,14]

Conclusions

Sweet syndrome is a rare entity that may appear as a sign of malignancy, as in the present case, in a young patient with fatal outcome. It is necessary to have a high index of suspicion to recognize it and identify the underlying disorder.

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