

Photoclinic

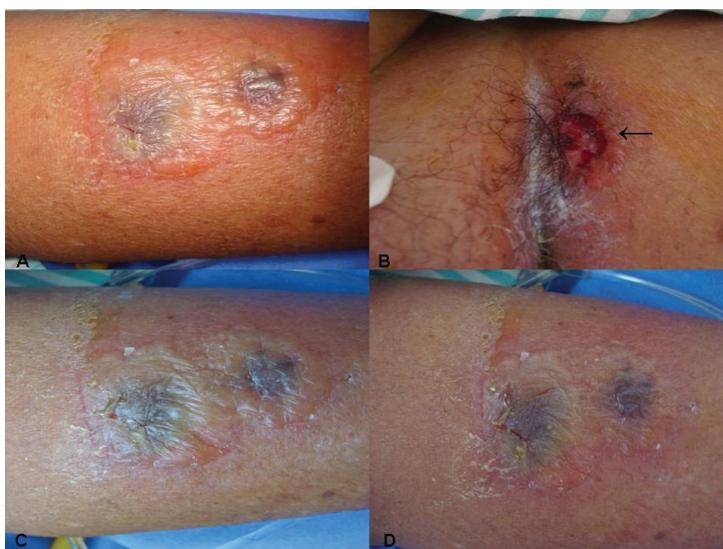


Figure 1. A) Serous vesicle blisters on an erythematous plaque which showed acute onset at the site of venipuncture in a patient receiving hydroxyurea to control chronic myeloid leukemia; B) Shallow vulvar ulceration (arrow) coexistent with left forearm skin lesions; C and D) Healing of skin changes two and three days after the use of corticosteroids.

In March 2009, a 79-year-old female presented with refractory anemia and excess blasts (MDS AREB-2) and was treated with cyclosporine (50 mg BID) at another hospital. In May, she was admitted to our Internal Medicine Ward for clinical and hematology surveillance. New bone marrow studies were performed, which revealed about 32% myeloblasts that contained Auer bodies, more than 20% basophils and negative for BCR-ABL mutation. Cyclosporine was withdrawn. She received hydroxyurea 500mg/day, which was increased up to 1,500 mg daily. Ten days later, the patient exhibited a high fever, along with erythema and painful vesicle-bullous lesions that appeared at the venipuncture sites in her left forearm (Figure 1A), in addition to vulvar ulcer with clean base (Figure 1B). Lesions were not found in

Vitorino Modesto dos Santos MD PhD^{1,2}, Natália Solon Nery MD², Gustavo Bettarello MD³, Israel Mauricio Neiman MD⁴, Flavia Campos de Brito MD², Cristiane Farias Ribeiro Souza MD¹
Authors' affiliations: ¹Internal Medicine Department, Catholic University, Brasília-DF, ²Internal Medicine Department, Armed Forces Hospital, Brasília-DF, ³Division of Hematology, Armed Forces Hospital, Brasília-DF, ⁴Division of Dermatology, Armed Forces Hospital, Brasília-DF, Brazil.

•**Corresponding author and reprints:** Vitorino Modesto dos Santos MD PhD, SMPW Quadra 14 Conjunto 2 Lote 7 Casa A. 71.745-140, Brasília-DF, Brazil. Tel: +61-33802666; Fax: +61-32331599. E-mail: vitorinomodesto@gmail.com
 Accepted for publication: 10 February 2010

the neck, trunk, eyes, mouth, nose, or anal region. Histopathology study was performed in biopsy samples from the skin lesions. Of note, microorganisms were not detected in tissue samples, blood, and urine cultures. Additionally, serologic tests for infectious agents were negative. Cutaneous changes showed rapid improvement (Figures 1C and 1D) after the use of prednisone 60 mg/day. Splenomegaly was not conspicuous and the lung field examination was unremarkable. However, despite nutritional, clinical, and intensive care support, the patient's course was downhill. Blood counts showed: leukocytes $28.7 \times 10^9/L$, 39% blasts, 2% myelocytes, 3% metamyelocytes, 18% bands, 22% segmented neutrophils, 3% basophils, 8% lymphocytes, erythrocytes $2.68 \times 10^{12}/L$, hemoglobin 8.3 g/dL, hematocrit 25.1%, MVC 94 fL, MCHC 33 g/dL, platelets $33.0 \times 10^9/L$, and ESR 38 mm/hour. Serum determinations showed: urea 117.8 mg/dL, creatinine 2.2 mg/dL, folic acid 6.99 nmol/L, vitamin B12 8, 440 pg/mL, beta-2 microglobulin 184.5 mg/L, and CRP 19.5 mg/dL. Death occurred on June 3rd, following acute atrial fibrillation and irreversible circulatory shock.

What is Your Diagnosis?
See the page 562 for the diagnosis

Photoclinic Diagnosis:

Bullous Sweet syndrome in chronic myeloid leukemia

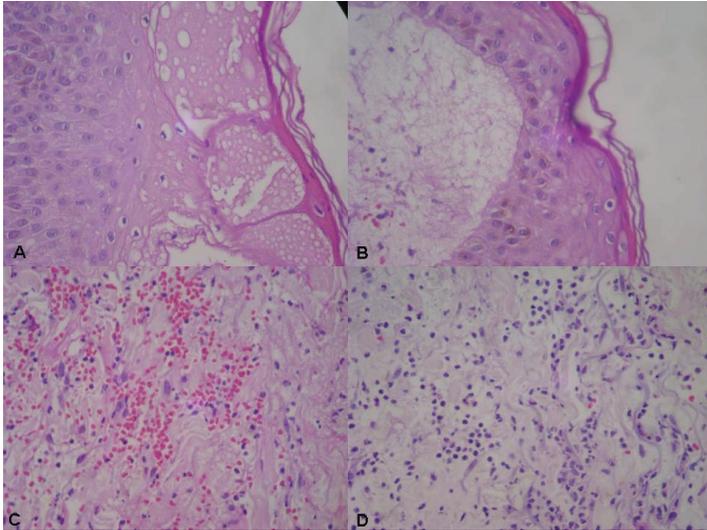


Figure 2. **A)** Skin sample showing epidermic bullae (H&E stain, original magnification 40×); **B)** Conspicuous subepidermal edema (H&E stain, original magnification 40×); **C)** Neutrophilic infiltrate in the upper dermis and moderate erythrocyte extravasation in some areas. Features of vasculitis are absent (H&E stain, original magnification 40×); **D)** The mixed infiltrate of upper dermis contains predominant mature neutrophils.

The patient was diagnosed with Sweet syndrome (SS), or acute febrile neutrophilic dermatosis. SS is a broad spectrum condition, typically characterized by fever, neutrophilia, and cutaneous, and mucous lesions (erythematous, solid, and bullous), in addition to diffuse neutrophilic infiltrate in the upper dermis.¹⁻⁵ Genital ulcerations have been scarcely reported in SS,^{2,4} which can be idiopathic, drug-induced, and associated with malignant tumors or hematologic malignancies.^{1-3,5} In this patient, the diagnosis of SS was established by clinical, laboratory, and typical skin biopsy data (Figure 2)^{1-3,5}; and characteristically, the conspicuous lesions improved rapidly after administration of corticosteroids.^{1,2}

This case report emphasizes some concerns about SS associated with treated chronic myeloid leukemia (CML). First, because the syndrome can be due to CML or associated with the use of hydroxyurea.⁶ Although leukemia cutis can mimic SS features,³ histologic data ruled out this possibility. Second, the high level of CRP suggested some associated infection, but the hypothesis was not confirmed by blood and urine cultures, serologic tests or histopathologic tissue samples. Autonomic dysfunction and anemia due to leukemia can play a role in heart arrhythmias⁷; in addition, anemia can predict death in elderly patients that present with atrial fibrillation.⁸

References

1. Cohen PR. Neutrophilic dermatoses: a review of current treatment options. *Am J Clin Dermatol.* 2009; **10**: 301 – 312.
2. Khodadad K, Sadeghipour A, Aghili N. Generalized neutrophilic dermatosis: a rare presentation of myelodysplastic syndrome. *Indian J Cancer.* 2005; **42**: 57 – 59.
3. Fitzgerald RL, McBurney EI, Nesbitt LT Jr. Sweet's syndrome. *Int J Dermatol.* 1996; **35**: 9 – 15.
4. Lindskov R. Acute febrile neutrophilic dermatosis with genital involvement. *Acta Derm Venerol.* 1984; **64**: 559 – 561.
5. Zamanian A, Ameri A. Acute febrile neutrophilic dermatosis (Sweet's syndrome): a study of 15 cases in Iran. *Int J Dermatol.* 2007; **46**: 571 – 574.
6. Vassallo C, Passamonti F, Merante S, Ardigò M, Nolli G, Mangiacavalli S, et al. Muco-cutaneous changes during long-term therapy with hydroxyurea in chronic myeloid leukaemia. *Clin Exp Dermatol.* 2001; **26**: 141 – 148.
7. Nevruz O, Yokusoglu M, Uzun M, Demirkol S, Avcu F, Baysan O, et al. Cardiac autonomic functions are altered in patients with acute leukemia, assessed by heart rate variability. *Tohoku J Exp Med.* 2007; **211**: 121 – 126.
8. Sharma S, Gage BF, Deych E, Rich MW. Anemia: an independent predictor of death and hospitalizations among elderly patients with atrial fibrillation. *Am Heart J.* 2009; **157**: 1057 – 1063.