

Sweet's Syndrome in an Agranulocytotic Patient: A Case Report.

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ABSTRACT:

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Sweet's syndrome is an inflammatory disease presented clinically as fever and cutaneous eruption of tender erythematous plaques together with abnormal laboratory finding i.e. leukocytosis with neutrophilia in the peripheral blood. The histology is characterized by a dense infiltration of mature neutrophils in the papillary dermis. It is unusual for a leukopenic patient to develop Sweet's syndrome. Here, we report a patient with acute myeloid leukemia at the stage of agranulocytosis who develops a cutaneous eruption that is consistent with Sweet's syndrome. Hence, Sweet's syndrome should also be considered when encountering patients with cutaneous eruptions and underlying hematologic malignancies, regardless of their peripheral blood neutrophil count.

Key words: Sweet's syndrome, agranulocytosis, acute myeloid leukemia

บทคัดย่อ :

วรดา ชูวีเชียร, รัชยานี คเนจร ณ อุทยา รายงานผู้ป่วยกลุ่มอาการสวิต ในผู้ป่วยที่อยู่ในภาวะไม่มีเม็ดเลือดขาวชนิดนิวโทรฟิลในกระแสเลือด วารสารโรคผิวหนัง 2552; 25: 245-250.

แผนกผิวหนัง กองอายุรกรรม โรงพยาบาลพระมงกุฎเกล้า

ผู้ป่วยกลุ่มอาการสวิต มักตรวจพบไข้ ผื่นแดงนูนและเจ็บ ร่วมกับเม็ดเลือดขาวชนิดนิวโทรฟิลสูงในเลือด และตรวจทางพยาธิวิทยาพบเม็ดเลือดขาวชนิดนิวโทรฟิลที่ชั้นหนังแท้ส่วนบน กลุ่มอาการสวิตมักไม่พบในผู้ป่วยที่มีระดับเม็ดเลือดขาวในเลือดต่ำ ในรายงานนี้ได้นำเสนอผู้ป่วยมะเร็งเม็ดเลือดขาว ซึ่งอยู่ในภาวะไม่มีเม็ดเลือดขาวชนิดนิวโทรฟิลในกระแสเลือด ที่ได้รับการวินิจฉัยว่าเป็นโรคกลุ่มอาการสวิต ดังนั้นกลุ่มอาการสวิตยังเป็นหนึ่งในโรคที่ต้องวินิจฉัยแยกโรค หากตรวจพบผื่นในผู้ป่วยมะเร็งเม็ดเลือดขาว โดยไม่จำเป็นต้องมีระดับเม็ดเลือดขาวในเลือดสูงเสมอไป

คำสำคัญ: กลุ่มอาการสวิต, ภาวะไม่มีเม็ดเลือดขาวชนิดนิวโทรฟิลในเลือด, มะเร็งเม็ดเลือดขาว

Introduction

Sweet's syndrome [acute febrile neutrophilic dermatosis] was first described in 1964 by Dr. Robert Douglas Sweet¹. Sweet's syndrome is characterized by pyrexia, neutrophilia, erythematous plaques of dense infiltration of mature neutrophils in the papillary dermis and usually associated with leukocytosis². Here we report a case of Sweet's syndrome with post-chemotherapy-agranulocytosis for the treatment of acute myeloid leukemia.

Case report

A 56-year-old Thai man was diagnosed as acute myelomonocytic leukemia and right pleural involvement for one month. He was admitted for an induction chemotherapy consisting of cytarabine and idarubicin. Seven days after the chemotherapy, he developed fever without any organ specific symptoms.

Septic work-up including blood, pleural fluid and urine cultures were done. With regard to the medical condition of the patient, infection could not be ruled out. As a result, antibiotics [tazobactam + piperacillin and amikacin] were administered. Three days later, he developed a cutaneous eruption.

Dermatological examination revealed generalized marked jaundice with multiple ill-defined erythematous edematous non-tender papules on the neck, right forearm and both inguinal regions which coalesced to form plaques on the left side of the neck and right forearm [Figure 1, 2]. There were widespread ill-defined maculopapular rash at the anterior trunk and back together with patches of petechiae at both legs.



Figure 1 ไม่ได้คำบรรยายได้ภาพ



Figure 2 ไม่ได้คำบรรยายได้ภาพ

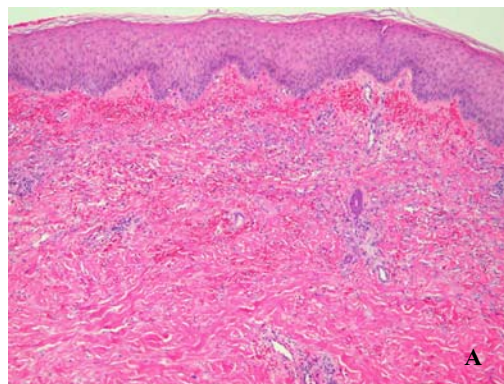
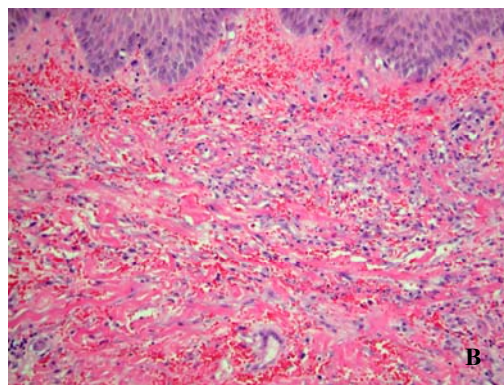
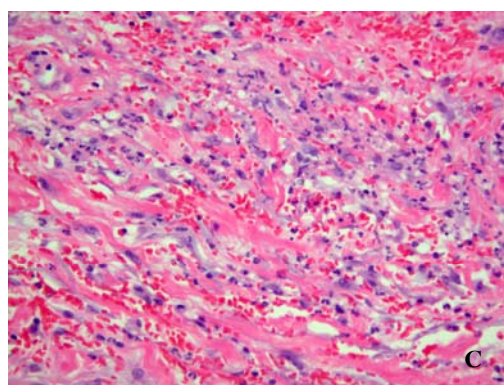


Figure 3[A,B,C] Histopathologic section from the plaque at the right forearm showed dermal edema with diffuse infiltration of predominantly neutrophils and nuclear dust and lymphocytes in the dermis with extravasation of red blood cells.(Original magnification: A,x10; B,x20; C,x40.)

Skin biopsy from a plaque at the right forearm showed dermal edema with a diffuse infiltration of predominantly neutrophils with nuclear dust and lymphocytes in the dermis and an extravasation of red blood cells compatible with Sweet's syndrome [Figure 3]. On the same day in which the skin biopsy was performed, the laboratory investigations were as followed i.e. total white blood cell count 300 / μ L [too low for differential count], absolute neutrophil count 0%, hematocrit 23.3%, platelet count 38,000/ μ L, aspartate aminotransferase 75 U/L, alanine aminotransferase 88 U/L, total bilirubin 17.6 mg/dL, direct bilirubin 16.2 mg/dL, alkaline phosphatase 93 U/L. Blood, urine, pleural fluid, and tissue culture for bacteria all revealed no growth for organisms.

Colchicine was prescribed at the dosage of 0.6 mg/day, adjusted for renal and hepatic impairment. Tazobactam + piperacillin was discontinued and replaced by ciprofloxacin and amphotericin B. Systemic corticosteroid was not prescribed as sepsis could not be ruled out. Four days later, fever and the skin lesions began to subside. On the 18th day of admission, skin

lesions completely subsided and the colchicine was discontinued.

Discussion

The skin lesions of Sweet's syndrome are described as tender erythematous or violaceous plaques or nodules³ often arising on extremities, head and neck⁴. Fever can precede the skin disease or occur concurrently during the entire episode of the dermatosis. Other symptoms include arthralgia, conjunctivitis, malaise, myalgia, and headache^{4,5}.

Von den Driesch proposed the criteria for the diagnosis of Sweet's syndrome in 1994[Table]³. Patients with Sweet's syndrome were generally classified into 3 categories: [1] Classic Sweet's syndrome, which may be associated with infection [gastrointestinal or upper respiratory tract], inflammatory bowel disease, or pregnancy, [2] Paraneoplastic Sweet's syndrome that is associated with the presence of hematologic or solid organ malignancies, and [3] Drug-induced Sweet's syndrome that is most frequently associated with the administration of granulocyte colony-stimulating factors [G-CSF]^{6,7}.

Table Criteria for diagnosis of Sweet's syndrome***Major Criteria:** required for diagnosis

- ☐ Abrupt onset of tender or painful erythematous plaques or nodules occasionally with vesicles, pustules, or bulla
- ☐ Predominantly neutrophilic infiltration in the dermis without leukocytoclastic vasculitis

Minor Criteria: two required for diagnosis

- ☐ Preceded by a non specific respiratory or gastrointestinal tract infection or vaccination or associated with:
 - ☐ Inflammatory diseases such as chronic autoimmune disorders, infections
 - ☐ Hemoproliferative disorders or solid malignant tumors
 - ☐ Pregnancy
- ☐ Accompanied by periods of general malaise and fever [$> 38^{\circ}\text{C}$]
- ☐ Laboratory values during onset: ESR > 20 mm; C-reactive protein positive: segmented-nuclear neutrophils $> 70\%$ in peripheral blood smear; leukocytosis $> 8,000$ [three of four of these values necessary]
- ☐ Excellent response to treatment with systemic corticosteroids or potassium iodide

*Taken from von den Driess P, J Am Acad Dermatol 1994; 31: 544

Our patient developed a cutaneous eruption 10 days after a course of chemotherapy during a period of agranulocytosis. The result of the skin biopsy from the plaque at his right wrist and quick response to the treatment with colchicine confirmed the diagnosis of Sweet's syndrome. Maculopapular rash at his back seemed to be due to an exanthematous drug eruption because the lesion improved after piperacillin and tazobactam had been switched to ciprofloxacin. As for the patient's jaundice, cytarabine was suspected. His jaundice has been improved ever since cytarabine was discontinued. Granulocyte-colony stimulating factor [G-CSF] was not prescribed for this patient.

Cohen et al. noted that neutrophilia might be absent in up to 50% of malignancy associated Sweet's

syndrome as well as Probert et al^{4,8}. They reported case series of 4 patients who developed Sweet's syndrome in neutropenic patient caused by chemotherapy for treating the underlying hematologic malignancy. Chatham-Stephens et al, also reported a case of an adolescent male with chronic pancytopenia that was secondary to Fanconi anemia who presented with acute respiratory distress and developed characteristic cutaneous lesions of Sweet's syndrome 4 months later. Thus, metachronous Sweet's syndrome was diagnosed due to neutrophilic infiltration in the lung parenchyma, dermis, and subcutis⁹.

The cause of Sweet's syndrome is unknown. Infectious processes, mechanical irritation, dysregulated cell signaling, and exaggerated immune response with

cytokine induced neutrophils release have been postulated as possible etiologies^{2,3}. Treatment with exogenous G-CSF has been associated with Sweet's syndrome, possibly due to the up-regulation of neutrophil function and secondary release of cytokines^{10,11}. The mechanism of malignancy-associated Sweet's syndrome may involve aberrant cytokine signaling to account for the pathologic lesions despite relative neutropenia^{8,12}. Piette et al. hypothesized that leukemic cells are able to differentiate into clonal neutrophils and that this differentiation may be prompted by chemotherapy¹³. Skin may also be a site of sequestration of viable neutrophils in spite of the intravascular neutropenia⁸.

Rapid resolution of Sweet's syndrome usually occurs after the treatment with systemic corticosteroids, potassium iodide, or colchicine¹⁴. Since sepsis could not be ruled out in our patient, colchicine was prescribed instead of prednisolone with complete resolution of lesions within 18 days.

In conclusion, we report a case of Sweet's syndrome in an agranulocytopenic patient as a result of chemotherapy for acute myeloid leukemia. Sweet's syndrome cannot be entirely ruled out in neutropenic patients with hematologic malignancies undergoing chemotherapy.

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