Case Report

Sweet's Syndrome Associated with Mycobacterium Tuberculosis and Cervical Cancer: A Case Report

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A case of Sweet's syndrome associated with pulmonary tuberculosis and cervical cancer was reported. A 34-year-old Thai woman had pulmonary tuberculosis. After treatment with anti-tuberculosis for two months, she developed erythematous papules, plaque, pustule-like lesions at face and limbs, extremities, palms and soles spare truncal area. She also had high fever and muscle pain. Biochemical test at that time showed only leukocytosis and thrombocytosis, no correlation to any other infections, malignancy or connective tissue disease was found. We continued treating with anti-tuberculosis, simultaneously with systemic steroid and occasional colchicin for her cutaneous and hematologic conditions. The disease flared up for few episodes which could be controled with systemic steroid before it subsided. However, she was diagnosed and treated for cervical carcinoma few years later. Eventhough is not very common, the chance of having tuberculosis and cervical cancer should be considered in patients presenting with Sweet's syndrome.

***Keywords** : Acute febrile neutrophilic dermatosis (Sweet's syndrome), Tuberculosis, Anemia, Thrombocytosis, Cervical cancer*

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Sweet's syndrome is a disorder characterized by tender raised erythematous plaques with pseudoblistering and occasionally pustules on the face, neck, chest and extremities accompanying by fever, general malaise, arthralgia, ocular involvement and sometimes flu-like symptoms. It is mainly found in middle-aged women.

Sweet's syndrome has been classified to three main clinical settings: classical or idiopathic, malignancy associated, or drug-induced Sweet's syndrome. Association with infections and pregnancy is less found. In this case the clinical symptoms of Sweet's syndrome were presented together with both tuberculosis and cervical cancer, which was very uncommon.

Case Report

A 34-year-old woman who was treated for pulmonary tuberculosis for 2 months, developed high grade fever and malaise and skin lesion show erythematous, tender, papulo-nodulo-plaque and targetoid lesions (Fig. 1-3) located at face, arms, legs and spare trunk. Histological specimen taken from a skin lesion revealed marked dermal infiltrated of neutrophils without evidence of vasculitis (Fig. 4,5). Skin culture for bacteria, fungus, mycobateria and atypical mycobacteria were all negative. Her blood constituent also showed marked elevation of leukocytes dominant in neutrophils and thrombocytosis. WBC count was 34.9 x 10^3 cells/μL with 80.0% neutrophils, 9.0% lymphocyte, 4.0% monocyte, 7.0% eosinophil, hemoglobin level was 8.5 g/dL, platelets count was 747 x 10^3 cells/μL, BUN concentration was 13 mg/dL, creatinine level was 0.5 mg/dL. Peripheral blood smear showed evidence of mature neutrophils with no immature myeloid forms and increased platelets. In addition, there was no evidence of acute leukemia on the peripheral blood smear. Anti-HIV was non-reactive with CD4 = 25.0% (2,450 cells/mm^3). ANA was negative. Rheumatoid factor was negative. Bone marrow biopsy revealed marked hypocelular trilineage marrow (10.0% of cellularity with gelatinous change, absence of megakaryocytes, and presence of hemosiderophage also negative for acid fast bacilli). Chromosome study was normal. Chest radiography demonstrated scattered nodular infiltrates

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throughout both lungs.

At that time she was treated by ciprofloxacin for suspected of atypical mycobacterium infection and both fever and skin lesion seemed to relieve. After that, symptoms and skin lesion recurred. This time a favorable outcome was observed following administration of systemic steroid. Subsequently, there were few episodes of attack few months later and each time the patient was successfully treated with systemic steroid and/or colchicines simultaneously. Continued anti-tuberculosis was needed according to her pulmonary tuberculosis and she was free of any symptoms after few attacks since then. Three years later, she was diagnosed and treated for cervical cancer.

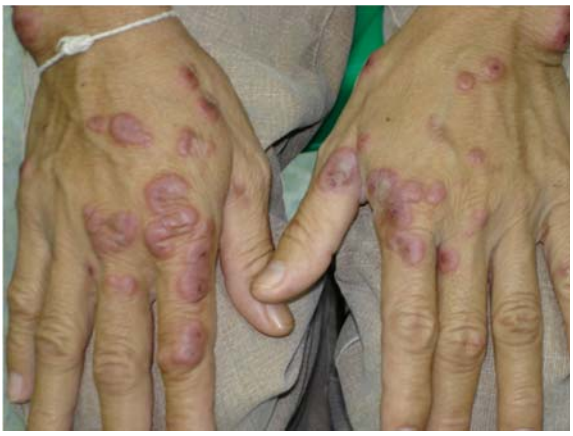

Fig. 1 A violaceous plaque on dorsal hands

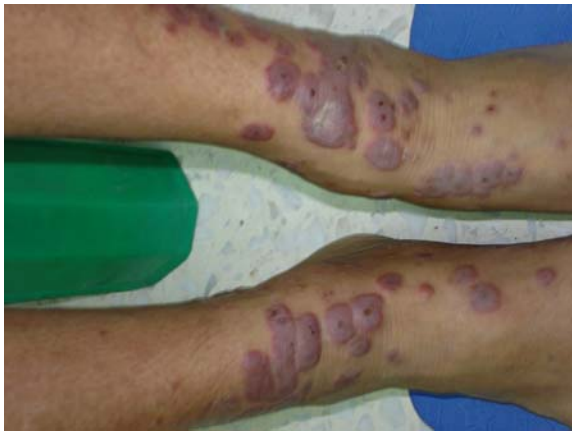

Fig. 2 Violaceus plaques on lower legs

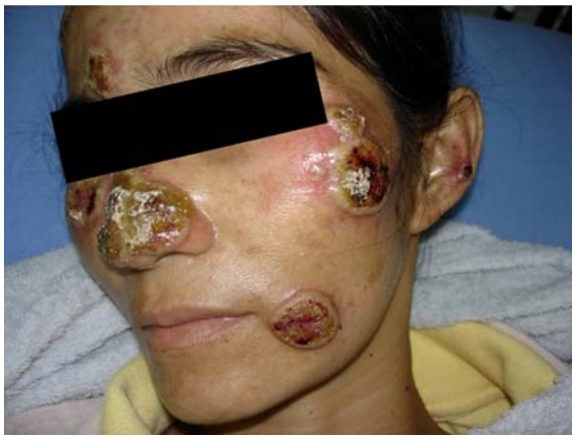

Fig. 3 Umbilicated bleb-like on face

Discussion

Sweet's syndrome or acute febrile neutrophilic dermatosis was described by Robert Douglas Sweet in 1964[1]. This type of disease is characterized by recurrent painful plaque-forming inflammatory papules, fever, peripheral leukocytosis and a diffuse dermal neutrophilic infiltrates of which well respond to glucocorticoid therapy. The disease has no racial predilection, it is classified into idiopathic, malignancy-associated and drug associated forms. For malignancy-associated Sweet's syndrome which occur about 20.0% of cases[2]. Hematologic malignancy is usually acute myelogenous leukemia[3,4] while other solid tumors frequently occurring in genitourinary organs (37.0%), breast (23.0%) and gastrointestinal tracts (17.0%)[5]. While malignancy-associated form equally affects both sex, idiopathic and drug-associated forms are predominant in women.

Although the disease is generally associated with malignancy or idiopathic, infections also have some roles in this dermatosis according to some evidences such as Yersinia enterolyica that can be treated with systemic antibiotics. Other infections like atypical mycobateria[6], cytomegalovirus, hepatitis (chronic active), histolasmosis, human immune deficiency virus, leprosy, salmonellosis, toxoplasmosis, tuberculosis[7], tonsillitis, valvovaginitis may possibly be the cause of disease. Although there are increasing reports[8] (mostly from Thailand) of non-Mycobacterium tuberculosis like Mycobacterium fortuitum, Mycobacterium absessus/ulceran, Mycobacterium tuberculosis is still prevalently associated with this disease.

The pathogenesis of this disease is not known. There is some postulation about the role of circulating autoantibodies, immune complexes, or cytokines. This may be pointed to hypersensitivity reaction to pathogen to bacteria, viral or even tumor antigens presented. Even not unequivocally proven, it is

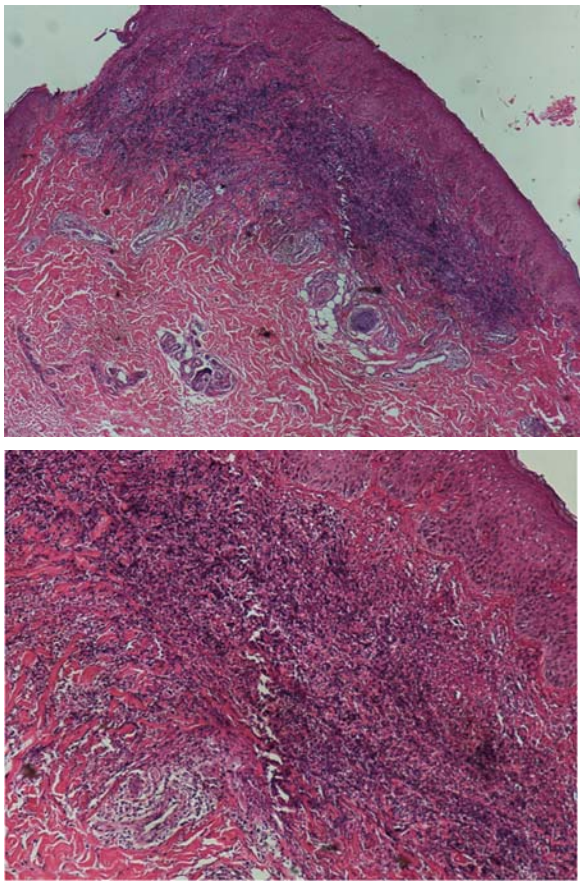

Fig. 4-5 Dense dermal infiltrate of neutrophils at upper dermid hematoxylin and eosin stain)

currently thought that cytokine dysregulation of interleukin(IL)1, IL-3, IL-6, IL-8, G-CSF, granulocyte macrophage colony stimulating factor (GM-CSF) and interferon gamma may potentially be involved in causing the lesions and symptoms of the disease[9]. While there are increasing reports about drug that participated with the disease such as all-trans retinoic acid, carbamazepine, hydralazine, levonorgestrel/ethinyl estradiol, minocycline,doxycycline, trimethoprime/sulfamethoxazole, granulocyte colony-stimulating factor (G-CSF) has been more commonly associated, supporting the idea of the autoantibodies reaction[4,5,10]. In this case, she had been previously diagnosed with tuberculosis as evident from the signs in her lung and some nonspecific lesions of chest x-ray. However, no concrete data was found to support the diagnosis. Her sputum AFB or culture was negaitive for tuberculosis. Thus, she may be purely idiopathic Sweet's syndrome with systemic manifestations. Pulmonary involvement may manifest as dyspnea, chronic cough or pulmonary infiltrates or effusion on chest radiograph[11]. Fortunately, most cases of sweet syndrome with pulmonary and other systemic involvement tend to highly responsive to glucocorticoid therapy[12].

Later, the patient was diagnosed with cervical cancer and this may be related to the rare type of malignancy-associated Sweet's syndrome. Only four cases were reported so far and one Asian patient was reported for this dermatosis preceding the initial diagnosis of cercival cancer like in our patient[13-14]. For malignancy associated-type, there is a tendency to develop more severe skin lesions, involvement of mucous membrane or other extracutaneous site. Abnormal platelet counts and high rate of recurrences are also involved[15-16]. Similarly, this case showed severe painful blisters, lung infiltrations by chest X-ray, symptoms mimicking tuberculosis, thrombocytosis and few recurrence episodes of this dermatosis. Malignancy associated Sweet's syndrome may either precede the occurrence of underlying disease or after or at the time of diagnosis. In this case cancer was found three years later. Therefore, repeated occurrence of symptoms, abnormal platelet count and anemia especially in elderly patient should be more considered in malignancy-associated Sweet's syndrome.

Potential conflicts of interest

None.

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รายงานผู้ป่วย Sweet's syndrome ร่วมกับวัณโรคปอดและมะเร็งปากมดลูก

อรศิริ เสรีรัตน์, ยุพิน ไทยพิสุทธิกุล

รายงานผู้ป่วย Sweet's syndrome ร่วมกับวัณโรคปอดและมะเร็งปากมดลูก ผู้ป่วยหญิงอายุ 34 ปี หลังจากรักษาโรควัณโรคปอด 2 เดือนได้เกิดตุ่มแดงเจ็บ ตุ่มหนองที่ หน้า แขน ขา พร้อมด้วยอาการไข้สูง ปวดกล้ามเนื้อ จากผลการตรวจทางห้องปฏิบัติการ พบ ภาวะโลหิตจาง เม็ดเลือดผู้ป่วยไม่มีอาการแสดงของโรคมะเร็งหรือ autoimmune disease และสามารถควบคุมอาการด้วย prednisolone และ colchicin ผู้ป่วยมีการกลับเป็นซ้ำ 2-3 ครั้ง ก่อนจะหายไปในที่สุดแต่ภายหลังตรวจพบว่าผู้ป่วยมีโรคมะเร็งปากมดลูกด้วย