Sweet's syndrome with idiopathic epididymitis

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Sweet's syndrome (SS), also known as acute febrile neutrophilic dermatosis, is a rare condition presenting with an abrupt onset of fever and tender skin lesions with neutrophilic infiltration in the dermis, accompanied by leukocytosis [1]. Although it is not always possible to determine the etiology, SS most commonly arises as a consequence of systemic disorders. Approximately 20% of SS cases are associated with solid tumor or hematologic malignancy, most often acute myelogenous leukemia [2–5]. Cases of drug-induced SS were described after exposure to a wide variety of medication, including granulocytecolony stimulating factor [6] and other anticancer agents, antibiotics, antiepileptic, antidepressant, antihypertensive drugs, and oral contraceptives [5–8]. Pharmacotherapy-associated SS accounts for approximately 12% of SS cases [3]. The classic (idiopathic) SS type may occur in association with infections, autoimmune disorders or pregnancy [4, 9].

A 54-year-old sexually inactive man presented with acute onset of skin rash, beginning on the chest 3 days before and spreading to the face, neck, back, shoulders and arms together with intermittent fever up to 40°C and malaise. Simultaneously, the patient complained of discomfort in the posterior part of the left testicle accompanied by redness and increased warmth of the scrotum. There was no history of dysuria or urethral discharge.

During the previous 3 years, the patient had several episodes of similar, but milder symptoms, but has never been diagnosed with SS. The patient underwent rheumatologic evaluation for Still's disease, which was excluded. Oral glucocorticosteroid therapy with prednisone (10 mg daily) was recommended, however it did not prevent further relapses.

Physical examination at admission to the Department of Dermatology, Sexually Transmitted Diseases and Immunodermatology, revealed multiple, tender, erythematous plaques located on the face, neck, trunk and both upper extremities (Figures 1 A, B). No mucosal lesions in the oral cavity were found. Histopathological examination of the skin sample obtained from the back demonstrated dense neutrophilic infiltration with intense papillary dermal edema (Figure 2). An elevated level of white blood cell count (12.66 × 10^3/µl; range: 4.0–10.0 × 10^3/µl) with 92% neutrophils, and mild anemia (hemoglobin 10.9 g/dl; range: 12.0–18.0 g/dl) were found in the whole blood count. The C-reactive protein (CRP) and procalcitonin plasma concentrations were increased (337.92 mg/l and 0.875 ng/ml, respectively; range 0.1–5.0 mg/l and 0–0.5 ng/ml). Tests for viral hepatitis, human immunodeficiency virus and lues yielded negative results. The patient serum was negative for ANA antibodies. Antineutrophil cytoplasmic and anti-cyclic citrullinated peptide antibodies, rheumatoid factor, complement C3 and C4, antistreptolysin O antibody, serum creatinine, liver function tests, creatine kinase and urinalysis were negative or in normal range. Expanded diagnosis for malignancies or infections was negative. No signs of endocarditis were found in transthoracic echocardiography. Gastroscopy, chest X-ray and abdominal ultrasound have not revealed any abnormalities. Bilateral epididymitis was confirmed by the urologist based on the ultrasound examination of testicles. Blood and urine cultures were negative and no infectious agent was identified.

Based on the above findings, a final diagnosis of SS associated with idiopathic epididymitis was established. Due to elevated concentrations of inflammatory markers and suspicion of sepsis, the patient was initially treated with intravenous antibiotics according to clinical microbiologist's recommendations. However, cloxacillin (8.0 g daily) and ceftriaxone (2.0 g daily), followed by vancomycin (3.0 g daily) combined with piperacillin-tazobactam (13.5 g daily) did not produce any improvement. Pyrexia, leukocytosis with neutrophilia and raised CRP have persisted. Oral prednisolone of 50 mg once daily was started

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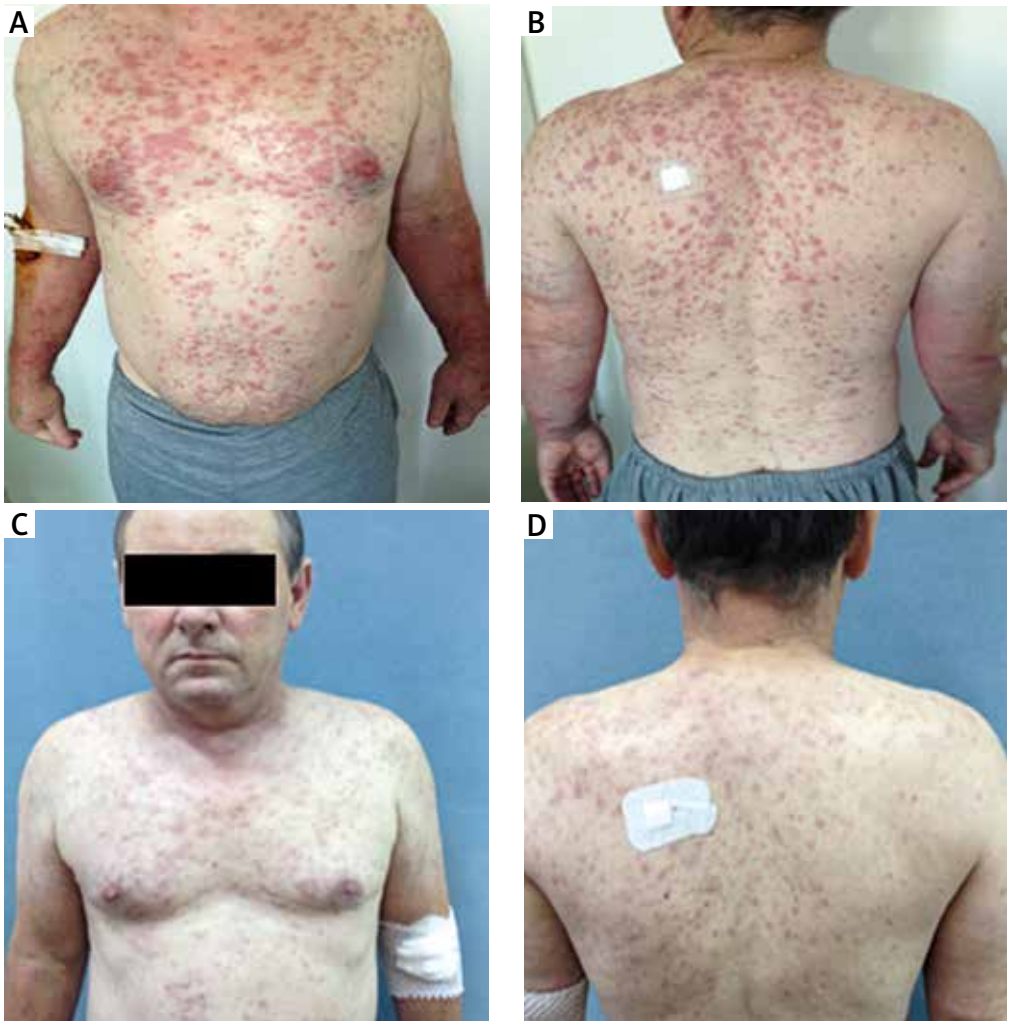

Figure 1. Erythematous skin lesions located on the chest, abdomen, back and both upper extremities (**A, B**). Rapid improvement of skin lesions on day 2 of systemic glucocorticosteroids (**C, D**)

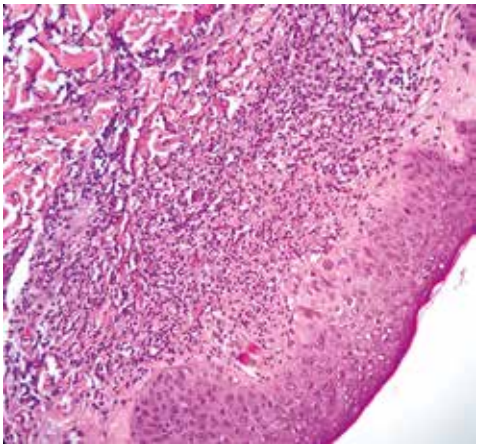

Figure 2. Histopathology of the skin biopsy taken from the trunk showed papillary dermal edema and diffuse infiltration of predominantly neutrophils, with no features of vasculitis (H + E staining, 100×)

when infectious investigation returned negative, leading to rapid resolution of fever and skin lesions (Figures 1 C, D) with normalization of laboratory parameters.

Classical SS occurs predominantly in females, aged between 30 and 50 years [4]. Diagnostic criteria for SS were introduced by Su and Liu in 1986 [10], and were modified by von den Driesch in 1994 [11] to include: (i) abrupt onset of painful erythematous plaques or nodules; (ii) histopathologic examination of dense neutrophilic infiltrate without evidence of leukocytoclastic vasculitis; (iii) pyrexia of > 38°C; (iv) association with underlying hematologic or visceral malignancies, inflammatory diseases, pregnancy, prior upper respiratory or gastrointestinal infections, or vaccination; (v) good response to treatment with systemic glucocorticosteroids or potassium iodide; and (vi) abnormal laboratory values at presentation (to include three of: erythrocyte sedimentation rate of > 20 mm/h; positive CRP; > 8000 leuko-

cytes; and > 70% neutrophils). Both of major (i and ii) and two out of four minor (iii–vi) criteria are required to establish diagnosis of classical SS. Noteworthy, in our patient, two major (i and ii) and three minor criteria (iii, v, vi) were fulfilled [10].

Various conditions, such as autoimmune disorders, including rheumatoid arthritis, Sjögren's syndrome, systemic lupus erythematosus, relapsing polychondritis, inflammatory bowel disease, have been associated with classical SS. This occurrence of SS has also been reported following infections, most frequently upper respiratory tract or gastrointestinal tract infections [4]. Other cases related to tuberculosis, otitis media, parotitis and cholangitis have been reported [11–13]. However, an association with epididymitis, up to our best knowledge, has never been described. Even though infectious background of epididymitis has not been confirmed in our case, inflammatory state connected with epididymitis might have been a causative factor of SS. Therefore, we assumed that the fourth criterion for SS has been fulfilled in the described patient.

Treatment of SS should be guided with consideration of the underlying cause. In our case application of antibiotics was unsuccessful, whereas treatment with corticosteroids, which are a gold standard for SS management, has resulted in a rapid alleviation of disease symptoms. Other agents that have been previously reported as effective in the treatment of SS are potassium iodide (900 mg daily) and colchicine (1.5 mg daily). Indomethacin, cyclosporine, dapsone, clofazimine, chlorambucil, cyclophosphamide may be considered as the second-line treatment [4, 14].

Faced with the occurrence of an SS, an inflammatory disorder has to be sought as a potential cause and epididymitis has to be added to the list of possible SS triggering conditions.

Conflict of interest

The authors declare no conflict of interest.

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