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A retrospective analysis of Sweet's syndrome in a tertiary care hospital in Nepal: A BPKIHS perspective

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Abstract

Sweet's syndrome (the eponym for acute febrile neutrophilic dermatosis) is characterized by a constellation of clinical symptoms, physical features, and pathologic findings which include fever, neutrophilia, tender erythematous skin lesions (papules, nodules, and plaques), and a diffuse infiltrate consisting predominantly of mature neutrophils that are typically located in the upper dermis without vasculitis.

To study the clinico-pathological features, clinical course and treatment of patients with sweets syndrome.
A retrospective observational analysis of 12 diagnosed cases of sweet's syndrome attending and admitted in the Department of Dermatology from June 2003- April 2009 were considered in this study.

The study comprised of 9 females and 3 males (3:1) between the age group of 22-73 years. Typical lesions of sweets syndrome were present in all cases and the duration of illness ranged from 3-8 days. Constitutional symptoms of fever, pain and malaise were present in all and the extremities were the most common site of involvement 12 (100%). Leucocytosis was present in 7 (58.3%), raised ESR in 9 (75%) and raised C reactive protein in 7(58.3%) patients. Characteristic histological features were recorded in specimens of all patients. 9 (75%) patients responded promptly to systemic oral corticosteroids while 3 (25%) were treated with intravenous steroids. Complete Response was seen in 7 (58.3%), partial response in 5 (41.6%) and recurrence in 1(8.3%) patient after therapy

Characteristic skin lesion, histopathological diagnosis and relevant abnormal laboratory parameters can act as a useful diagnostic tool in patients with sweet's syndrome.

Key words: Sweets syndrome, acute febrile neutrophilic dermatosis, malaise.

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Introduction

Sweet's Syndrome (SS) or acute febrile neutrophilic dermatosis) is characterized by typical erythematous, tender, papulonodulo - targetoid plaque lesions, with or without pseudovesiculation, associated with fever and malaise of acute onset. A neutrophilic dermal infiltrate without vasculitis, peripheral neutrophilia, and a dramatic response to systemic corticosteroid therapy are diagnostic. The clinical appearance, course, and histopathology suggest that it may represent a form of hypersensitivity reaction to bacterial, viral, or, perhaps, tumor antigens.[1] SS presents in three clinical settings: classical (or idiopathic), malignancy-associated, and drug-induced. Classical Sweet's syndrome (CSS) usually presents in women between the ages of 30 to 50 years, it is often preceded by an upper respiratory tract infection and may be associated with inflammatory bowel disease and pregnancy. [1-4] The malignancy-associated Sweet's syndrome (MASS) can occur as a paraneoplastic syndrome in patients with an established cancer such as hematologic malignancies, including acute myelogenous leukemia, lymphoma, and dysproteinemia, comprise most cases, but adenocarcinomas of the lung, breast, and colon are also important to rule out in addition to testicular, ovarian, bladder, and prostatic malignancies.[5]

Drug-induced Sweet's syndrome (DISS) most commonly occurs in patients who have been treated with granulocyte-colony stimulating factor, however, other medications may also be associated with DISS like furosemide, hydralazine, trimethoprim-sulfamethoxazole, minocycline, nitrofurantoin, co-trimoxazole, carbamazepine, diazepam, isotretinoin, levonorgestrel/ ethinyl estradiol, and all-trans retinoic acid. [2]

The current diagnostic criteria for SS recognize the variable presentation of this dermatosis (Table 1).[1] The minor criteria identify the associations, clinical and laboratory findings. The distribution of Sweet's syndrome cases is worldwide and there is no racial predilection. [1, 2] This case series is thus the first of its kind being reported from Nepal.

Materials and methods

This is a retrospective study of patients from B.P. Koirala Institute of Health Sciences, Dharan, a tertiary care hospital in eastern Nepal, between June 2003 and April 2009. Patients were identified from the hospital pathology and clinical dermatology databases. Case histories, along with investigation results and histology slides, were reviewed. Patients meeting the clinicopathological criteria for a diagnosis of Sweet's syndrome were included in this analysis. Their presenting symptoms, cutaneous lesions, histopathologic features, laboratory investigations, associated diseases, treatment, and clinical course were recorded (Table 2, 3)

Age and Sex distribution

All patients were between 22-73 years (mean 46.53±18.55) of age. There were 9 females (35 days to 57 years) and three males (10–40 years) and the female to male ratio was 3: 1.

Duration of disease

The mean duration of the disease was 3-8days (mean 6.08±1.62)

Cutaneous/ extracutaneous lesions and systemic features

All patients presented with multiple, typical, tender erythematous skin lesions including papules, nodules, and plaques with pseudovesiculations. The lesions were bilaterally symmetrical involving the hands, forearms, arms, legs, and thighs in 8/12(66.6%) patients. The trunk was involved in 6/12 (50%), face in 6/12 (50%) and the genitalia was involved in 1/12(8.33%) patient. 1 patient presented with localised sweets syndrome involving the right forearm. Constitutional symptoms of fever (temperature ≥38 °C) and myalgia was present in all patients.

Associated comorbidity and Drug intake

History of upper respiratory tract infection, pain abdomen, pain over the bilateral hip joint and loose motion was present in 1(8.33%) patient each. 1 patient also presented with history of lesions during the third trimester of pregnancy with fetus loss at 35 weeks of gestation. Drug history of ciprofloxacin intake was present in 1 patient.

Laboratory Findings

Haemoglobin (Hb)d" 9gm% was present in 2/ 12(16.6%) patients while an erythrocyte sedimentation rate (ESR) of ≥ 20 mm was present in 11/12(91.6%) patients. 9/12 (75%) patients presented with a total leucocyte count (TLC) ≥ 8000/cm^3 and absolute neutrophil count ≥ 70%. Elevated C reactive protein d" 8mg/L was also present in 8/12 (66.6%) patients. (Table 3)

Histopathologic Findings

All patients underwent skin biopsies and had histological findings of a dense neutrophilic infiltrate within the dermis and the absence of leukocytoclasis. (Fig 2 and 3)

Treatment and Clinical Course

Nine out of twelve (75%) patients were started on oral corticosteroids with clinical response seen in 1-3 weeks (mean 2.11 ± 0.78days). Intravenous dexamethasone was started in 3/12 (25%) patients. Complete resolution was seen in 7/12 (58.33%) patients while partial resolution of lesions was seen in 5/12 (41.66%) patients after commencing of the therapy.

Discussion

The syndrome was originally described by Dr. Robert Douglas Sweet in the August September 1964 issue of the British Journal of Dermatology as an "acute febrile neutrophilic dermatosis"[2]

Sweet's syndrome (SS) can present in several clinical settings: classical (or idiopathic) Sweet's syndrome, malignancy associated Sweet's syndrome, and drug-induced Sweet's syndrome with a worldwide distribution with no racial predilection. [1,2] Though sweet syndrome occurs without any predilection for age or sex, the initial episode of classical Sweet's syndrome most frequently occurs between the ages of 30 to 60 years [3] and predominantly affects women.It may be associated with infection (upper respiratory tract or gastrointestinal tract), inflammatory bowel disease or

Table 2: Demographic and Clinical spectrum of patients with sweets syndrome

Case	Age / Sex	Duration (days)	Symptoms	Distribution of skin lesion	Associated conditions/ Drug intake	Treatment / Remarks	Follow up / Outcome (weeks)
1	28 / F	5	Fever, pain, myalgia	Upper and lower extremities	-	Oral prednisolone	Complete resolution (CR) in 3 weeks
2	22/F	7	Fever, pain, myalgia	Face	-	Oral prednisolone	CR in 1 weeks
3	65/F	7	Fever, pain	Upper extremitis	-	Oral prednisolone	CR in 2 weeks
4	63/F	8	Fever	Upper and lower extremities	Pain abdomen	Intravenous Dexamethasone	Partial resolution (PR) in 2.2 weeks
5	55/F	5	Fever, pain, myalgia	Upper and lower extremities, trunk, face	-	Intravenous Dexamethasone	CR in 3 weeks
6	25/F	3	Fever, pain	Lower extremities, face, trunk, genitalia	Pregnancy	Oral prednisolone	PR in 2 weeks
7	30/M	7	Fever, pain	R forearm	-	Oral prednisolone	CR in 3 weeks, Recurrence
8	73/M	7	Fever, pain, myalgia	Upper and lower extremities, trunk, face	Drug Ciprofloxacin	Intravenous Dexamethasone	PR in 1.3 weeks
9	27/F	8	Fever, pain	Upper and lower extremities	-	Oral prednisolone	CR in 1.5 weeks
10	53/F	5	Fever, pain	Upper and lower extremities, trunk, face	Pain hip joint	Oral prednisolone	PR in 1 week
11	40/F	4	Fever, pain, myalgia	Upper and lower extremities, trunk, face	Throat pain	Oral prednisolone	CR in 3 weeks
12	63/M	7	Fever, pain	Upper and lower extremities, trunk, face	Loose motion	Oral prednisolone	PR in 2.4 weeks

Table 3: Investigation profile of patients with sweet's syndrome

Case No	Hb (g %)	ESR (mm 1st hr)	TLC (/cm^3)	Neutrophils	CRP(IU)	Histopathology
1	11.6	34	15 000	70	96	Dense neutrophilic infiltration in the dermis and absence of leukocytoclasis. Compatible with Sweet's syndrome
2	12.1	50	9700	88	-	Compatible with Sweet's syndrome
3	10.1	33	11900	85	24	Compatible with Sweet's syndrome
4	14.1	55	18400	81	30	Compatible with Sweet's syndrome
5	9.7	40	7000	80	-	Compatible with Sweet's syndrome
6	10.5	46	3000	42	26	Compatible with Sweet's syndrome
7	10.2	50	12000	68	40	Compatible with Sweet's syndrome
8	6.5	14	9000	60	-	Compatible with Sweet's syndrome
9	10.5	50	22000	85	34	Compatible with Sweet's syndrome
10	11.0	23	13000	76	40	Compatible with Sweet's syndrome
11	9.2	50	15000	80	35	Compatible with Sweet's syndrome
12	8.5	20	12000	77	-	Compatible with Sweet's syndrome

ESR: Erythrocyte Sedimentation Rate ; **Hb**: Haemoglobin; **TLC**:Total leucocyte count, **CRP**:C-Reactive Prot

pregnancy [2,4]. This case series, in the idiopathic subgroup, also showed a female preponderance (4.5:1) with patients in the 22-65 year group.

The most frequently affected sites of SS are known to be the upper extremities, head and neck.[2,3,6] The upper extremities were almost universally involved in our study population, seen in 66.6% of the patients. (Table 1) Fever was the most common symptom in this report seen in all patients, which was comparable to the study done by Anavekar et al [8] and Mahajan et al [9] followed by generalized pain and myalgia. Loose motion, pain abdomen, upper respiratory tract infection and bilateral hip joint pain were observed in one patient each. The association of pregnancy with SS is not uncommon.[3] Pregnancy in the third trimester was associated in one patient. She gave history of recurrent lesions of SS in the past two successive pregnancies which resulted in still birth. Only one patient gave history of appearance of lesions after the intake of ciprofloxacin for an ill defined swelling on the right earlobe two days back.There was a similar history about a year back but the patient was lost to follow up for rechallenge However malignancy induced SS and extra cutaneous manifestations were not found among the study population.

Although the etiology of SS is unknown, an immunologic mechanism with an abnormal tissue response to certain unknown antigens may play a role. A hypersensitivity reaction to an eliciting bacterial, viral, or tumor antigen may promote the development of SS.[1,2]

Similarly Circulating autoantibodies, cytokines, dermal dendrocytes, human leukocyte antigen serotypes, immune complexes, and leukotactic mechanisms have all been postulated to contribute to the pathogenesis of Sweet's syndrome.[2]

The most consistent laboratory abnormalties in patients with Sweet's syndrome are peripheral leukocytosis with neutrophilia and elevated erythrocyte sedimentation rate.[7] However, an elevated white blood cell count is not always observed in all patients with biopsy-confirmed Sweet's syndrome [8]

Similarly 9/12 (75%) patients presented with a total leucocyte count (TLC) $\geq$ 8000/cm^3 and absolute neutrophil count $\geq$ 70% in the study while the reports vary from 68% [10]- 33.3% [9] Evaluation of acute phase reactants (such as the erythrocyte sedimentation rate or C-reactive protein) should be done in all patients [3] ESR was raised in 11/12 patients and CRP detected in eight cases indicate some infective focus.

All patients in this study underwent a histopathological examination to confirm the clinical diagnosis and showed report consistent with SS.

Systemic corticosteroids are the "gold standard" of therapy for SS. Dermatosis-associated symptoms improves promptly after treatment has been started and the cutaneous lesions resolve subsequently. [2.3.7] The response to prednisolone in this report was prompt, leading to the resolution of clinical symptoms and lesions. Oral corticosteroids with 1 mg/kg/day of prednisolone as a single oral morning dose, have been the main stay of treatment options for most patients in the study while those who had presented with extensive lesions were started on intravenous steroids on dexamethasone equivalent and one patient was treated with pulse 100mg of dexamethasone. The patients were then tapered or switched to the oral prednisolone therapy. All showed clinical response within a week of starting therapy. (Table 3)

Steroid-sparing agents may play a role in systemic diseases and include potassium iodide (30-300 mg thrice a day), dapsone (200 mg per day), colchicine (1-1.5 mg per day), and nonsteroidal antiinflammatory drugs. Cyclosporine (4 mg/kg per day), mycophenolate mofetil, thalidomide, clofazimine, methotrexate, and interferon a combined with hydroxyurea and chlorambucil can also be used. [2,7] It was but not seen to be used in this case .

The retrospective nature of this analysis has prevented the acquisition of a complete set of data, with imperfect investigation results. Patients were not followed up long term with regard to their SS. Only a small number of patients were recruited, perhaps a reflection of the infrequency of this syndrome, thus this descriptive study is being reported for the first time from Nepal. Still their overall clinicopathologic and therapeutic spectrum does not appear to differ from the established picture of SS reported worldwide.

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