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Case Report

A rare association of Sweet syndrome in a diagnosed case of pemphigus vulgaris

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Abstract Sweet syndrome (SS) is a rare neutrophilic dermatosis. It is characterized by acute onset of fever and painful erythematous papules, plaques and nodule on skin. SS may affect other organs. Pemphigus Vulgaris is an immune mediated condition which is characterized by the flaccid blisters affecting mainly trunk and mucosae with painful erosions. A 59 years old male, diagnosed case of Diabetes Mellitus and Pemphigus vulgaris, presented to our outpatient department with fever and multiple painful erythematous plaques, nodules and ulcers on both lower limbs. He was in remission phase of pemphigus vulgaris with immunosuppressants namely steroids and azathioprine. Patient fulfilled diagnostic criteria of Sweet syndrome. During his stay in the department of dermatology, he developed neurological manifestations in the form of weakness of the left proximal upper limb with altered sensorium. Cerebrovascular infarct was confirmed on computed tomography (CT) scan. Cerebrovascular infarct is a very rare manifestation of neuro-Sweet disease. SS is associated with many conditions. It is reported in various autoimmune conditions. But as far as pemphigus vulgaris is concerned SS is reported very rarely with pemphigus vulgaris.

Key words
Sweet Syndrome; Pemphigus vulgaris; Neutrophilic dermatosis.

Introduction

Sweet syndrome (SS), also known as acute febrile neutrophilic dermatoses, is characterized clinically by fever, abrupt onset of tender, erythematous, papules, plaques or nodules and peripheral neutrophilia.[1] SS affects mostly upper limbs, trunk, head and neck and is usually accompanied by arthralgia. Other systems may be involved in sweet syndrome.[2]

SS is usually idiopathic but many triggering factors may precede the onset of SS which include infections, vaccinations, drugs, pregnancy, malignancy, and inflammatory conditions.[3]

Skin biopsy shows papillary dermal edema and dense dermal infiltrate with mature neutrophils.[4] Lesions of Sweet syndrome respond to systemic steroid therapy effectively.[3,4]

Pemphigus Vulgaris is an immune mediated blistering condition characterized by flaccid blisters which lead to painful erosions. Pemphigus vulgaris mainly affects trunk, oral and genital mucosae. These blisters develop due to immunoglobulin (Ig) G antibodies against desmoglein. These antibodies cause acantholysis in basal cell layer of epidermis. Histopathology shows suprabasal cleft with acantholytic cells.[5-7]

Here we present a rarely reported association of Sweet syndrome with pemphigus vulgaris, diagnosed in the Dermatology Department of Lahore General Hospital (LGH), Lahore.

Case Report

Our patient, 59 years old, married male, resident of Kasur City, teacher by profession, diagnosed

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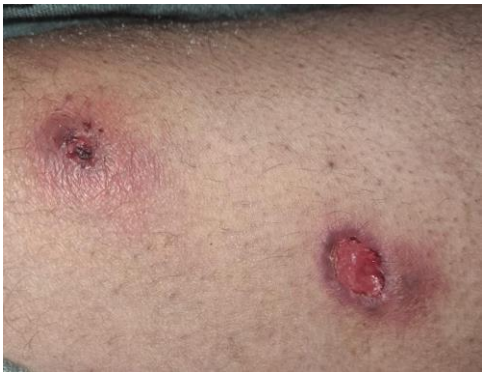

Figure 1

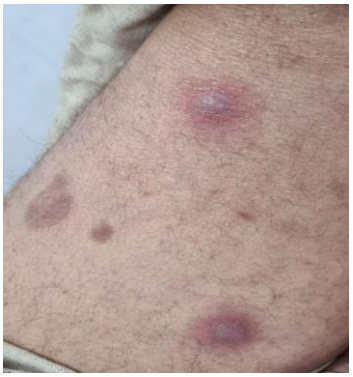

Figure 2

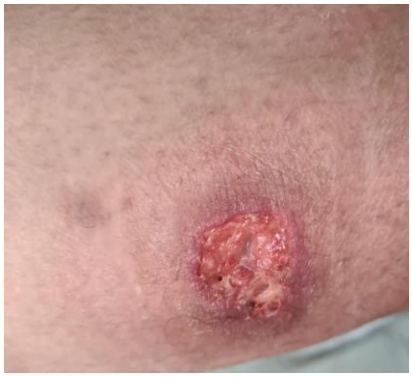

Figure 3

case of Diabetes Mellitus for past 08 years and pemphigus vulgaris for the last 02 years, presented in Out Patient Department of Dermatology, LGH. His presenting complaints were multiple, painful, erythematous plaques, nodules and ulcers on both lower limbs associated with fever for the last 2 months. Lesions of pemphigus vulgaris were in remission with medicines namely deltacortil and azathioprine.

History revealed that presenting lesions appeared spontaneously as erythematous, painful plaques and nodules on medial aspects of legs. They gradually increased in size in a few days and later on appeared on thighs and hips. Lesions on legs ulcerated in a few weeks. Pain in lesions was aggravated with movement and relieved by painkillers. These lesions were accompanied with fever, intermittent in pattern, with a record of 101°F. There was no history of mucosal involvement, weight loss, change in appetite or lumps and bumps anywhere on the body. His systemic examination was unremarkable.

He was in poor compliance with anti-diabetic drugs i.e., metformin 500mg TDS and Insulin Retard 10+10+10. Furthermore, he was taking tablet azathioprine 50mg BD and deltacortil 15mg daily for pemphigus vulgaris.

Examination revealed multiple ulcers on the medial aspect of the right leg, 4cm above the medial malleolus, with the largest one measuring 4x3cm, with yellowish granulation tissue at the floor, sloping edges and surrounding erythema. Also, he had similar ulcers of varying sizes on both thighs. These nodules and ulcers are shown in **Figure 1-3**. He had multiple pigmented patches of variable sizes and shapes affecting trunk, which were indicative of pemphigus vulgaris in resolution phase. He had temperature of 101°F, intermittent in pattern. His systemic examination was unremarkable.

His blood tests showed Hemoglobin 12.9mg/dl, Total Leukocyte Count (TLC) 12.5x 10^9/L with neutrophils 81%, platelets 486 x 10^9/L and ESR was 80 mm in first hour, HbA1c was 8.5%, while rest of investigations were within normal limits. His biopsy report showed papillary edema and infiltrate in dermis consistent of mature neutrophils, which was indicative of Sweet syndrome. Dosage of tablet deltacortil was increased to 50mg daily in divided doses, whilst rest of the treatment continued as such.

During his stay in hospital, while being treated for SS, he developed sudden weakness of the left proximal upper limb and developed progressive altered state of consciousness. Computed Tomographic (CT) scan of brain showed right sided ischemic infarct in brain and patient was referred to medical unit for further management. He was treated there for three days with addition

of Tab loprin 75 mg but after 4th day of the development of neurological symptoms he passed away due to sudden cardiac arrest.

Discussion

Sweet syndrome is a rare, non-infectious, inflammatory skin condition.[2] Exact etiology of SS is unknown. The adaptive immune system including IL-17, IL-1β, and pro_ inflammatory cytokines has a significant role in neutrophil recruitment and activation.[1,2]

While pemphigus vulgaris is an immune mediated disorder, in which suprabasal keratinocytes detach from each other (a process called acantholysis) due to IgG auto antibodies against desmoglein 3. Desmogleins cause adhesion between basal keratinocytes.[5-7]

Many conditions are associated with SS which include i). infections (like acute respiratory infections, Hepatitis B and C virus), ii). vaccinations (like BCG, measles), iii). drugs (like colony stimulating factor, retinoids, contarceptive pills, azathioprine, minocycline), iv). pregnancy, v. malignancy (like acute myeloid leukemia, acute lymphoid leukemia, myelodysplastic syndrome) and vi. inflammatory conditions (like Systemic Lupus Erythematosus, Autoimmune hepatitis, Crohns disease).[3]

A thorough review of the literature yielded only two documented cases of pemphigus vulgaris with Sweet syndrome.[6,7]

The possible explanation of Sweet syndrome in our patient, previously diagnosed with pemphigus vulgaris, include the following (i) The involvement of autoantibodies in the development of SS, (ii) Immune complexes have been referred in several reports as the cause of Sweet's lesions and in some cases of pemphigus vulgaris immune complexes have been seen, (iii) A case of Sweet syndrome has been reported with azathioprine therapy. Our patient was taking azathioprine which might be a potential cause, (iv) The neutrophilic activation and chemotaxis is rarely seen in pemphigus vulgaris, (v) The excessive elaboration of interleukin-1 might be the potential factor involved in pathogenesis.[6]

Sweet syndrome is diagnosed according to the clinical criteria, which was first devised by Su and Liu in 1986 and later on modified by von Der Driesch in 1992. This criteria requires the fulfillment of two major and two minor criteria. Major criteria include classical lesions, characteristic histopathological features. Four minor criteria include i presence of associated factors, fever more than 38°C, raised inflammatory markers, peripheral leukocytosis, neutrophilia and lesions respond to systemic steroids effectively. Skin biopsy shows papillary dermal edema and dense dermal infiltrate with mature neutrophils.[4] Our patient fulfilled two major and two minor criteria of SS.

Neuro-sweet disease is a rare complication of Sweet syndrome. The most common neurologic associations in Sweet disease are encephalitis and meningitis, although few cases showed peripheral neuropathy, the disturbance of consciousness, hemiparesis, memory disturbances, epilepsy and headache. Diagnosis of Neuro-Sweet disease is confirmed with the help of a criteria.[2]

Thus case probably developed a complication of SS as neuro sweet disease. As cerebrovascular infarcts may be rarely seen in neuro-sweet disease. But other comorbid condition, uncontrolled Diabetes Mellitus and systemic steroid therapy were also present in this case which may lead to cerebrovascular infarct.

Conclusion

In summary, we report a case of Sweet syndrome in a patient of pemphigus vulgaris. More cases are required to confirm this rare association of Sweet syndrome with pemphigus vulgaris, and for clarification of the neutrophilic activation mechanisms in these processes.

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