SKIN

BRIEF ARTICLE

# Drug-Induced Sweet's Syndrome by Xcopri

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## ABSTRACT

**Background:** Sweet's syndrome (SS) is a relatively rare, self-limiting dermatological condition predominantly affecting women aged 30-50. It is characterized by the sudden onset of erythematous plaques, nodules, or papules on the skin and is often accompanied by fever, leukocytosis, and systemic symptoms. While most SS cases are idiopathic, approximately 5% are drug-induced.
**Case:** This case report describes a 34-year-old female with a medical history significant for epilepsy who presented with diffuse erythematous papules on the bilateral upper extremities. The onset of these symptoms coincided with the initiation of Xcopri (cenobamate tablets) in her medication regimen.
**Conclusion:** To our knowledge, this report highlights the first case of Xcopri-induced SS. We interpret this patient's presentation as a cutaneous response secondary to an adverse drug reaction and aim to emphasize the importance of obtaining a thorough medication history at each clinical consultation.

## INTRODUCTION

Acute febrile non-vasculitic neutrophilic dermatosis, also known as Sweet's syndrome (SS), is a rare dermatologic condition that disproportionately affects middle-aged women. It is characterized by the sudden onset of painful erythematous bumps or plaques of various sizes in an asymmetric distribution, often accompanied by fever, leukocytosis, and diffuse neutrophilic infiltration in the reticular dermis. Although rare, some patients may present with extracutaneous manifestations such as arthritis, conjunctivitis, osteomyelitis, pleural effusions, or gastrointestinal disease. SS is present in various clinical settings and is further classified into three types: classic Sweet's, malignancy-associated, and drug-induced. The exact pathogenesis is not well understood; however, it is thought to be related to genetic factors, upper respiratory infections, inflammatory bowel disease, and pregnancy. Clinical symptoms of SS are typically self-limiting; persistent lesions may require addressing any underlying causes and managing symptoms with a 2–6-week tapering course of oral prednisone. In some refractory cases, topical potassium iodide, colchicine, dapsone, or indomethacin may also be effective.[1]

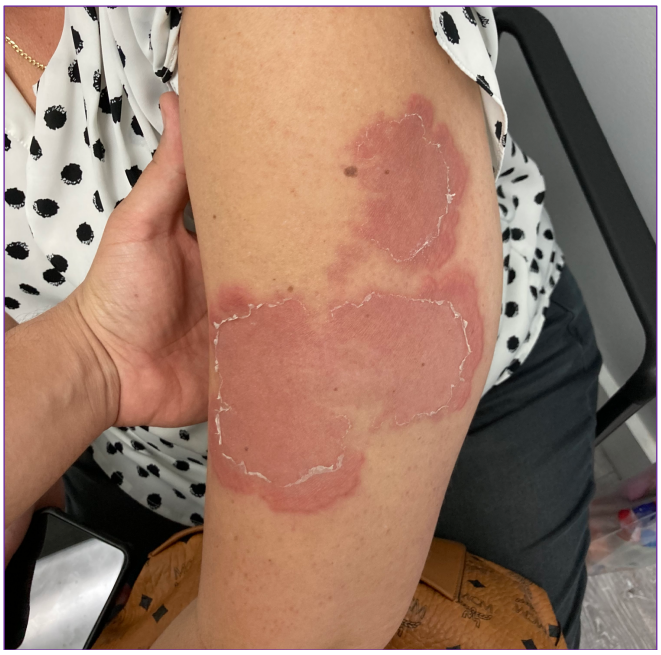

**Figure 1.** Sweet's Syndrome Clinical Photographs. Photo of the left upper lateral arm as she presented in the clinic.

This report highlights a case of a patient who presented with clinical symptoms of SS after starting a relatively new anti-epileptic medication on the market, Xcopri (cenobamate tablets). Xcopri is currently FDA-approved for the adjunctive treatment of partial-onset seizures in adults with epilepsy.[2] To our knowledge, our patient represents the first case of Xcopri-induced SS. Although drug-induced SS represents 5% of SS cases, we aim to stress the importance of inquiring about recent drugs and updating the medication history for a patient with suspicion of SS.

## CASE REPORT

A 34-year-old female patient with a history of epileptic seizures presented to the clinic with scattered erythematous bumps on her bilateral upper arms, which have been present for one month. The patient had no previous history of similar lesions. Although she denied any traumatic injury and notable exposures, the patient reported symptoms appearing the day she added Xcopri (cenobamate tablets), a relatively novel anti-epileptic medication, to her treatment regimen. The patient also reported experiencing fevers; however, no objective temperature measurements were recorded. Dermatological examination revealed closed vesicles on an erythematous base with a trailing scale on the lateral left upper arm (**Figure 1**). Erythematous raised nodules and plaques with extensive edema were observed on the lateral right upper arm. Furthermore, a 0.3 cm punch biopsy of the lesion on the right upper lateral arm confirmed a diagnosis of neutrophilic dermatosis consistent with Sweet's syndrome. Serum protein electrophoresis (SPEP) and urine protein electrophoresis (UPEP) were negative. The patient was on Xcopri for a total of one month, during which the rash persisted; subsequently, she was advised to discontinue the medication and apply clobetasol 0.05% topical cream once daily to the affected areas. After one month of treatment, the patient revisited the clinic with improved symptoms and was

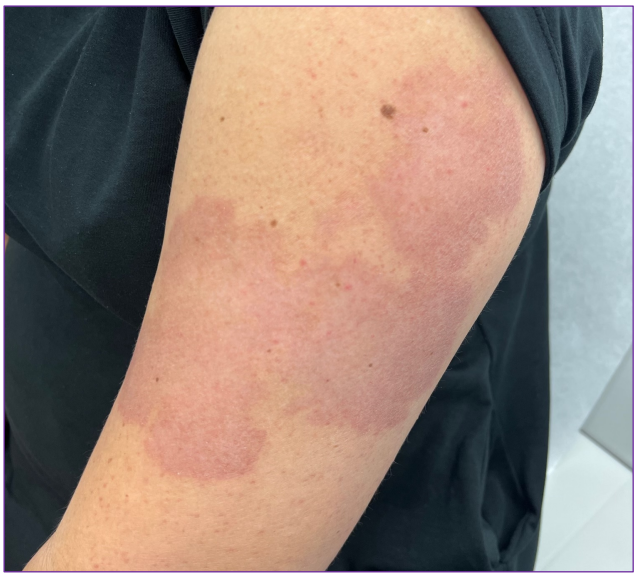

**Figure 2.** Sweet's Syndrome Clinical Photographs. After consistent use of topical clobetasol and one-month discontinuation of Xcopri.

discharged with instructions to return if the lesions worsened (**Figure 2**).

## DISCUSSION

The complete pathogenesis of SS is largely incomplete; however, recent research has provided valuable insights into the contributions of inflammatory activation, abnormal cellular signaling, malignant transformation, and genetics to the development of neutrophilic dermatoses.[3] For instance, endogenous hematopoiec growth factor G- CSF regulates innate immune system activation by promoting neutrophil differentiation, chemotaxis, maturation, and activation within the bone marrow.[4] Elevated levels of G-CSF in the serum have also been correlated with increased disease severity.5 Moreover, culturing neutrophils with G-CSF-containing serum from SS patients can inhibit apoptotic pathways and prolong neutrophil survival.[4,5] More recently, the onset of the COVID-19 pandemic in 2019 has led to an increase in atypical SS cases, likely caused by an exaggerated reactive neutrophilic response that manifests as SS on the skin.[6]

The diagnostic criteria proposed by Walker and Cohen for drug-induced SS include the abrupt onset of painful erythematous plaques or nodules, histological evidence of dense neutrophilic infiltration of the dermis, and a fever exceeding 38 degrees Celsius.[1] Our patient met two out of three criteria for the diagnosis of drug-induced SS. Our patient recently completed a one-month course of Xcopri (cenobamate tablets), an anti-epileptic medication indicated for the use of partial-onset (focal) seizures in adults. Although the exact mechanism of Xcopri is unknown, studies have suggested that Xcopri may amplify both the inactivated state of voltage-gated sodium channels and γ-aminobutyric acid (GABA)- mediated inhibition on GABA receptors.[7] We hypothesize that anti-epileptic medications may induce a hypersensitivity syndrome, modulating humoral and cellular immunity and upregulating cytokine levels in SS. Our patient's acute onset of erythematous nodules raises suspicion of SS secondary to Xcopri use. To our knowledge, this case report highlights the first reported

case of Xcopri-induced Sweet's Syndrome. We believe our patient's case represents a reactive dermatological manifestation of an underlying drug reaction and hope to emphasize the importance of inquiring about recent medication use when there is suspicion of SS.

**Conflict of Interest Disclosures:** None

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