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Sweet Syndrome: A Comprehensive Review of Pathogenesis, Clinical Manifestations, Diagnosis, and Management Strategies

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ABSTRACT

Sweet syndrome, also known as acute febrile neutrophilic dermatosis, is a rare and inflammatory disorder characterized by fever, neutrophilia, and tender, erythematous skin lesions. The pathogenesis of Sweet syndrome involves an exaggerated immune response, with evidence suggesting a role for cytokines, particularly granulocyte colony-stimulating factor (G-CSF). Clinical manifestations vary widely, but commonly include abrupt onset of painful, raised plaques or nodules, often on the upper limbs, face, or neck. Histopathological examination reveals dense neutrophilic infiltrates in the dermis without evidence of vasculitis.

Diagnosis is primarily clinical, supported by histopathology and exclusion of other similar conditions. Treatment typically involves corticosteroids, which often lead to rapid resolution of symptoms. However, relapses are common, necessitating long-term management strategies. This review aims to provide a comprehensive overview of the pathogenesis, clinical manifestations, diagnosis, and management of Sweet syndrome, highlighting recent advancements and areas requiring further research.

KEYWORDS: syndrome, skin, neutrophilic, dermatosis

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INTRODUCTION

Sweet syndrome was first described by Dr. Robert Douglas Sweet in 1964 as an acute febrile neutrophilic dermatosis characterized by fever, neutrophilia, and tender, erythematous skin lesions. Since its initial description, the understanding of this rare condition has evolved, with significant advancements in its pathogenesis, clinical presentation, diagnosis, and management.1,2

Sweet syndrome is now recognized as a reactive dermatosis, often associated with underlying infections, inflammatory diseases, malignancies, and drug exposures. The exact pathogenesis remains incompletely understood, but evidence suggests an exaggerated immune response, particularly involving cytokines such as G-CSF.1,2

Clinically, Sweet syndrome presents with a constellation of symptoms, including fever, neutrophilia, and characteristic skin lesions. The skin lesions are typically painful, raised plaques or nodules, commonly located on the upper limbs, face, or neck. These lesions can evolve rapidly and may exhibit a pseudovesicular appearance.1,2

Histopathological examination of skin lesions is a key component in the diagnosis of Sweet syndrome, revealing dense neutrophilic infiltrates in the dermis without evidence of vasculitis. The diagnosis is primarily clinical, supported by histopathology and exclusion of other similar conditions such as infection, vasculitis, and other neutrophilic dermatoses.1,2

Treatment of Sweet syndrome typically involves corticosteroids, which often lead to rapid resolution of symptoms. However, relapses are common, necessitating long-term management strategies. Other treatment options, such as non-steroidal anti-inflammatory drugs (NSAIDs), colchicine, and immunosuppressive agents, may be considered in refractory cases.1,2

Sweet syndrome is a rare and intriguing dermatological disorder with a complex pathogenesis and diverse clinical manifestations. This review aims to provide a comprehensive overview of the current understanding of Sweet syndrome,

highlighting recent advancements and areas requiring further research.2,3

EPIDEMIOLOGY

Sweet syndrome, also known as acute febrile neutrophilic dermatosis, is a rare and inflammatory disorder with an estimated annual incidence ranging from 0.27 to 2.7 cases per 100,000 individuals. The condition can affect individuals of any age, although it most commonly occurs in adults between the ages of 30 and 60 years, with a slight female predominance.3,4

Several underlying conditions have been associated with Sweet syndrome, including infections (particularly upper respiratory tract infections), inflammatory diseases (such as inflammatory bowel disease and rheumatoid arthritis), malignancies (most commonly hematologic malignancies), and medications (such as granulocyte colony-stimulating factor, certain antibiotics, and non-steroidal anti-inflammatory drugs).3,4

The prevalence of Sweet syndrome in patients with hematologic malignancies, particularly acute myeloid leukemia, is higher compared to the general population, suggesting a potential association with immune dysregulation in these conditions.3,4

The exact pathogenesis of Sweet syndrome remains incompletely understood, but it is thought to involve an exaggerated immune response, with evidence suggesting a role for cytokines, particularly granulocyte colony-stimulating factor (G-CSF), in the development of the condition.3,4

Further epidemiological studies are needed to better understand the risk factors, natural history, and optimal management strategies for Sweet syndrome.5

CLINICAL MANIFESTATIONS

Sweet syndrome, also known as acute febrile neutrophilic dermatosis, is characterized by a constellation of symptoms, including fever, neutrophilia, and tender, erythematous skin lesions. The classic skin lesions of Sweet syndrome are painful, raised plaques or nodules, often with a pseudovesicular appearance. These lesions typically occur on the upper limbs, face, or neck, but can also affect other areas of the body.6,7

The onset of Sweet syndrome is often abrupt, with the skin lesions evolving rapidly over a period of days to weeks. The lesions may be associated with a burning or itching sensation and can vary in size from a few millimeters to several centimeters.6,7

In addition to the skin manifestations, patients with Sweet syndrome may also experience systemic symptoms, including fever, malaise, and arthralgias. The fever is usually high-grade and may precede the development of skin lesions. Neutrophilia is a common laboratory finding, but other inflammatory markers, such as elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), may also be present.6,7

Sweet syndrome can be classified into several subtypes based on the clinical presentation. The classical or idiopathic form of Sweet syndrome occurs in the absence of an underlying cause and is often associated with a good response to treatment. Drug-induced Sweet syndrome occurs in response to medications, most commonly granulocyte colony-stimulating factor (G-CSF), and typically resolves upon discontinuation of the offending drug.6,7

Sweet syndrome can also occur in association with underlying conditions, such as infections (particularly upper respiratory tract infections), inflammatory diseases (such as inflammatory bowel disease and rheumatoid arthritis), malignancies (most commonly hematologic malignancies), and pregnancy. In these cases, treatment of the underlying condition may lead to resolution of Sweet syndrome.6,7

Overall, the clinical manifestations of Sweet syndrome are diverse and can mimic other inflammatory and infectious conditions. A thorough evaluation, including a detailed medical history, physical examination, and laboratory investigations, is essential for accurate diagnosis and appropriate management of this rare condition.7,8

DIAGNOSIS

The diagnosis of Sweet syndrome, also known as acute febrile neutrophilic dermatosis, is primarily clinical, supported by histopathology and exclusion of other similar conditions. A thorough evaluation is essential to differentiate Sweet syndrome from other inflammatory and infectious disorders that may mimic its clinical presentation.9,10

Clinical features that are suggestive of Sweet syndrome include the abrupt onset of painful, erythematous skin lesions, fever, and neutrophilia. The skin lesions typically have a raised, edematous appearance and may be accompanied by a burning or itching sensation.9,10

Histopathological examination of skin lesions is an important diagnostic tool for Sweet syndrome. Biopsy specimens typically show dense neutrophilic infiltrates in the dermis, with no evidence of vasculitis. The presence of papillary dermal edema and a predominantly neutrophilic infiltrate are characteristic features of Sweet syndrome on histopathology.9,10

Laboratory investigations may also be helpful in supporting the diagnosis of Sweet syndrome. Neutrophilia is a common finding, although it is not specific to Sweet syndrome. Elevated inflammatory markers, such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), may also be present.9,10

The diagnosis of Sweet syndrome is often one of exclusion, as other conditions can mimic its clinical presentation. Conditions that should be considered in the differential diagnosis include infections (such as cellulitis and erysipelas), vasculitis (such as leukocytoclastic vasculitis), and other neutrophilic dermatoses (such as pyoderma gangrenosum and erythema elevatum diutinum).11,12

In cases where the diagnosis of Sweet syndrome is unclear, additional investigations may be warranted. These may include blood cultures to rule out infection, serological tests for autoimmune diseases, and imaging studies to evaluate for underlying malignancy. 11,12

Overall, the diagnosis of Sweet syndrome requires a high index of suspicion, and a multidisciplinary approach involving dermatologists, rheumatologists, and hematologists may be necessary for accurate diagnosis and management.11,12

TREATMENT

The treatment of Sweet syndrome, also known as acute febrile neutrophilic dermatosis, aims to control symptoms, promote resolution of skin lesions, and prevent recurrence. The choice of treatment depends on the severity of symptoms, underlying conditions, and response to initial therapy.13,14

1. Corticosteroids:

Corticosteroids are the mainstay of treatment for Sweet syndrome and are highly effective in most cases. Oral prednisone is typically used at a starting dose of 0.5-1 mg/kg/day, with gradual tapering over several weeks to months based on clinical response.

Topical corticosteroids may be used for localized skin lesions, although systemic therapy is often required for more widespread or severe cases.13,14

2. Immunosuppressive Agents:

In cases where corticosteroids alone are insufficient or not well tolerated, immunosuppressive agents such as colchicine, dapsone, or methotrexate may be used as steroid-sparing agents.

Azathioprine and cyclosporine have also been used in refractory cases of Sweet syndrome, particularly in patients with underlying inflammatory or autoimmune conditions.13,14

3. Biologic Therapies:

Biologic agents such as tumor necrosis factor (TNF) inhibitors (e.g., infliximab, adalimumab) and interleukin-1 (IL-1) inhibitors (e.g., anakinra) have shown efficacy in some cases of Sweet syndrome, particularly in patients with associated inflammatory diseases.

These agents are typically reserved for severe, refractory cases due to their cost and potential for adverse effects.13,14

4. Treatment of Underlying Conditions:

In cases where Sweet syndrome is associated with an underlying condition, such as infection, inflammatory disease, or malignancy, treatment of the underlying condition is essential for resolution of Sweet syndrome.

Close collaboration with specialists in infectious diseases, rheumatology, and oncology may be necessary to optimize treatment.

5. Supportive Care:

Supportive measures, such as analgesics for pain relief and antipyretics for fever, may be used to alleviate symptoms.

Wound care for ulcerated lesions and psychological support for patients experiencing emotional distress can also be beneficial.13,14

6. Monitoring and Follow-up:

Regular monitoring of symptoms, laboratory parameters (e.g., complete blood count, inflammatory markers), and response to treatment is essential for guiding therapy and detecting any complications or relapses.13,14

Long-term follow-up is recommended, as Sweet syndrome can recur in some patients, particularly those with associated malignancies or autoimmune diseases.

In conclusion, the treatment of Sweet syndrome is multifaceted and often requires a tailored approach based on the individual patient's clinical presentation and underlying conditions. Early recognition and prompt initiation of treatment are key to achieving favorable outcomes and preventing complications.13,14

CONCLUSION

Sweet syndrome, also known as acute febrile neutrophilic dermatosis, is a rare and intriguing inflammatory disorder characterized by fever, neutrophilia, and tender, erythematous skin lesions. Despite its rarity, Sweet syndrome serves as a clinical entity that highlights the complex interplay between the immune system, inflammatory pathways, and various underlying conditions.

The pathogenesis of Sweet syndrome remains incompletely understood, with evidence suggesting a dysregulated immune response, particularly involving cytokines such as granulocyte colony-stimulating factor (G-CSF). This dysregulation can lead to the recruitment and activation of neutrophils, resulting in the characteristic skin lesions and systemic symptoms seen in Sweet syndrome.

Diagnosis of Sweet syndrome requires a high index of suspicion, as it can mimic other inflammatory and infectious conditions. Clinical features, histopathological findings, and exclusion of other similar conditions are key components of the diagnostic workup. Collaboration between dermatologists, rheumatologists, and hematologists is often necessary for accurate diagnosis and management.

Treatment of Sweet syndrome is primarily aimed at controlling symptoms, promoting resolution of skin lesions, and preventing recurrence. Corticosteroids are the mainstay of treatment, although other immunosuppressive agents and biologic therapies may be used in refractory cases or in patients with underlying conditions.

Long-term management and follow-up are important aspects of Sweet syndrome care, as relapses can occur, particularly in patients with associated malignancies or autoimmune diseases. Further research is needed to better understand the underlying pathophysiology of Sweet syndrome and to develop more targeted and effective therapies.

In conclusion, Sweet syndrome is a rare but important dermatological disorder that underscores the complex interplay between the immune system and inflammatory pathways. Advances in our understanding of Sweet syndrome have improved diagnosis and management, but further research is needed to optimize outcomes for affected patients.

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