Moxifloxacin-Induced Sweet Syndrome in an 85-year-old Female with Prosthetic Joint Infection

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Case Presentation

An 85-year-old female with history of recurrent *Streptococcus Agalactiae* bacteremia with cardiovascular implantable electronic device lead vegetations and bilateral hip arthroplasties presented to the Emergency Department with concern for right hip cellulitis. Culture of joint aspirate was performed and grew *Strep. Agalactiae.* The patient declined orthopedic surgical intervention and was started on intravenous antibiotics then transitioned to daily moxifloxacin 400 mg by mouth. After several weeks of moxifloxacin therapy, the patient developed low-grade fevers, malaise, and painful cutaneous lesions on both hands (Figure 1 and 2). Laboratory evaluation was significant for an elevated ESR (86 mm/hr), CRP (22 mg/dL) and a normal WBC count. She was referred to dermatology for evaluation and a biopsy of a representative lesion was performed with a clinical differential diagnosis of Sweet syndrome, Janeway lesions, and erythema muliforme.

Histology

Hematoxylin-eosin (H+E) staining of the shave biopsy revealed nodular and diffuse neutrophilic infiltrate with karyorrhexis and papillary dermal edema consistent with an acute neutrophilic dermatosis (Figure 3 and Figure 4). GMS and Gram stain were negative for bacteria or fungal elements.

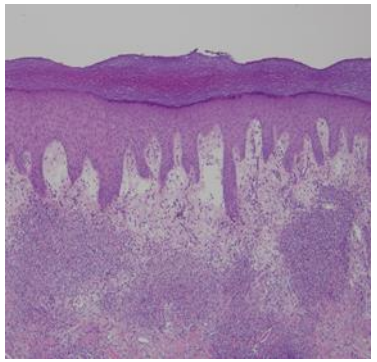

Figure 3: H+E 40x.

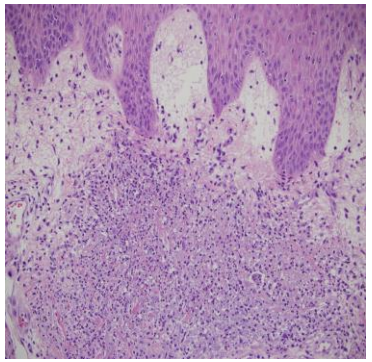

Figure 4: H+E 200x

Clinical Presentation

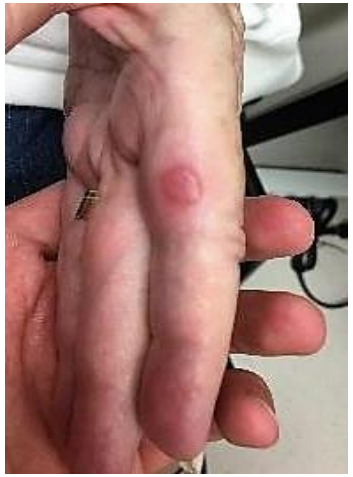

Figure 1

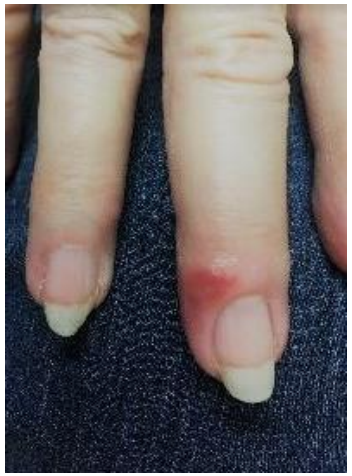

Figure 2

Table 1: Drug-Induced Sweet Syndrome Criteria
All 5 criteria required for diagnosis

1.) Abrupt onset of typical cutaneous lesions
2.) Histopathology consist with Sweet Syndrome
3.) Presence of fever and constitutional signs and symptoms
4.) Temporal relationship between drug ingestion and clinical presentation OR temporarily-related recurrence after oral rechallenge
5.) Resolution of lesions after drug withdrawal or treatment with systemic corticosteroids

Table modified from Walker and Cohen

Table 2. Common Drug-Induced Causes of Sweet Syndrome

NSAIDS	celecoxib, diclofenac, ibuprofen
Salicylates	aspirin and sulfasalazine
Antibiotics	cephalexin, azithromycin, clindamycin, amoxicillin, ciprofloxacin, levofloxacin, norfloxacin, ofloxacin, bactrim, doxycycline, minocycline, nitrofurantoin
Antineoplastic	ipilimumab, capecitabine, sorafenib, imatinib, vemurafenib
Cardiovascular	furosemide, captopril, enalapril, hydralazine
Immunostimulants	G-CSF, GM-CSF, pegylated G-CSF
TNF-α inhibitors	adalimumab and infliximab
Systemic Retinoids	all-trans retinoic acid and 13-cis-retinoic acid

Table 2 adapted from *JAAD CME December 2018, Neutrophilic Dermatoses*

Discussion

Acute febrile neutrophilic dermatosis, also known as Sweet syndrome, is a distinct dermatologic condition characterized by an abrupt onset of painful erythematous plaques, associated systemic findings and a sterile, predominantly neutrophilic infiltrate on histopathology. Although the pathophysiology is not completely understood, there are multiple causes of Sweet syndrome to include infectious, autoimmune, malignancy-associated and drug-induced[1] (Table 2).

Given clinical and histologic findings, our patient met diagnostic criteria for Sweet syndrome (Table 1). Traditionally, first-line treatment for Sweet syndrome is systemic corticosteroids[2] (prednisone 0.5 to 1mg/kg/day) tapered based on disease severity. If steroid-sparing systemic therapy is indicated, other therapies include colchicine (1.5 mg/day), dapsone (100-200 mg/day), and potassium iodide (900 mg/day).[3] Given on-going treatment for chronic infection, our patient was started on high-potency topical steroids to treat the cutaneous lesions.

Sweet syndrome may also resolve following treatment of the underlying etiology in the context of malignancy, infection, or drug-induced causes.[4] Given the abrupt onset of symptoms that coincided with initiation of moxifloxacin, we suspected drug-induced Sweet syndrome. The patient was switched to amoxicillin by Infectious Disease for long-term antibiotic therapy. Over the next few weeks, her cutaneous lesions and systemic findings resolved and her ESR and CRP returned to within normal limits. In drug-induced cases, fever and neutropenia typically resolve within 1-3 days after discontinuation of the offending agent, with cutaneous lesions improving over 3-30 days.[4]

There are many drug-induced causes of Sweet syndrome (Table 2). Our patient represents the first reported case of moxifloxacin-induced Sweet syndrome. Drug-induced causes of Sweet syndrome can be difficult to identify and treatment should be tailored to the individual, taking into account associated diseases and comorbidities.[3]

References

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2. Sweet RD. An acute febrile neutrophilic dermatosis. *Br J Dermatol*. 1964;76:349-356
3. Nelson CA, Stephen S, Ashchyan HJ, James WD, Micheletti RG, Rosenbach M. Neutrophilic dermatoses: Pathogenesis, Sweet syndrome, neutrophilic eccrine hidradenitis, and Behçet disease. *J Am Acad Dermatol*. 2018 Dec;79(6):987-1006
4. Walker DC, Cohen PR. Trimethoprim-sulfamethoxazole-associated acute febrile neutrophilic dermatosis: case report and review of drug-induced Sweet's syndrome. *J Am Acad Dermatol*. 1996;34(5 pt 2):918-923