SKIN

BRIEF ARTICLE

Recognizing Multiple Diagnoses: Von Zumbusch Generalized Pustular Psoriasis Flare And Adverse Drug Effect

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ABSTRACT

Von Zumbusch generalized pustular psoriasis (GPP) is a rare and severe type of psoriasis that presents as superficial pustules which coalesce into lakes of pus with erythema and scaling, with associated fever and life-threatening complications including sepsis. Here we describe a patient with a history of von Zumbusch GPP who presented with erythroderma, neutrophilic leukocytosis, and hyperbilirubinemia in the setting of missed medication dose and hip surgery. While her laboratory abnormalities were initially attributed to a flare of her underlying skin disease, when treatment of her psoriasis flare failed to correct the laboratory abnormalities, review of her biopsy showed evidence of a concomitant adverse drug effect and the patient ultimately expired due to sepsis.

INTRODUCTION

Von Zumbusch generalized pustular psoriasis (GPP), also known as acute generalized pustular psoriasis, is a rare and severe type of pustular psoriasis characterized by superficial pustules on the trunk and extremities which coalesce into lakes of pus with erythema and scaling. GPP presents with fever and leukocytosis, and can be associated with life-threatening complications including sepsis. Triggers include infection, medications, operations, and hypocalcemia.[1, 2] We present a patient with von Zumbusch GPP who flared in the setting of a gap in etanercept dosing and hospitalization for hip fracture. We discuss the importance of considering additional diagnoses in patients with this condition who present with laboratory abnormalities that fail to improve with treatment of their GPP.

CASE REPORT

A 74-year-old woman with von Zumbusch GPP was transferred from an outside hospital for a diffuse desquamating rash. She had been managed with etanercept 50 mg twice weekly for 10 years with good response, but unfortunately had a lapse in etanercept two months prior to admission due to insurance issues. During outside hospital admission for hip fracture, she developed a psoriasis flare. Post-operatively, she developed progressive leukocytosis (WBC increased from 13.7K/uL on admission to 37.7K/uL prior to transfer), conjugated hyperbilirubinemia and mild transaminitis (TBili 0.8 mg/dL, ALT 11 IU/L, AST 18 IU/L on admission increased to Tbili 4.4 mg/dL, ALT 49 IU/L, AST 38 IU/L prior to transfer), low-grade fever, and urinary tract infection (UTI) treated with cefazolin,

ceftriaxone, piperacillin-tazobactam, and vancomycin. Given these systemic findings as well as a progressive rash, she was transferred to our institution for further management.

On arrival, she was afebrile and hemodynamically stable. Exam revealed erythroderma with light-yellow, thick scaly plaques on the trunk and extremities with superficial desquamation and superficial pustules coalescing into lakes of pus in the right groin fold (Figure 1). Oral and ocular mucosa were clear. There were no new medications or dose changes prior to outside hospital admission.

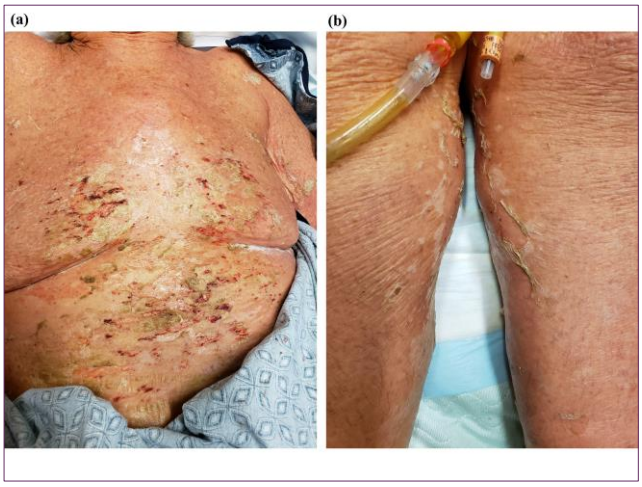

Figure 1. Patient's initial presentation of erythroderma with thick scaly plaques and superficial desquamation A) with pinpoint pustules coalescing into lakes of pus in the skin folds B)

Labs showed leukocytosis (42.5K/uL with 93% neutrophils), direct hyperbilirubinemia (Tbili 6.6 mg/dL, Dbili 5.3 mg/dL), transaminitis (ALT 41 IU/L, AST 88 IU/L), and normal calcium (8.9 mg/dL). Blood cultures were negative. CT Abdomen/Pelvis revealed no biliary duct dilation. Punch biopsy revealed vacuolar interface change with focal subepidermal split, scattered apoptotic keratinocytes, epidermal dysmaturation, diffuse parakeratosis with intracorneal neutrophils, consistent with a drug-related eruption on a background of psoriasis (Figure 2).

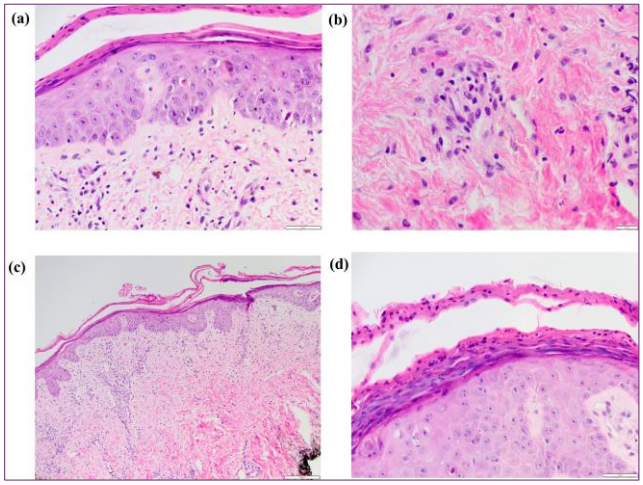

Figure 2. Punch biopsy showing A) vacuolar interface change, rare apoptotic keratinocytes, epidermal dysmaturation (H&E, original magnification x40), B) rare intermixed eosinophils and neutrophils (H&E, original magnification x100) compatible with a drug reaction, and C) mild epidermal hyperplasia, spongiosis, diffuse parakeratosis, superficial predominantly lymphocytic infiltrate (H&E, original magnification x20), and D) rare intracorneal neutrophils within the parakeratotic scale (H&E, original magnification x40) suggesting a psoriatic diathesis in addition to a drug eruption

She was started on cyclosporine 2.5 mg/kg/daily in two divided doses and high-potency topical steroids under occlusion, with plan to transition back to etanercept. Within two days of starting cyclosporine, her white blood cell count decreased from 42.5 K/uL to 24.8 K/uL; however subsequently rebounded, peaking at 46 K/uL (Figure 3). She was found to have polymicrobial bacteremia and a UTI. Additionally, liver function tests continued to rise (Tbili peaked at 10.9 mg/dL), prompting further

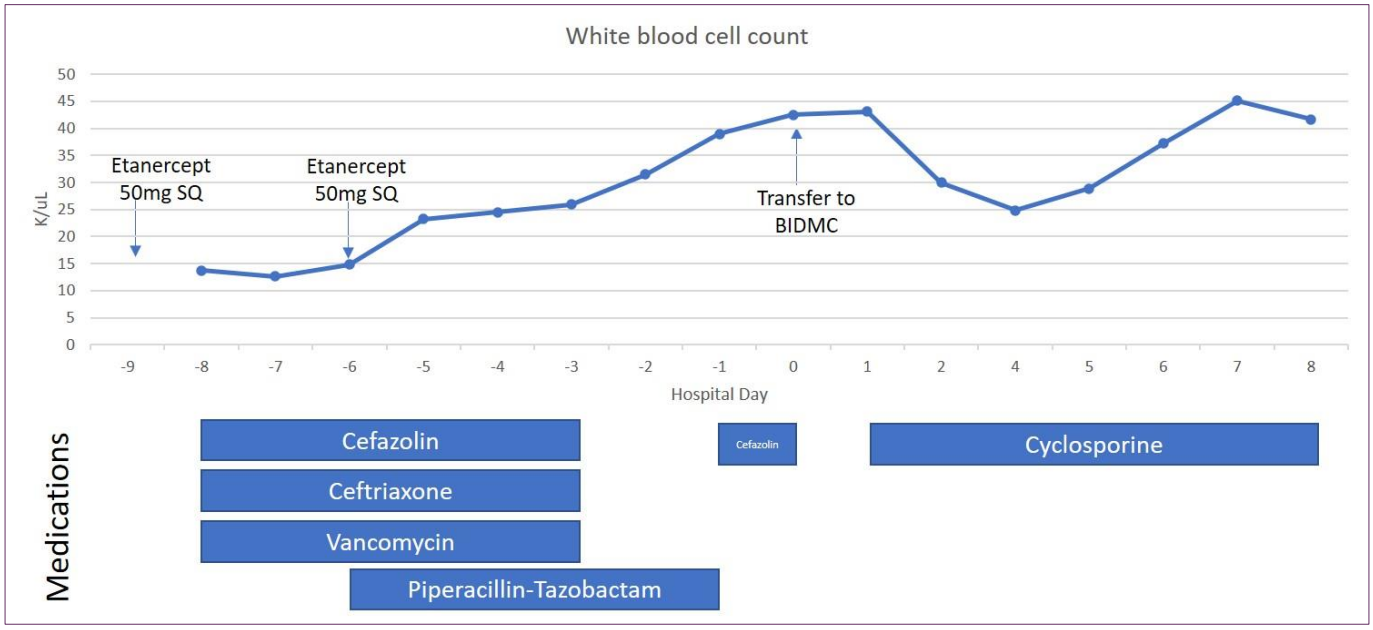

Figure 3. Patient's laboratory value trends for white blood cell count (K/uL) during her hospital admission, paired with recently administered medications.

investigation. MRCP was unremarkable, so she underwent a CT-guided liver biopsy.

Post-procedurally, she became hypotensive with an acute drop in her hematocrit. Chest CT revealed a right-sided hemothorax, attributed to the recent liver biopsy, but no source of active bleeding. She was transferred to the ICU, where a chest tube was placed. She became hypotensive and pulseless, and resuscitation attempts were unsuccessful. Post-mortem, liver biopsy revealed a biliary pattern of liver injury with neutrophils and patchy lymphocytic cholangitis suggestive of drug effect with superimposed sepsis.

DISCUSSION

Neutrophilic leukocytosis and liver abnormalities have been reported in patients with GPP, paralleling the evolution of skin lesions and returning to normal upon remission of pustular psoriasis.[2] This patient's significant leukocytosis and direct hyperbilirubinemia were initially attributed to her GPP. Review of outside records revealed a steady rise in bilirubin and white blood cell count paralleling the flare of her skin disease (Figure 3). Given some pathological evidence of drug reaction on skin biopsy coupled with transaminitis, DIHS was considered however there was no evidence of eosinophilia or facial edema and transaminitis was relatively mild. After starting cyclosporine, her leukocytosis decreased concordant with improvement in skin lesions. However, her leukocytosis then rebounded to higher than admission levels and her liver function test abnormalities remained elevated despite notable improvement in her skin. These abnormalities were later found to be related to sepsis and drug effect, supporting the confluence of multiple factors (GPP, sepsis, and drug-induced liver injury) in her passing. It was challenging to identify the culprit drug for the cutaneous adverse reaction in this case given the patient was recently exposed to multiple antibiotics for her UTI (Figure 3). The patient had no other known allergies or prior adverse drug reactions.

CONCLUSION

In summary, we describe a patient with a history of von Zumbusch pustular psoriasis whose leukocytosis and hyperbilirubinemia failed to resolve despite treatment of her underlying psoriasis, and were ultimately found to be related to a concomitant adverse drug effect as well as sepsis. Although significant laboratory abnormalities can be associated with a GPP flare, we suggest that when laboratory abnormalities no longer parallel the skin condition, it is critical to investigate other causes such as infection or adverse drug reaction. Moreover, because it can be challenging to differentiate between GPP and other diagnoses based on laboratory findings alone, it is critical to engage early in an interdisciplinary approach for the care of these complex patients.

Conflict of Interest Disclosures: None

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