COMA BLISTER FOLLOWING TRAZODONE MISUSE: A CASE REPORT

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1. Introduction

Coma blisters are epidermal and subepidermal bullous lesions that can arise throughout the body following prolonged impairment of conscious level. Coma blisters- like lesions have been well documented in adults following barbiturate-induced intoxication. More recently in literature, other drugs and substances have been associated with the development of these bullae, which has broadened the scope of medications that put patients at risk for developing coma blisters-like lesions. Here, we present a unique case of a non-comatose patient who developed coma blisters-like lesions after trazodone misuse. This case illustrates the need to further investigate the mechanism behind drug-induced coma bullae-like lesions, so that clinicians can better identify and discontinue drugs that precipitate such lesions.

2. Case

A 61-year-old female presented with asymptomatic pink patches scattered on the body, along with swelling and blistering on her left foot that appeared overnight and persisted for a few days. Her past medical history was notable for anxiety, depression, breast cancer, and arthritis, status-post right shoulder arthroplasty with revision. She was on an extended course of doxycycline due to infection of her right shoulder bone graft, but otherwise denied new medications. She later revealed taking an extra dose of trazodone the evening prior to onset of the presenting lesions, resulting in a fifteen-hour period of sleep.

3. Clinical Examination

- Erythematous dusky patch on the right posterior thigh.
- Erythematous patches on right posterior heel and left dorsal foot (Figure 1).
- Swelling of the bilateral feet with tense bullae on the left lateral hallux and medial second toe that drained serous fluid upon incision (Figure 2).

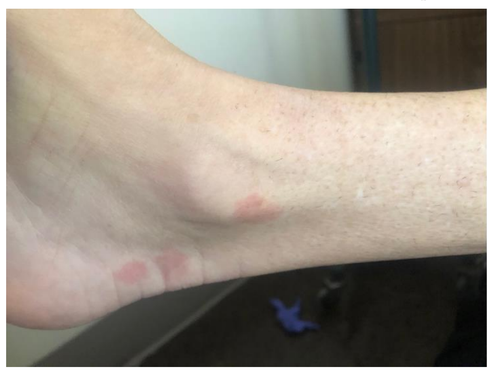

Figure 1. Erythematous dusky patches on the right posterior heel.

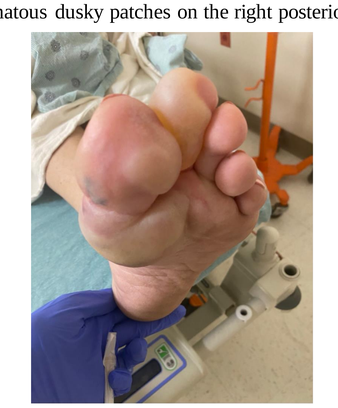

Figure 2 Tense bullae on the left foot lateral hallux and medial second toe.

4. Histological Findings

- Punch biopsy from the right posterior thigh revealed sweat gland necrosis of the deep dermis with a hint of leukocytoclastic vasculitis (Figure 3a-c).

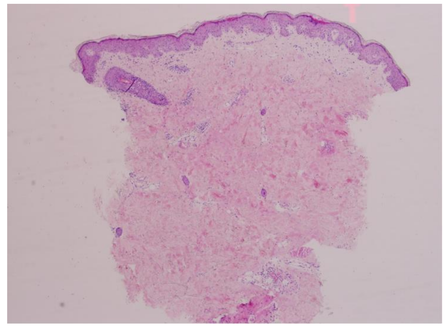

Figure 3a. Punch biopsy of erythematous patch on right thigh (hematoxylin and eosin, original magnification, ×40) showing papillary dermal edema with mild inflammation and sweat gland necrosis at the deep edge of the specimen.

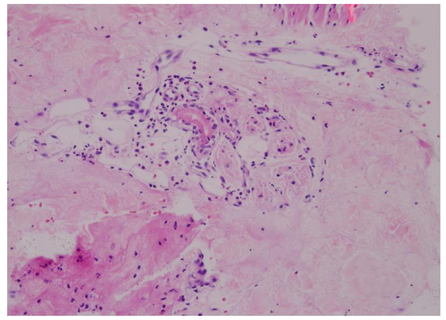

Figure 3b. Eccrine gland necrosis (hematoxylin and eosin, original magnification, ×200).

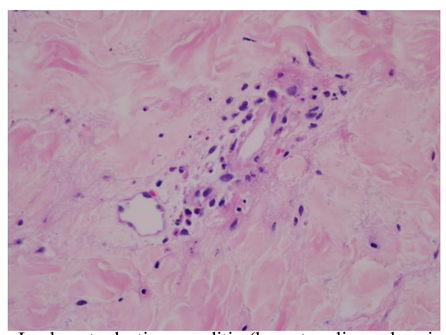

Figure 3c. Leukocytoclastic vasculitis (hematoxylin and eosin, original magnification, ×200).

5. Laboratory Values

- Complete blood count, complete metabolic panels, C3 and C4 complement levels within normal limits.
- Work-up for connective tissue disease, including ANA profile was unremarkable.
- ESR elevated at 95 mm/h.
- Bacterial culture of the interdigital skin of the left foot grew mixed skin flora.
- Bullae fluid culture negative.

7. Clinical Course

- At follow up, interval improvement to rash, decrease of left foot bullae, and no new lesions.
- Diagnosis of bullous disease with sweat gland necrosis, suspected to be secondary to prolonged immobilization from trazodone use.
- Treated with triamcinolone ointment for use on pruritic lesions on the flank with a continued hold on trazodone use.

8. Discussion

The exact pathogenesis of coma blisters remain unknown.

- The exact pathogenesis of coma blisters remains unknown.
- Current theories suggest that these lesions develop from varying combinations of dermal pressure damage, drug toxicity, local anoxic damage, and immune mediated mechanisms [1].
- One hypothesis is that uninterrupted pressure compounded by arterial hypotension from vasoactive drugs lead to local tissue injury and bullae formation [2].
- Coma blisters are self-limiting.
- Stopping the offending drug has been useful for the healing process and prevention of new blisters.

It is important to note the accompanying histological finding of small vessel leukocytoclastic vasculitis, which may be drug-induced as well.

- The mechanism of drug-induced vasculitis is not clearly understood, however it appears to require an environmental trigger with genetic predisposition [3].
- Trazodone is not commonly associated with drug-induced vasculitis.
- Leukocytoclastic vasculitis is not commonly seen in coma blisters, hence we suggest that this finding in addition to the sweat gland necrosis favor a drug-induced coma-blister like lesion.

Trazadone is FDA-approved for major depressive disorder but has also been used off-label to induce sedation and treat anxiety [4].

- While there are many reported side effects of trazodone, some of which include drowsiness, somnolence and anticholinergic effects, dermatological reactions are not commonly reported.
- To the best of our knowledge, there have been no reports on trazodone-induced bullae eruptions.
- Cases of coma bullae following overdose of other anxiolytics have been reported [5], illustrating the contribution of central nervous system depression to bullae development.

9. Conclusion

With the increasing use of sleeping aids and anti-anxiety medications over the past few years, the risk of anxiolytic misuse and associated sequelae is more relevant than ever [6]. This case highlights the importance of including drug-induced coma bullae-like lesions in the differential of acute bullae presentation for patients with a history of depression or anxiety, and obtaining a detailed medication history. It also suggests a potential role for further studies to explore the possibility that trazodone, along with its sedating effects, may have other pharmacological effects at the dermal level that put patients at risk for the formation of bullae lesions.

10. References

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