A Rare Case of Terlipressin-Induced Skin Necrosis in Hepatorenal Syndrome on Second Encounter

Rafla Hassan, MD[1]; Atul Bali, MD[1]
1. Geisinger Health System, PA

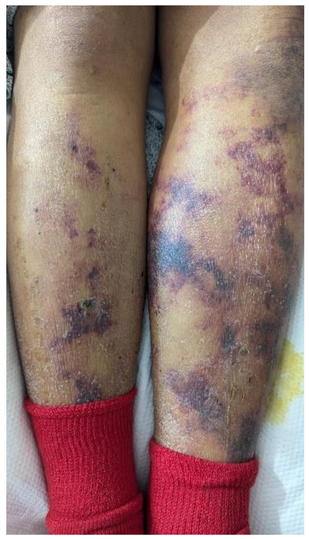
Introduction

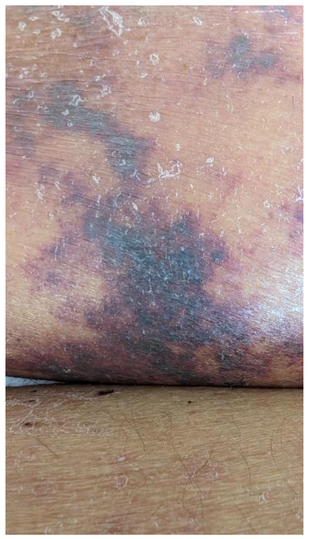
Terlipressin is a synthetic vasopressin analogue newly approved drug by the FDA in September 2022 for the treatment of Hepatorenal Syndrome (HRS) which improves renal function and survival [1–3]. While having a generally a safe profile, Terlipressin induced skin necrosis has been reported as a rare complication with a 0.08% occurrence [4].

Case Presentation

A 55-year-old male presented with Acute Kidney Injury attributed to HRS in the setting of a recent diagnosis of alcoholic liver cirrhosis and spontaneous bacterial peritonitis (SBP). The patient was referred to the emergency department due to decreased mentation and lethargy with increasing creatinine levels from 1.2 mg/dL one month ago to 3.0 mg/dL at presentation, in the context of spontaneous bacterial peritonitis with Pseudomonas sp. on culture. The patient was hospitalized 1 month prior to this with HRS where he responded well to treatment with intravenous Albumin and Terlipressin. For this reason, he was restarted on the same regimen in addition to Midodrine. Terlipressin was administered intravenously at a 0.85mg dose 6 hourly.

He noted new onset lower extremity discomfort on day 2 of hospitalization, but with no clinically apparent change on exam. On day 3 of hospitalization, he developed dark discrete areas and skin discoloration along with worsening pain of the bilateral lower extremities (BLE).





Venous duplex showed no clots. CT of the BLE revealed subcutaneous edema, without fluid collections or subcutaneous gas. Terlipressin was discontinued and modest improvement in pain without progression of skin lesions was noted on the subsequent day. Octreotide was started. Unfortunately, the patient continued to deteriorate with worsening liver and kidney function and was not a candidate for transplantation, and thus opted to pursue hospice.

Discussion

Skin necrosis is a rare but serious adverse event of Terlipressin. This can be attributed to the vasoconstrictive property of the drug on the systemic circulation in addition to the splanchnic circulation. In prior reports, skin manifestations were noted from a few hours to 21 days of treatment as in our case which began on the day 3 of treatment [5,6]. SBP has been reported as a risk factor (which was present in our patient) amongst others such as venous insufficiency and obesity [7]. To our knowledge, skin necrosis happens on the first encounter with Terlipressin in patients with HRS. However, our case is unique with the patient developing this complication on the second encounter with the drug.

Conclusion

Terlipressin induced skin necrosis is a rare complication which warrants discontinuation of the drug. Our study emphasizes the importance of vigilant monitoring for this complication, especially those with risk factors, even in patients with no prior history of adverse events.

References:
1. Wong F, Pappas SC, Curry MP, Reddy KR, Rubin RA, Porayko MK, et al. Terlipressin plus Albumin for the Treatment of Type 1 Hepatorenal Syndrome. New England Journal of Medicine. 2021 Mar 3;384(9):818–28.
2. Karvellas CJ, Subramanian R, Olson JC, Jamil K. Role of Terlipressin in Patients With Hepatorenal Syndrome-Acute Kidney Injury Admitted to the ICU: A Substudy of the CONFIRM Trial. Crit Care Explor. 2023 Mar 28;5(4):e0890.
3. Moreau R, Durand F, Poynard T, Duhamel C, Cervoni JP, Ichaï P, et al. Terlipressin in patients with cirrhosis and type 1 hepatorenal syndrome: A retrospective multicenter study. Gastroenterology. 2002 Apr 1;122(4):923–30.
4. Kulkarni AV, Ravikumar ST, Tevethia H, Premkumar M, Kumar K, Sharma M, et al. Safety and efficacy of terlipressin in acute-on-chronic liver failure with hepatorenal syndrome-acute kidney injury (HRS-AKI): a prospective cohort study. Sci Rep. 2022 Apr 1;12:5503.
5. Zhou Y, Zeng J, Song L, Wang C. Clinical characteristics and treatment of terlipressin-induced ischemic skin necrosis: A synthesis of 35 literature reported cases. J Clin Pharm Ther. 2022 Aug;47(8):1270–5.
6. Macedo SS, Cabral C, Novais A, Teixeira M, Knock A. Terlipressin-related Ischaemic Necrosis of the Skin: A Rare Complication. Eur J Case Rep Intern Med. 2019;6(11):001247.
7. Coskun BDO, Karaman A, Gorkem H, Buğday I, Poyrazoğlu OK, Senel F. Terlipressin-Induced Ischemic Skin Necrosis: A Rare Association. Am J Case Rep. 2014 Oct 31;15:476–9.

Geisinger