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Terlipressin-related Ischaemic Necrosis of the Skin: A Rare Complication

Sara Simões Macedo[1], Cátia Cabral[2], António Novais[1], Mónica Teixeira[1], Anna Knock[3]
[1]Department of Internal Medicine, Centro Hospitalar Tondela-Viseu, Viseu, Portugal
[2]Department of Internal Medicine, Hospital Trofa Saúde Vila Real, Vila Real, Portugal
[3]Department of Internal Medicine, Hospital de Braga, Braga, Portugal

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ABSTRACT

Terlipressin is used for the treatment of bleeding oesophageal varices and hepatorenal syndrome in patients with cirrhosis. Adverse effects are usually minimal. However, potentially serious side effects such as skin necrosis involving the extremities, scrotum, trunk and abdominal skin can rarely occur. Our patient had greater skin involvement than other described cases. We present the case of a patient with extensive skin necrosis, unrelated to the infusion site, in the lower and upper limbs, scrotum and abdomen after the use of terlipressin. Skin necrosis secondary to terlipressin is a rare complication and early identification is essential so the drug can be immediately suspended.

LEARNING POINTS

- Skin necrosis secondary to terlipressin is a rare complication.
- Early identification is essential so the drug can be immediately suspended.
- Death is not directly related to the skin necrosis but to the secondary complications of advanced liver disease.

KEYWORDS

Terlipressin, vasoconstrictor agents, skin necrosis, hepatorenal syndrome, liver cirrhosis

CASE DESCRIPTION

A 71-year-old man presented with hypovolaemic shock due to ruptured oesophageal varices. He had alcoholic cirrhosis (Child-Pugh C), type 2 hepatorenal syndrome, thrombocytopenia, oesophageal varices and atrial fibrillation. He was currently on dicumarinic and amiodarone. There was no history of peripheral or coronary artery disease.

Haemodynamic stabilization and endoscopic procedures were immediately carried out. The following terlipressin protocol was initiated: 3 mg on the 1st day, 10 mg on the 2nd day, 9 mg on the 3rd day and 3 mg on the 4th day. However, on the 5th day of treatment, the patient presented extensive purpuric cutaneous lesions involving the lower and upper limbs, scrotum and abdomen. A biopsy of the involved skin showed necrosis of the entire epidermal thickness with vesicles and areas of detachment of the underlying dermis that was largely in the re-epithelialization phase; vasculitis was excluded. The terlipressin treatment was suspended on the 7th day. The lesions had improved 7 days after terlipressin withdrawal, without additional treatment. The patient eventually died from decompensated cirrhosis.

DISCUSSION

Terlipressin is a synthetic vasopressin analogue used in the treatment of upper gastro-intestinal bleeding from oesophageal varices. It has a half-life of approximately 6 hours[1]. This drug also has high affinity for type V1 receptors located in the smooth muscles of blood vessels

mostly in the splenic, renal, myometrial, bladder, adipocyte and cutaneous circulations[1–3]. Its vasoconstrictor effect is similar to that of vasopressin but requires a lower dosage with fewer side effects. The most common adverse effects are pallor, headache, abdominal pain, bradycardia and hypertension. There are more serious rare complications such as myocardial infarction, ischaemic colitis and skin necrosis[3]. Reports in the literature generally describe one or two affected body areas such as the abdominal wall, thigh, leg, toes, tongue, scalp, scrotum, breast and oesophagus. Other areas less frequently affected are the feet, breasts, back, forearms (except the hands and fingers), scalp and tongue[3]. Our patient had greater skin involvement affecting the upper and lower limbs, scrotum and abdomen. This atypical localization of necrotic areas could be explained by the existence of areas of thicker skin, extra fatty tissue[1] and the hypothesis of a heterogeneous distribution of V1 receptors.

The risk factors for ischaemic skin complications described in the literature include ischaemic disease, obesity, ascites, venous insufficiency, spontaneous bacterial peritonitis, hypotension, vasopressor drugs administered concomitantly, and continuous infusion of terlipressin[1,2]. Our patient presented with venous insufficiency and episodes of hypotension secondary to gastro-intestinal haemorrhage, which could cause tissue hypoxia.

A recent study comparing the administration of intravenous boluses and continuous terlipressin perfusion[4] suggested that continuous perfusion may avoid side effects, due to a lower total dose of the drug. Cutaneous necrosis was not detected in either of the two groups analyzed and only one recorded event of peripheral ischaemia was noted in the continuous perfusion group.

In the literature, skin manifestations were described on the 2nd and 3rd days of terlipressin treatment. In our case, we also considered the hypothesis of a cumulative dose effect due to the extent and late appearance of the lesions (5th day of administration).

The pathological anatomy of the lesions is non-specific and so is less useful for ruling out other vasculitic pathologies[2]. In our case, it was possible to identify epidermal necrosis. Macroscopically, the lesions are characteristically blackish in colour. Consequently, such lesions in a patient treated with terlipressin should raise immediate suspicion of this adverse effect[3].

Treatment with terlipressin should be discontinued if there is suspicion of skin necrosis. Most published cases reported improvement after withdrawal of the drug. Treatment with alprostadil (10 µg/day), sildenafil (50 mg/12 h) and nitrates can be given if lesions do not improve[3].

Mortality at 30 days was high (16 out of 22 patients, including ours). The majority of deaths were not directly related to cutaneous necrosis but to secondary complications of the advanced liver disease usually present in patients receiving terlipressin[3].

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