Cutaneous Necrosis Secondary to Terlipressin Therapy

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Sir,

Hepatorenal syndrome (HRS) is defined as a functional renal failure complicating end-stage cirrhosis. Its prognosis is very poor, liver transplantation being the only definitive treatment. During recent years, vasoactive agents such as terlipressin have been used as a bridge to transplantation (1–6). Terlipressin is currently licensed for the management of acute variceal bleeding (3, 6), but its effects on survival outcomes in HRS are still undefined (4). Only case reports and small series are available, but the results are promising and suggest terlipressin as an efficacious and safe choice (1, 2, 4).

CASE REPORT

We report here a case of a 39-year-old man with a medical history of alcoholic cirrhosis, who was admitted to the gastroenterology department on account of ascites and high acute digestive bleeding secondary to double antral ulcer, which resolved after endoscopic treatment. There was no evidence of oesophageal varices or any signs of encephalopathy. Laboratory tests revealed severe secondary anaemia and leucocytosis with neutrophilia, but complementary tests disclosed infection. High levels of creatinine were also remarkable. Diagnosis of HRS was made and terlipressin therapy was administered intravenously (0.5 mg/4 h). The renal failure then improved slightly. However, 48–72 h after the start of vasoactive therapy, the patient suffered from cyanosis and pain in the acral areas and purpuric lesions appeared on the lower legs. These cutaneous lesions evolved rapidly into large necrotizing areas, presenting as a livedoid pattern involving the entire surface of the lower extremities (Fig. 1). Cutaneous biopsy revealed necrosis of epidermis and upper dermis, with haemorrhage and epidermal detachment. There was no evidence of thrombi or vasculitic signs in the dermal vessels. A scanty non-specific inflammatory infiltrate was present (Fig. 2). Despite lowering the dose of terlipressin, and subsequent drug withdrawal, the cutaneous lesions remained invariable. No study of the arterial circulation was made, apart from physical examination, which showed present and symmetrical pulses. Arteriography, the gold standard test, could not be performed due to the acute renal failure. The patient died a few days later secondary to recurrent digestive bleeding and impairment of renal function in the context of hepatic failure. No autopsy was performed.

Fig. 1. Large purpuric lesions presenting as a livedoid pattern involving the patient's thigh.

DISCUSSION

The use of vasoconstrictor agents for HRS may be complicated by ischaemic side-effects. Its use is not recommended in patients with a medical history of ischaemic diseases (1).

Terlipressin is a non-selective V1 vasopressin analogue (2, 3). Compared with vasopressin and other analogues, it is known to have similar vasoconstricting potency but much less severe ischaemic complications (3–5, 7). Case reports and small series published in the literature

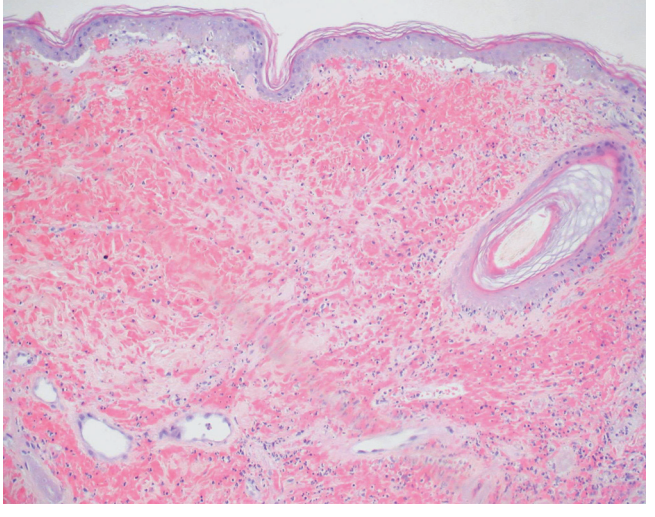

Fig. 2. Necrosis of epidermis and upper dermis, with haemorrhage and epidermal detachment. Dermal vessels were not involved, and there was no evidence of thrombi or vasculitic changes (haematoxylin and eosin ×200).

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since 1990 have reported the use of terlipressin for the treatment of HRS with good outcomes and low risk of adverse effects. Incidence of secondary ischaemic events in HRS differs depending on series from 5% to 29% (1, 2, 8, 9). Significantly, a recent meta-analysis revealed that no permanent interruption of terlipressin was needed because of intolerance (1).

Undesirable effects are usually mild and disappear by lowering the dose of the drug, i.e. paleness, acral cyanosis, abdominal pain, diarrhoea, headache and self-limiting cardiac arrhythmias. However, serious ischaemic events, such as skin necrosis involving the extremities, scrotum, penis or abdominal skin have been documented (1–3, 5, 6, 8, 9). Obesity, venous insufficiency and spontaneous bacterial peritonitis have been proposed as possible risk factors for the development of ischaemic cutaneous complications (3, 5).

Our patient did not have a medical history of ischaemic disease and, at physical examination, he was not obese and showed no signs of venous insufficiency. Repeated negative ascitic cultures ruled out a spontaneous bacterial peritonitis. The doses of terlipressin administered were low. This case is of clinical importance due to the large area of cutaneous necrosis and its rapid occurrence, without resolution after terlipressin withdrawal.

In conclusion, we report here a new case of cutaneous necrosis secondary to terlipressin therapy for management of HRS. Although rare, we must bear in mind the possibility of ischaemic complication of terlipressin.

The authors declare no conflict of interest.

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