Toxic Epidermal Necrolysis Associated with High Intake of Sildenafil and its Response to Infliximab

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Sir,

Toxic epidermal necrolysis (TEN) is a rare, but well-known acute and life-threatening disorder first described by Lyell (1). It is defined as epidermolytic necrosis induced most commonly by drugs (1, 2). If the loss of epidermis exceeds 30%, it is called TEN, whereas less than 30% skin affection is called either Stevens-Johnson (SJ) syndrome (<10%) or intermediate SJ-TEN (10–30%). It can involve the internal surfaces of the gastrointestinal tract (1, 2). We describe here a classical case of TEN induced by poly-pharmacy including the intake of aphrodiasic herbal drugs and sildenafil. Treatment with infliximab led to a rapid recovery.

CASE REPORT

A 67-year-old man was admitted with an extensive mucocutaneous eruption of large erythematous areas and bullae leading to denudation consistent with TEN (Fig. 1a). He had no history of skin disease or allergies. He suffered from cardiac insufficiency, diabetes mellitus, gout, hyperlipidaemia, hypertension, obesity and had 5 months earlier undergone replacement of knee joints due to osteoarthritis. At the time of the skin eruption he took eight drugs for the diseases mentioned above. As he had recently married he took an aphrodiasic drug of Chinese herbal medicine (2 + 2 capsules over 2 days). Simultaneously, he had also taken 100 mg and 200 mg sildenafil over a 2-day period.

A few days after this intake and approximately 10 days before admission at our hospital he developed oral ulcers and a rash on the upper part of the back. He was admitted to a local hospital and diagnosed as having Lyell’s syndrome and started prednisolone 60 mg p.o. daily, which was given for 2–3 days. Due to progressive symptoms, he was admitted to our hospital. We observed a universal skin rash including severe erosions of the oral cavity. Approximately 40–50% of his skin was eroded, especially the back, buttocks and feet. The rest of his skin was also affected. Our clinical diagnosis of TEN was based on his history of poly-pharmacy and confirmed by histological examination, which showed epidermal necrosis of keratinocytes and intra-epidermal blister formation (Fig. 2). Immunofluorescence was negative. Biochemical investigations including liver enzymes were normal.

We stopped all medication except antihypertensive medicine and insulin. He was admitted to our intensive care unit for i.v. fluids and nursing care with sulfadiazine cream on eroded skin. We gave infliximab (Remicade®) 3 mg/kg (total dosage 300 mg) over a 3-h infusion.

Multiple cultures were obtained from skin, and these showed colonization with a sensitive strain of Pseudomonas aeruginosa. His course in the intensive care unit was complicated by the development of septic shock secondary to a catheter-related infection, as blood cultures and the femoral central vein line tip grew P. aeruginosa. The patient responded

Fig. 1. The patient (a) before and (b) 10 days after injection of infliximab 3 mg/kg during the first day of admission.
well to meropenem 1 g three times daily, with prompt resolution of septic shock after 48 h. Within 1 week re-epithelization had started (Fig. 1b) and i.v. administration of analgesics was discontinued. The patient was transferred to a stationary ward after 10 days and recovered fully.

Toxicological investigation of the Chinese herbal medicine (Fu Yauan Chun capsules) revealed that each capsule (0.5 g) contained 95 mg sildenafil. Thus the maximal dosage of sildenafil per day just prior to his skin symptoms may have been close to 300–400 mg. Additionally, each capsule contained osthole, which belongs to derivatives of coumarin that are effective in treatment of erectile dysfunction (3).

We measured tumour necrosis factor-alpha (TNF-α) on his arrival before treatment and after 1 week. The first sample showed 16.5 ng TNF-α/ml (normal range 0–8.5 ng/ml). The second sample was negative for TNF-α.

REFERENCES