Toxic epidermal necrolysis following chlorpromazine ingestion complicated by SIADH

Sir, Toxic epidermal necrolysis (TEN) is an often fatal condition most frequently caused by adverse drug reactions. We report what we believe is the second case of TEN caused by chlorpromazine, an aminothiazine. This case was complicated by inappropriate antidiuretic hormone secretion (SIADH). This has not been reported with TEN although there is one report of SIADH after chlorpromazine.3

Case report
A 23-year-old caucasian man with a history of personality disorder and suicide attempts received chlorpromazine 100 mg nocte for two nights, for sedation, while in prison. There was no history of allergy. Two days later he developed a haemorrhagic buccal blister with influenza-like symptoms. On day 6 he was released from prison and he noted erythematous spots on his limbs and trunk. He received amphotericin, nystatin, amoxycillin and chloramphenicol eye drops. On day 8 he was admitted as an emergency with pyrexia (39.6°C), crepitations and a bullous eruption involving over 50% of his skin. Nikolsky’s sign was present. He had SIADH (plasma sodium was 125 mmol/l), urine osmolality = 543 mOsm/kg and plasma osmolality = 268 mOsm/kg. On day 12 he was commenced on prednisolone and minoxidil for suspected TEN. His condition deteriorated and he was transferred to intensive care. There was a lack of hydration, and he was commenced on fluid replacement. His skin lesions were confirmed histologically as toxic epidermal necrolysis. In view of the poor response to treatment, the patient died on day 16. The autopsy confirmed the diagnosis of toxic epidermal necrolysis and a review of six cases. Burns 1990; 16: 97–104.

PATRICK PURCELL

Toxic epidermal necrolysis associated with indomethacin therapy

Sir, Toxic epidermal necrolysis (TEN) is a rare and sometimes fatal disease first described in 1956 by Lyell.1 Drugs are a major cause. Other associations include viral infections, measles, immunisation, lymphoma, radiotherapy and graft-versus-host disease.2 The precise pathophysiology of the condition is still not known. We report a case of TEN secondary to indomethacin which has been rarely reported in the UK.

Case report
A 60-year-old man presented with a generalised purpuric eruption two days after starting indomethacin, 50 mg tid, for osteoarthritis. There was no history of sord throat or sepsis elsewhere and no viral prodrome. Initially he had hypertension and a transurethral resection of the prostate 10 years earlier. His only other medication was atenolol, 50 mg once daily, which he had taken for 10 years. He had no known allergies. Examination showed sheeted erythema with numerous bullae and pustules over most of his body. There was no mucosal involvement. His temperature was 38°C. The rest of the examination was unremarkable. Investigations showed a haemoglobin of 15.2 g/dl, white cell count 16 x 10^9/l (90% neutrophils, 2%, eosinophils), erythrocyte sedimentation rate 10 mm/h. Liver function tests, urinalysis and electrolytes were normal. Blood, urine, throat and skin cultures were unremarkable. A skin biopsy showed sub-epidermal bullae with epidermal necrosis and a mild lymphocytic infiltrate which was felt to be compatible with TEN. Indomethacin was stopped and he was treated with flumazaine and prednisolone 40 mg once daily and a moderate-potency topical steroid. Within two days his rash was beginning to improve and no new pustules developed. The prednisolone was stopped after one week and he was discharged. In view of the severity of the eruption the patient was not rechallenged with indomethacin.

There have been three cases of TEN from indomethacin reported to the Committee on Safety of Medicines in the UK. A patient developing TEN four days after indomethacin has been published.3 TEN is usually characterised by large areas of erythema followed by a bullous phase. Our case was slightly atypical in that there was little erythema and more predominant blister formation early in the course. We believe this is an example of toxic follicular pustuloderma, which is associated with drug therapy,4 was considered but the subsequent course of the disease and histology confirmed a diagnosis of TEN. Drugs associated with TEN include barbiturates, phenytoin, phenobarbitone, phenytin, penicillin, sulphonamides, dapsone, chloramphenicol, quinine, allopurinol and tetracyclines.5 One study has shown that, amongst nonsteroidal anti-inflammatory drugs, indomethacin had the lowest risk of TEN.6 There is no specific treatment. The suspected drug should be withdrawn, fluid and electrolyte loss replaced and topical antibacterials

Table Drugs reported as causing TEN3-7 (most commonly reported in bold type)

<table>
<thead>
<tr>
<th>Nonsteroidal anti-inflammatory drugs</th>
<th>Antibacterials</th>
<th>Anticoagulants</th>
<th>Analgesics or drugs used in treatment of gout</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>isoxicam</td>
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<td>phenobarbital</td>
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P. Purcell and A. Valmana

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