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Letters to the Editor

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.[1] We report what we believe is the second case of TEN caused by chlorpromazine, an aminoalkyl phenothiazine. 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.[2]

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 positive. 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 aggressive, refused treatment and tried to leave. The psychiatrist considered he was suicidal and detained him. Virtually 100% of the skin was involved. It was felt he would die of sepsis if he left. He tried removing his own necrotic skin and toe nail. He received diazepam intravenously under common law. It was decided to change his detention order to a treatment order for life-saving treatment. A decision was then made (under common law) that it was imperative to ventilate the patient forthwith, rather than wait for the treatment order, which was completed shortly afterwards. Ventilation lasted 22 days, complications included anaemia, pulmonary oedema, granulocytosis and clotting abnormalities. A definitive histological diagnosis of TEN was made. Immunofluorescence studies were negative. After 16 days in the intensive care unit there was almost total epidermal regeneration. On leaving the intensive care unit he suffered a confusional state which resolved over six days. He was intermittently challenging but was discharged 14 days after leaving the intensive care unit. Dermatologists and psychiatrists quickly discharged him from follow-up and 18 months later the only sequelae are occular (symblepharon).

As chlorpromazine is commonly used, the rare[1] but serious side-effect of TEN should be considered. It is unclear whether the SIADH was associated with TEN or chlorpromazine in this case. SIADH has been described with other phenothiazines,[2] but no other known causes of SIADH applied in this case.

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Table Drugs reported as causing TEN[1,3–7] (most commonly reported in bold type[4])

Nonsteroidal anti-inflammatory drugs	*Antibacterials*	*Anticonvulsants*	*Analgesics & drugs used in treatment of gout*	*Others*
isoxicam	**ampicillin**	**phenobarbital**	**aspirin**	fluoxetine
fenbufen	**amoxicillin**	carbamazepine	**paracetamol**	fluvoxamine
piroxicam	**cotrimoxazole**	phenytoin	diflunisal	indapamide
oxyphenbutazone	sulfasalazine		**allopurinol**	omeprazole
diclofenac	sulfadiazine		colchicine	etrenitrate
indomethacin	sulfamethoxy-pyradizine			vincristine
flurbiprofen	erythromycin			chloropropramide
phenylbutazone	rifampicin			cyclophosphamide
				clofibrate
				chlorpromazine

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 pustular eruption two days after starting indomethacin, 50 mg tid, for osteoarthritis. There was no history of sore throat or sepsis elsewhere and no viral prodrome. In the past 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 16×10^9/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 flamazine 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 disease. Initially a diagnosis 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, phenylbutazone, phenytoin, penicillin, sulphonamides, dapsone, chloramphenicol, quinine, allopurinol and tetracyclines.[5] One study has shown that, amongst nonsteroidal anti-inflammatories, 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