Fatal adverse drug reaction to trimethoprim

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BACKGROUND
Trimethoprim is the antibiotic of choice for treating uncomplicated community acquired urinary tract infections. However, before prescribing any drug it is vital to obtain a detailed drug history to exclude possible drug allergy.

OBJECTIVE
We present the case of a fatal adverse drug reaction due to trimethoprim. We discuss some of the problems that led to the patient's death, and consider how to prevent similar events.

DISCUSSION
Re-exposing a patient to a drug suspected of causing an adverse reaction is associated with considerable risk of morbidity and mortality. A detailed history is vital to correctly diagnose drug allergies but, even so, it is not always possible to identify the causative agent. Following an adverse drug reaction, health professionals must take appropriate steps to avoid inadvertently re-prescribing the culprit drug. This is essential to avoid the tragic outcome highlighted in this case.

Case history

An Asian man, 70 years of age, was seen by an on-call general practitioner with symptoms typical of an urinary tract infection (UTI). He was prescribed trimethoprim. Within a few hours of the first dose his skin became sore and itchy. Twenty-four hours later he was admitted to hospital with large blisters involving the trunk, buttocks, thighs and perineum (about 60% body surface area). The skin was painful and extremely tender to touch. There was extensive epidermal loss revealing raw, oozing dermis (*Figure 1*). Blood tests and chest X-ray were normal.

The patient had smoked 20 cigarettes a day for 50 years, had chronic obstructive pulmonary disease and used regular inhalers. Two years previously he had been admitted with a chest infection. For 5 days before that admission he had been taking his daughter's trimethoprim to help treat his fever. On admission he was prescribed amoxycillin and 2 days later developed a pruritic bullous eruption with epidermal loss on the perineum, hands and back. This resolved spontaneously. A dermatologist made a diagnosis of severe drug induced erythema multiforme, secondary to either trimethoprim or amoxycillin. The patient was counselled about the potentially serious consequences of re-challenge with either antibiotic. A discharge letter detailing this information was sent to his GP.

On this hospital admission, we diagnosed toxic epidermal necrolysis (TEN) due to trimethoprim. We stopped the drug and implemented aggressive supportive management. He was given fluid replacement via a central line and high oral protein supplementation. The necrotic epidermis was debrided and dressed and he was nursed on a 'pressure relieving' mattress. By day 2, there was no further skin loss. By day 10, most of the denuded areas were re-epithelialising. However, on day 14 he deteriorated suddenly, suffered a cardiac arrest and died.

Discussion

TEN is a rare, adverse cutaneous drug reaction with an estimated mortality rate of 30–70%.[1–3] The most common causes are antibiotics, anticonvulsants and nonsteroidal anti-inflammatory drugs. The condition usually occurs within 1–3 weeks of commencing the culprit drug, but can occur within 24

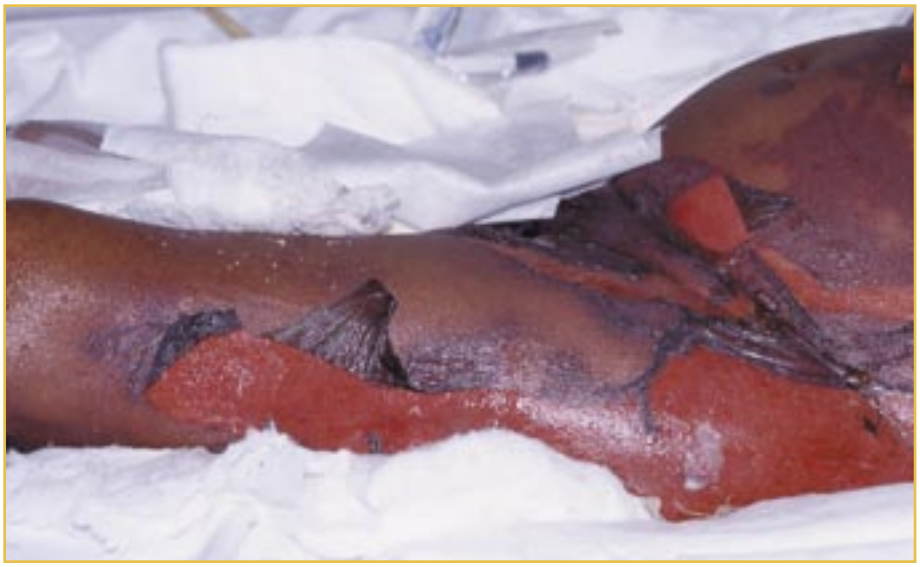

Figure 1. Toxic epidermal necrolysis with extensive epidermal loss and raw, oozing dermis

hours upon rechallenge. Ninety percent of patients suffer erosions of the oral, genital, and ocular mucosa. A third of survivors have ocular sequelae ranging from sicca syndrome to blindness.[4] The respiratory and gastrointestinal tracts may also be involved.[5] Prompt diagnosis of TEN and the immediate withdrawal of the suspected drug are essential.[6] Patients should be managed in an intensive care setting, with aggressive supportive measures.[1]

Adverse drug reactions are common, but fatal drug reactions are rare. Re-challenge with a drug suspected of causing an adverse reaction is associated with considerable risk. As there is no diagnostic test that can reliably identify the culprit drug, a detailed clinical history is vital to establish a diagnosis. Even so, it is not always possible to identify a single causative drug from a 'short list' of two or three 'contenders'. The decision to re-administer a drug suspected of causing an adverse reaction must be carefully evaluated in terms of risks and benefits.

Our patient was treated by an on-call GP, who did not have access to the patient's medical records. In the absence of records, often a GP relies solely on the patient (and relatives) for a drug history. Unfortunately our patient had a poor command of the English language and it is unclear how much he understood about the initial problem. Without the knowledge of the previous adverse drug reaction, trimethoprim would be the antibiotic of choice with which to treat an uncomplicated community acquired UTI.

This case emphasises the importance of good communication between health professionals and patients. It is imperative that, following recovery from an adverse drug reaction, patients and their relatives are counselled about the need to avoid the drug(s) thought to be responsible, and all chemically related compounds. If necessary this should be done via an interpreter. Adverse reactions should be clearly documented in an easily visible place in the patient's medical records, and the patient's GP informed in writing. Hospital discharge information needs to be entered into the patient's notes immediately rather than when the patient next presents. The front page of paper records or the summary sheet of computer records containing allergies, could be given to the patient to be used when attending a hospital or other GPs. Medical alert bracelets documenting drug allergies are a useful adjunct to the above, serving as a reminder to both patients and medical staff. In cases where a language barrier hampers an accurate history or where the patient is too unwell to communicate, alert bracelets may be the only way to warn medical practitioners of drug allergies.

It is the responsibility of every health professional to ensure that, following adverse drug reactions, appropriate steps are taken to minimise the risk of inadvertent drug re-challenge. This is essential to avoid the tragic, but preventable, outcome demonstrated in this case.

Summary of important points

- Although adverse drug reactions are common, fatal drug reactions are rare.
- Re-challenging a patient with a drug suspected of causing an adverse reaction is potentially dangerous.
- If a patient is seen without the benefit of their medical records, particular care should be taken to elicit details about the past medical history, including drugs and drug allergy.
- Following an adverse drug reaction, appropriate steps must be taken to minimise the risk of inadvertent drug re-challenge. This includes counselling/educating the patient and family about the diagnosis and risk of re-exposure (via an interpreter if needed), clearly documenting allergy details in the medical records and using medical alert bracelets.

Conflict of interest: none.

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