Case 1—A 56 year old man with mild hypertension sustained a cerebrovascular event in 1980 after which he had a mild right facial weakness and mild right hemiparesis. In 1981 he presented to this clinic with shooting pains affecting the right side of his body. He was successfully treated with sodium valproate and amitriptyline for three years. In 1984 the pain recurred and was worse and he also complained of hyperaesthesia of the right side of his body. Treatment with haloperidol and clomipramine was unsuccessful, and a transcutaneous nerve stimulator provided only temporary relief. In January 1985 he started a course of naloxone infusions; this resulted in partial improvement, which was maintained for six months. A second course of infusions gave greater relief for a further six months, and a third course gave him complete relief from pain for another six months. The pain then recurred and he started a fourth course of treatment. Results were equally good.

Case 2—A 49 year old obese woman taking the oral contraceptive pill presented in 1981 with a right hemiparesis. She made a partial recovery but was left with a constant nagging pain in her right arm and leg. After being seen in several departments and by several practitioners she presented to this clinic and started a course of naloxone infusions, which resulted in considerable but not complete improvement during the treatment and for the next four months.

Comment

The thalamic syndrome, first described in 1906,[3] is a rare but severely disabling complication of cerebrovascular events. It often produces severe pain, usually dysaesthetic or shooting. Concentrations of endogenous opioids in cerebrospinal fluid are increased in patients with the syndrome, and naloxone is believed to act by antagonising the effect of these opioids, especially in the region of the locus coeruleus.[4] Single doses of naloxone have been shown to be of great benefit in 54% of patients studied, their effect lasting for from four days to two and a half years.[1] Our cases indicate that increasing both the duration of treatment and the total dose of naloxone improves pain relief but does not increase the duration of the beneficial effect.

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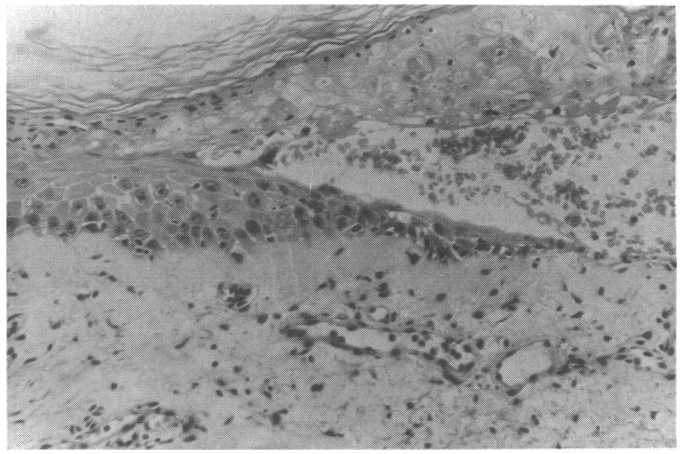
Toxic epidermal necrolysis occurring during treatment with trimethoprim alone

Trimethoprim is increasingly being used to treat infections of the urinary tract. After reports that trimethoprim is as effective and has fewer side effects when used alone as when combined with sulphamethoxazole (as co-trimoxazole) trimethoprim alone has increasingly been used to treat infections of the urinary tract. We report a case of toxic epidermal necrolysis occurring during treatment with trimethoprim alone. To the best of our knowledge this is the first published report of this side effect of this drug.[1]

Case report

A 74 year old woman with senile dementia was treated with trimethoprim 200 mg twice daily because of a urinary infection with *Escherichia coli*. She was not taking any other drugs. On the third day of treatment she developed an extensive erythematous eruption. The inflamed skin stripped off to leave large eroded areas, and in other areas there were flaccid blisters. Nickolsky's sign was present. She had severe mucosal ulceration and mild conjunctival inflammation. Apart from recurrent infections of the urinary tract, which had been treated with antibiotics including co-trimoxazole, she had no relevant medical history.

Toxic epidermal necrolysis was suspected, and she was admitted for prophylactic treatment, rehydration, intensive nursing on a continuous fluidisation bed, and analgesia to keep her comfortable. A skin biopsy (figure) confirmed the diagnosis; the specimen showed a subepidermal split and complete necrosis of the separated epidermis, which was invaded by mononuclear cells. A mild mononuclear perivascular infiltrate was present in the upper dermis.[2] Coexistent staphylococcal infection was excluded by culture of blood, urine, stools, and skin swabs. Full blood count, urea and electrolyte concentrations, autoimmune profile, and results of direct and indirect epidermal fluorescence were all normal. Oral steroids were not given; supportive treatment alone resulted in a gradual but complete recovery.



Skin biopsy specimen showing subepidermal split with complete necrosis of separated epidermis and mononuclear dermal infiltrate consistent with toxic epidermal necrolysis.

Comment

Toxic epidermal necrolysis was first described in 1956 as a blistering syndrome causing epithelial shearing with its attendant clinical complications.[3] It has a mortality of 10-40%.[4] Many drugs have been implicated as a cause, including sulphonamides, penicillins, derivatives of pyrazalone, and barbiturates. When toxic epidermal necrolysis has occurred with co-trimoxazole the sulphonamide component has been thought responsible. In view of our report some of these cases may have been due to the trimethoprim component of co-trimoxazole. We think that trimethoprim should be added to the list of drugs capable of causing toxic epidermal necrolysis and that doctors should be alerted to this complication, especially as trimethoprim is widely used.

Since we reported this case to the Committee on Safety of Medicines in August 1987 it has received four reports of epidermal necrolysis associated with trimethoprim; whether these were cases of toxic epidermal necrolysis is not known. The manufacturer of the drug used in this case and two other manufacturers have not received any other reports of this complication.

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