use of intravenous cidofovir, we think it should be used in serious cases of recalcitrant molluscum contagiosum when other therapeutic choices have failed. The resolution of the lesions in our patient suggests that further studies are necessary to demonstrate the utility of intravenous cidofovir in immunodepressed patients and those with extensive lesions. However, Scolaro and Gordon (6) have recently described a promising alternative to the medical treatment of recurrent MCV lesions by the use of electron-beam radiation.

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Fatal Toxic Epidermal Necrolysis Associated with Ceftazidine and Vancomycin Therapy: A Report of Two Cases

Sir,

Toxic epidermal necrosis (TEN) is a condition most often induced by drug hypersensitivity. Some authors suggest that TEN and Stevens–Johnson syndrome are a continuum of the same condition (1). If less than 30% of the skin surface is involved, it is classified as Stevens–Johnson syndrome, whereas if more than 30% is involved, it is called TEN. Both conditions include mucosal involvement. Erythema multiforme is on clinical grounds believed to be a different entity (1, 2).

We report 2 fatal cases of TEN, which were associated with ceftazidine and vancomycin therapy. Ceftazidine has not previously been reported with TEN, and only a few case reports exist on vancomycin and TEN. Ceftazidine belongs to the cephalosporines, which structurally and pharmacologically are related to penicillin. Cross-allergenicity with penicillin is considered to happen in 5–16%. Cephalosporines may be nephrotoxic.

CASE REPORTS

Case 1

An 8-year-old boy was admitted because of malaise and vomitus. He had meningo-myelocle from birth and had developed hydrocephalus, treated with a v-p shunt, a neurogenic bladder and, as a consequence of this, uroemia. He had no known allergies. Culture from blood and urine showed Enterococcus faecalis and Actinobacter being sensitive to penicillin. Therefore, he was given i.v. ceftazidine 800 mg × 2 for 9 days. Owing to continued culture of E. faecalis and later Staphylococcus aureus from the skin, he also received i.v. vancomycin 150 mg, but only once. Seven days later he was given 500 mg i.v. ampicillin for 10 days. The day after ampicillin was initiated ceftaazidine was stopped and gentamycin 80 mg i.v. was given once. The same day an erosion was noted on the buttocks which spread to the trunk and extremities, together with low-grade fever. The clinical changes were peeling and blistering of the skin leaving erosions and bleeding. Mucosal sites were also involved, with bleeding from the gastrointestinal tract. At the height of the rash up to 80% of his skin was affected, leaving large denuded areas.

Histological examination of the affected skin showed necrosis of the epidermis with blistering. Other drugs were furosemide, valium, phenytoin (given after the rash occurred) and benadryl, but none of these drugs was considered causal to the skin rash.

The condition deteriorated clinically. He had leukocytosis around 25 × 10⁹/l and a severe thrombocytopenia with bleeding from the skin and the gastrointestinal tract. On the suspicion of “immune activation” and the possibility of an overactivity of the neutrophil granulocytes, a short-term intensive course of systemic immunosuppressive therapy was given with 25 mg prednisone i.v. daily for 3 days, cyclosporine 25 mg bid for 3 days and methotrexate 7.5 mg once. This treatment seemed temporarily to halt the progression of skin lesions, but the condition deteriorated with leukopenia. Within a few days hemorrhage was found in the ventricular system of the brain and therapy was stopped. He died after 5 weeks in the hospital.

Case 2

A 36-year-old woman was diagnosed with acute myeloid leukemia (AML) in 1991, for which she had a successful allogeneic bone marrow transplantation. She was readmitted in 1998 with a relapse of her AML confirmed through bone marrow aspiration. She had no previous history of allergy.

At admission she received ceftazidine 2 g × 3 i.v. for the next 5 days. A newly diagnosed herpes labialis was treated in parallel with acyclovir. Five days later an itchy rash of macular patches was observed on the legs. Her treatment was changed to imipenem 500 mg × 4 i.v. for 5 days, vancomycin 1 g × 2 i.v. for 3 days, chemotherapy (idarabubicin, ARA-C, etoposide, endosetron and dexamethasone for 3 days) and gentamycin 2 mg/kg i.v. for 3 days, and fluconazole 200 mg i.v. for 2 days. Within a few days the rash developed into blisters and erosions affecting more than 80% of her skin. Clinically, it was fully compatible with TEN. Histological

Acta Derm Venereol 80
examination of non-eroded skin on the forearm showed changes compatible with erythema multiforme. Her skin condition deteriorated rapidly. Antibiotics were stopped and she was given i.v. hydrocortisone, but she died from shock only 10 days after admission.

DISCUSSION

Two cases of fatal TEN are reported. Case 1 received intensive i.v. therapy with ceftazidime and vancomycin prior to the development of TEN, while case 2 received only ceftazidime and acyclovir. It is not possible with certainty to establish which compound elicited the drug rash as drugs with a possible cross-reactivity were given after the rash occurred. In case 1 ceftazidime and vancomycin may have had an additive effect. The patient was also uremic, which is a complicating factor when intensive i.v. therapy is given. In case 2 only ceftazidime was given prior to the development of TEN, apart from aciclovir, which is a highly atoxic drug.

A Medline search gave 1.522 articles on TEN (November 22, 1999). The combination of TEN and ceftazidime yielded 0 articles, TEN and cephalosporins 22 articles, TEN and vancomycin 3 articles, and TEN and gentamycin 7 articles. This shows that TEN is rarely seen after these compounds, and fatal TEN has not been reported. Cefazidime (3) and vancomycin (4, 5) have been associated with pustuloderma and TEN, respectively.

A recent study has documented that short-term therapy with phenytoin, phenobarbital and carbamazepine is associated with TEN or Stevens–Johnson syndrome among 16% of patients (6). TEN occurs during the first 8 weeks of treatment. Vancomycin is known to induce a number of side-effects, and it could have been the eliciting drug in case 1, who had uremia with impaired drug excretion (7). Severely ill patients undergoing multiple i.v. medications are at high risk for complications, as confirmed in this report. In addition, patients after bone-marrow transplantation and HIV/AIDS patients have an increased risk of TEN (1).

The immunosuppressive therapy in our patients was of no value, corresponding to a double-blind study of immunosuppression in patients with severe bullous erythema multiforme or TEN (8). Patients given intensive i.v. drug therapy in whom skin rashes develop should be evaluated acutely, and if TEN is diagnosed, only life-saving medication should be used.

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Randomized Double-blind Comparison of Short-term Itraconazole and Terbinafine Therapy for Toenail Onychomycosis

Sir,

I read with interest a recent study in Acta Dermato-Venereologica (1) comparing itraconazole and terbinafine in the treatment of onychomycosis. Several comments come to mind.

1. In previous studies (2) the duration of follow-up was 46 weeks and the mycological cure rates for itraconazole declined after week 36 as those of terbinafine increased.
2. There is no “black-box” warning in the package insert with terbinafine as compared to itraconazole. In addition, the alleged “rare cases of serious hepatotoxicity...” are not included in the terbinafine package insert of terbinafine, presumably because of the remote likelihood of such an occurrence.
3. Terbinafine is the only fungicidal agent in the treatment of dermatophytosis, while itraconazole is clearly fungistatic. No amount of machination can change this fact.

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