

## Efficacy of Cidofovir in the Treatment of Recalcitrant Molluscum Contagiosum in an AIDS Patient

Sir,

Molluscum contagiosum is a cutaneous skin lesion exclusive to humans, caused by molluscum contagiosum virus (MCV), a DNA virus of the poxvirus family. Among HIV patients, the prevalence of MCV is from 5 to 18% (1). This illness is usually limited and characterized by small, nodule-shaped lesions, indolent and umbilicated, and it can affect every part of the body except the palms and soles (1). The treatment is often unsatisfactory and there is no proven, specific antiviral therapy. We describe here a patient with recalcitrant molluscum contagiosum who was resolved with intravenous cidofovir.

In November 1996, a 32-year-old man with AIDS (CDC stage C3) and previous history of recurrent pneumonia and pulmonary tuberculosis came to our service because of the appearance of rounded, umbilicated papules and plaques on his face, which subsequently grew in number and size (Fig. 1). A biopsy specimen was examined, and confirmed the diagnosis of MCV. CD4 cell count was 76 cell/mm<sup>3</sup> and his HIV RNA level was 427,764 copies per ml. From May 1996 to June 1997 he was treated with zidovudine (ZDV) plus zalcitabine (DDC), and from then to November 1997 with ZDV plus lamivudine (3TC) plus saquinavir (SQV). He also received prophylactic therapy against *Pneumocystis carinii* with trimethoprim—sulfamethoxazole 3 days a week. The patient had never followed the treatment properly because he usually stopped taking the prescribe medications. Finally all treatment (antiretroviral and prophylaxis) was stopped definitively in November 1997, as this was decided by the patient. His lesions were treated in several occasions without success with curettage and podophyllin. In February 1998, he presented with extensive MCV lesions covering more than 60% of his face. This produced in our patient a severe depression, even with a suicide attempt, beginning treatment with paroxetine. Treatment with cidofovir (5 mg/kg once per week followed by 5 mg/kg once every 2 weeks for maintenance therapy) and probenecid (2 g, 3 h before the administration of cidofovir, and 1 g, 2 and 8 h later) was initiated in spite of not having a clear indication due to the



Fig. 1. Extensive, nodular, crusting plaques of molluscum contagiosum virus confluent on the cheek and chin.

great extension of the lesions and his severe depression. Dosage of cidofovir was maintained as renal function was normal. In June 1998, after 9 cycles, the lesions had disappeared (Fig. 2). So far, he is in a complete remission and there is no evidence of MCV, although he refuses any antiretroviral or prophylactic treatment and continues to have severe immunological failure (CD4 count less than 45 cell/mm<sup>3</sup> and HIV RNA level 1,363,445 copies per ml).

MCV is common in HIV-infected patients (1). The occurrence of opportunistic infection occur in 35% of these patients before the diagnosis of MCV, mainly in those patients with a mean CD4 count less than 100 (1). Treatment of MCV in HIV patients is often difficult and so far there is no ideal treatment (2). Cidofovir, a nucleotide analogue of deoxycytidine monophosphate with broad spectrum against DNA-viral, is an active treatment against MCV (3). When this drug is given intravenously, its prolonged half-life allows dosing every 2 weeks. Adverse effects associated with cidofovir are nephrotoxicity and, less common, neutropenia, fever and metabolic acidosis. Renal toxicity can be reduced by prehydration (1–2 l saline) and probenecid, a uricosuric drug that reduces the tubular excretion of cidofovir and so reduces renal dysfunction (4).

We began treatment with 5 mg/kg of cidofovir although 2 mg/kg had been employed by Meadows (3), as our patient had good renal function, extensive lesions, and the necessity for a quick resolution because of his severe depression. It is not clear if nucleoside analogues, non-nucleoside analogues or protease inhibitors contributed to the disappearance of the MCV lesions (3), but in our case the patient did not have an effective adherence to the treatment because he refused any antiretroviral treatment. Furthermore, the remission of the MCV did not correlate with either the use of antiretroviral treatment or improvement of the immune status, so in our opinion the remission of the MCV was due to cidofovir.

So far, intravenous cidofovir is only indicated in retinitis due to CMV in AIDS patients without renal functional disorder (5). Cidofovir also could be used topically or intralesionally (2, 3, 5), but in extensive lesions intravenous use may be necessary. According to our result and the literature (3), in spite of not having a great experience in the



Fig. 2. Resolution of lesions after intravenous cidofovir therapy.

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 Cefazidime and Vancomycin Therapy: A Report of Two Cases

*Sir,*

Toxic epidermal necrolysis (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 cefazidime and vancomycin therapy. Cefazidime has not previously been reported with TEN, and only a few case reports exist on vancomycin and TEN. Cefazidime belongs to the cephalosporines, which structurally and pharmacologically are related to penicillin. Cross-allergenicity with penicillin is considered to happen in 5–16%. Cephalosporins may be nephrotoxic.

#### CASE REPORTS

##### *Case 1*

An 8-year-old boy was admitted because of malaise and vomitus. He had meningo-myelocele from birth and had developed hydrocephalus, treated with a v-p shunt, a neurogenic bladder and, as a consequence of this, uraemia. 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. cefazidime 800 mg  $\times$  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 cefazidime 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  $25 \times 10^9/l$  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 cefazidime 2 g  $\times$  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  $\times$  4 i.v. for 5 days, vancomycin 1 g  $\times$  2 i.v. for 3 days, chemotherapy (idarubicin, ARA-C, etoposide, endoxan and dexamethazone 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