Failure of foscarnet in disseminated herpes zoster

Sir,—It is now rare for immunocompromised patients to die from any form of varicella-zoster virus (VZV) infection. However, acyclovir-resistant VZV has recently been recovered from HIV patients with indolent skin lesions, and foscarnet has been shown to be potentially effective.1,2

A 13-year-old girl had an allogeneic bone marrow transplant (BMT) from an HLA-identical sibling for acute myeloid leukemia (M4, myelomonocytic) in first remission. 46 days after BMT herpes zoster developed on her left flank and was treated successfully with acyclovir for 12 days. She then developed grade III acute graft-versus-host disease (GVHD) of the skin, which was controlled by corticosteroids. While she was being weaned off corticosteroids, at 89 days post-BMT, she developed acute GVHD of the liver. Two 5-day courses of antithymocyte globulin were given with minimal response, followed by 5 days of methylprednisolone 250 mg/m² per day and cyclosporin, which improved her liver function. The cyclosporin dose was adjusted to keep concentrations between 200 and 400 µg/L. On day 129 her aminotransferases and bilirubin increased. She was given another 5-day course of methylprednisolone (300 mg/m² per day) followed by prednisone (200 mg/m² per day) with no improvement in liver function. 4 days later scattered vesicles developed over her left flank and her liver function deteriorated substantially. She was started on intravenous acyclovir 1500 mg/m² per day and her immunosuppression drugs were reduced. She developed cutaneous dissemination 24 h later, but over the next 48 h her skin lesions resolved and her liver function improved. On the third day of acyclovir she had tachycardia, palpitations, tinnitus, and shortness of breath immediately after the infusion. Despite decreasing the dose and increasing the infusion time, there were similar but more severe symptoms with hypotension after the next two doses. Anaphylaxis to acyclovir was presumed and it was discontinued. Within 18 h intravenous foscarnet 40 mg/kg per 24 h was started, last administration 24 h after foscarnet vesicles were seen. Over the next 56 h she was stable with continued improvement in liver function but no resolution of the new skin lesions. 60 h after starting foscarnet she developed more skin lesions, neurological deterioration, pulmonary infiltrates, and heart failure. Desensitization to acyclovir was done but she died of heart failure within 24 h of resuming acyclovir. Necropsy was refused. Positive cultures for VZV were obtained from blood and vesicles before starting acyclovir; however, further cultures from blood, urine, and cerebrospinal fluid were negative. No vesicles were cultured after starting antiviral therapy. The VZV strain from her blood was sensitive to acyclovir and foscarnet (median inhibitory concentration [IC₅₀] 1.7 and 63 µmol/L, respectively). Retrospective analysis of her cerebrospinal fluid for the day of neurological deterioration showed a foscarnet concentration of 195 µmol/L, which was three times greater than the IC₅₀ of her isolate and indicated that abnormally rapid metabolism of foscarnet did not cause the clinical failure. Times of the foscarnet infusions and spinal taps were known, so the predicted plasma concentration was 346 µmol/L based on data from our laboratory and others.3

Our case demonstrates failure of foscarnet in herpes zoster, despite apparent clinical control of the infec- tion.3 Because acyclovir and foscarnet are virostatic with different mechanisms of action, the time needed to accumulate virostatic concentrations of foscarnet, after discontinuing acyclovir, may have allowed the virus unihibited replication that overwhelmed our patient. We found one other case of an HIV-infected patient with zoster secondary to acyclovir-resistant VZV whose lesions did not respond to foscarnet despite in-vitro susceptibility of the viral strain.1 Although foscarnet is a potential treatment for VZV infections, these two cases demonstrate the need for further studies to evaluate the optimum dose and to correlate in-vitro sensitivity with clinical efficacy. Of additional interest is the unusual reaction our patient had to acyclovir, consistent with anaphylaxis or cardiac toxicity.

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References

HIV-2 cultured from blood 16 days after death

Sir,—There are few data on post-mortem persistence of viable HIV in blood and tissues, mainly because of the short time that the infected bodies stay in mortuaries. Viable HIV-1 has been isolated 18 h,1 21 h,1 6 days,2 and 11 days3 after death, suggesting the possibility of post-mortem contamination. The viability of HIV-2 after death has not been evaluated.

A heterosexual West African patient with AIDS died from acute myelomonocytic leukemia in hospital. He was infected by HIV-2 but not HIV-1 as shown by methods that included two enzyme-linked immunosorbent assays (ELISA; third generation Abbott ELISA) that recognize HIV-1 and HIV-2 antibodies were positive; wellcome recombinant HIV-1 ELISA that recognizes HIV-1 antibodies was negative, the PBEPTI-LAV test (Pasteur

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References