Manic Symptoms Caused by Acyclovir in a Hemodialysis Patient

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Dear Sir,

Some patients with end-stage renal disease (ESRD) show a tendency toward secondary depression of the immune function. Not infrequently, such depressed immune functions lead to infections with the herpes zoster virus or other types. Herpes zoster virus infection is often chemically treated with acyclovir [1-3]. Acyclovir is a selective antiherpes agent. Its selective activity is by exploitation of differences between the herpes-specific and host cell enzymes. Toxic reactions to acyclovir consist of phlebitis, local irritation, and occasionally, reversible renal dysfunction [3]. There are a few reports that acyclovir has caused, though only rarely, side effects of central nervous system such as delirium, tremor, and abnormal electroencephalo-graphy [3]. However, there has been no report on the occurrence of psychiatric symptoms due to oral administration of acyclovir. This paper reported one case receiving hemodialysis (HD) therapy in which the oral administration of acyclovir produced a manic state.

The case was a male patient, 59 years of age. The patient has been receiving HD therapy due to since 53 years of ago. Information of his family, the patient's premorbid character was rather modest and quiet. Suddenly, he suffered from the infectious disease. In addition to pain, papules and blisters were observed on the left facial area under the control of the trigeminal nerve. The dermatologist diagnosed the case as herpes zoster virus infection from the clinical symptoms and the increase of herpes zoster virus antibody in the blood. He immediately, prescribed acyclovir (15 mg/kg/day) orally. After 2 days, the patient abruptly changed and became restless and talkative. Furthermore, he became irritable and hyperkinetic. He was admitted for further examinations. At the psychiatric interview on the second hospital day, his con-

sciousness was clear and psychiatric symptoms such as flight of idea and delusion of grandeur were observed. From the third hospital day, we stopped the acyclovir treatment. The manic symptoms continued for 3 days and then gradually subsided.

No abnormalities were found in the laboratory parameters except for those related to ESRD (BUN 82.3 mg/dl, creatinine 13.5 mg/dl). Cerebrospinal fluid showed nothing remarkable. Antibody of herpes zoster virus in the cerebrospinal fluid was negative. Blood concentration of acyclovir using high-performance liquid chromatography was 10.9 µg/ml (the 2nd day),

3.0 µg/ml (the 4th day before HD therapy), 1.0 µg/ml (the 4th day after HD therapy) (normal range of acyclovir, 2.02-2.30 µg/ml).

We have concluded that the manic symptoms observed in the present case were caused by the oral administration of acyclovir on several grounds: (1) no clinical or laboratory findings indicative of herpes encephalitis have been obtained while the cerebrospinal fluid was within a normal range; (2) the blood concentration of acyclovir was extremely high, indicating evidence of an accumulation of acyclovir due to ESRD; (3) as a premorbid personality, he had no cyclothymic disposition tending toward a manic state; (4) HD therapy may be indeed a treatment method involving a stress load, but HD therapy was economically stable and well adapted to his family environment or workplace, and did not involve any psychological or social factors that may have led to psychic symptoms at least for the least few years. Moreover, discontinuation of acyclovir tended to ameliorate the manic state, which was actually ameliorated by a decrease in the blood concentration of acyclovir. Two weeks after the discontinuation of acyclovir, the patient returned to his natural state.

Although there have been some sporadic reports on the appearance of side effects of central nervous system such as delirium caused by intravenous infusion of acyclovir [3], there was no report on the occurrence of manic symptoms due to the oral administration of acyclovir. Under these circumstances, the present case may be a valuable example. Several studies have demonstrated the accumulation of acyclovir in patients with impaired renal function [3-5]. Acyclovir enters the cerebrospinal fluid, and vaginal secretions at concentrations inhibitory to herpes simplex virus. In the present case with ESRD as well, the accumulation of acyclovir associated with the elevated blood concentration of acyclovir may be related to the appearance of manic symptoms. In consultation-liaison psychiatric service for ESRD patients, we should be always mindful of the possibility of the appearance of psychic symptoms due to acyclovir.

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