A Case of Methotrexate-Induced Acute Renal Failure Successfully Treated with Plasma Perfusion and Sequential Hemodialysis

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Dear Sir,

Recent successful results using high-dose methotrexate (MTX) followed by leucovorin in the treatment of head and neck carcinomas and osteosarcomas have led to a more widespread use of this therapy in patients with these and other tumors. A major complication of high-dose MTX therapy has been impairment of the renal function. This toxicity has led to delayed renal excretion of MTX which subsequently produces myelo-suppression in spite of standard leucovorin therapy [1]. Removing MTX from patients with impaired renal function would be beneficial in decreasing the risk of myelosuppression. We report a case of acute renal failure after a sudden fall in blood pressure during infusion of MTX.

A 45-year-old woman with osteosarcoma was treated with high-dose MTX therapy at another hospital. She was admitted for her seventh treatment, and after hydration and urine alkalization, she started receiving 16.4 g MTX. Three hours later she developed nausea, vomiting, and facial edema. She then lost consciousness, and no blood pressure could be detected. Immediately infusion of MTX was stopped and hydrocortisone was administered intravenously. Her consciousness and blood pressure recovered gradually, but her urine volume remained decreased. The next day, she was referred to our hospital for treatment of acute renal failure and removal of MTX.

Laboratory data at that time were as follows: urea 17.4 mg/dl, creatinine 1.88, uric acid 1.8 mg/dl, Na⁺ 137 mEq/l, K⁺ 3.5, Cl⁻ 98 mEq/l, creatinine clearance 2.4 ml/min, fractional excretion of sodium 18.3%, and serum MTX concentration 5.11×10^{-4} mol/l. Oliguria persisted.

Leucovorin treatment was begun according to the protocol of Bleyer [1], and plasma perfusion was performed (plasma separator Plasmacure®, absorber Meisorba BL®, Krara-ry, Osaka, Japan; purified plasma volume 8,400 ml). Subsequently, hemodialysis was performed (dialyzer KF 201-1201®; Krara-ry). By this procedure, the serum MTX concentration was reduced from 5.11×10^{-4} to 2.06×10^{-4} mol/l (fig. 1). By combined plasma perfusion and hemodialysis repeated for 3 days, the serum MTX concentration was reduced to 1.40×10^{-5} mol/l on the 4th day after admission, and thereafter hemodialysis alone was performed. The serum MTX concentration was further reduced to 5.00×10^{-6} mol/l hemodialysis alone. The rebound of the serum MTX concentration was only about 10% of the value after hemodialysis. Daily hemodialysis was performed not only to remove MTX from the blood, but also to correct metabolic disturbances associated with renal dysfunction. Three days after admission, severe mucositis, paralytic ileus, and myelosuppression had appeared. As the serum MTX concentration became lower, these adverse effects of MTX gradually disappeared. According to Bleyer [1], leucovorin treatment is necessary if the serum MTX concentration is over 1.0×10^{-7} mol/l. As the serum MTX concentration became lower, hemodialysis treatment removed lesser MTX. The serum MTX concentration decreased to $1.1 - 1.2 \times 10^{-7}$ mol/l, but not

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Hemodialysis

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Fig. 1. Clinical course.

further (fig. 1). Although the serum MTX concentration was still elevated, we stopped leucovorin treatment on the 22nd day after admission, since the patient was free of adverse drug effects. The renal function recovered gradually, and hemodialysis was stopped on the 29th day after admission.

The cause of the episode of cardiovascular collapse associated with high-dose intravenous MTX was unclear, but an anaphylactoid-type reaction to MTX was highly suspected, considering the other symptoms [2, 3]. The most effective method for removal of MTX is a difficult issue [4-6]. In this patient, plasma perfusion with sequential hemodialysis was more effective than hemodialysis alone. Hemodialysis did not significant decrease the MTX blood levels, but this method was warranted to correct life-threatening disturbances associated with secondary renal failure. Plasma perfusion is superi-

or to hemoperfusion in that the former causes lesser thrombocytopenia. In patients with MTX intoxication who suffer from myelosuppression, we consider plasma perfusion with sequential hemodialysis one of the best methods in dealing with both MTX intoxication and secondary renal dysfunction.

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