Fulminant Wilson's Disease Treated With Postdilution Hemofiltration and Orthotopic Liver Transplantation

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A 22-yr-old woman presented with fulminant Wilson's disease. The diagnosis was suspected clinically and was later confirmed with chemical and pathologic studies. She presented with acute hepatic failure, hemolysis, and acute anuric renal failure. Postdilution hemofiltration and continuous arteriovenous hemofiltration with oral D*-penicillamine allowed removal of a total of 95,700 μg of copper; 78,665 μg of the total were removed via postdilution hemofiltration alone. On the 57th day, the patient received successful liver and renal transplants. We found that the determination of serum copper was instrumental in the diagnosis of fulminant Wilson's disease, that postdilution hemofiltration allowed a rapid removal of copper in the presence of renal failure, and that, finally, orthotopic liver transplantation should be performed early in the clinical course of these patients. This patient is the longest survivor of this serious condition.*

Wilson's disease may initially present as acute hepatic failure (1). Until recently, this diagnosis was made postmortem and no therapeutic maneuvers were attempted. However, McCullough and associates (2) have recently demonstrated the usefulness of serum copper in diagnosing Wilson's disease and separating these patients with acute hepatic failure from other patients with hepatitis due to viruses or drugs. Several authors have reported a total of 5 patients in whom the diagnosis of Wilson's disease was suspected antemortem and treatment was initiated before their fatal outcome (3,4).

We report a patient without previous history of liver disease who presented for the first time with fulminant hepatitis due to Wilson's disease complicated by hemolysis and acute anuric renal failure. The renal and hepatic failure were treated initially with postdilution hemofiltration (HF) until the patient finally underwent a successful orthotopic liver transplantation and renal transplantation.

Case Report

A 22-yr-old woman was admitted to Rochester Methodist Hospital on November 20, 1984, with jaundice, hepatic encephalopathy, hemolysis, and renal failure. About 2 wk before admission, the patient had nausea, vomiting, and increasing jaundice. Two days before admission, she experienced mental confusion.

On physical examination, the patient was found to be deeply jaundiced, in a stage III coma, and only responsive to nociceptive stimuli. No stigmata of chronic liver disease were present. The liver edge was not palpable, and hepatic dullness was 4 cm in the right midclavicular line. The spleen was not palpable. Kayser–Fleischer rings were subsequently identified by slit-lamp examination.

Laboratory tests revealed the following values: total bilirubin, 73.1 mg/dl; direct bilirubin, 41.6 mg/dl; aspartate transaminase, 257 U/L; alanine transaminase, 110 U/L; and alkaline phosphatase, 90 U/L. Prothrombin time was 37 s prior to her transfer to the Mayo Clinic (November 20, 1984) and 19 s after transfusion of 4 U of fresh frozen plasma. Albumin was 2.6 g% and γ-globulin was 1.43 g%. Serum copper was 3.54 μg/ml (normal 0.75–1.45); serum ceruloplasmin was 25 mg/dL (normal 22.9–43.1); hemoglobin was 6 g/dl; and hematocrit was 21%. Blood smear revealed features consistent with active hemolysis. Red blood cell glucose-6-phosphate dehydrogenase was negative. Coombs' test was negative. Serum creatinine was 6.9 mg/dl. Urinalysis revealed unremarkable findings. Sero-

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Abbreviation used in this paper: HF, hemofiltration.

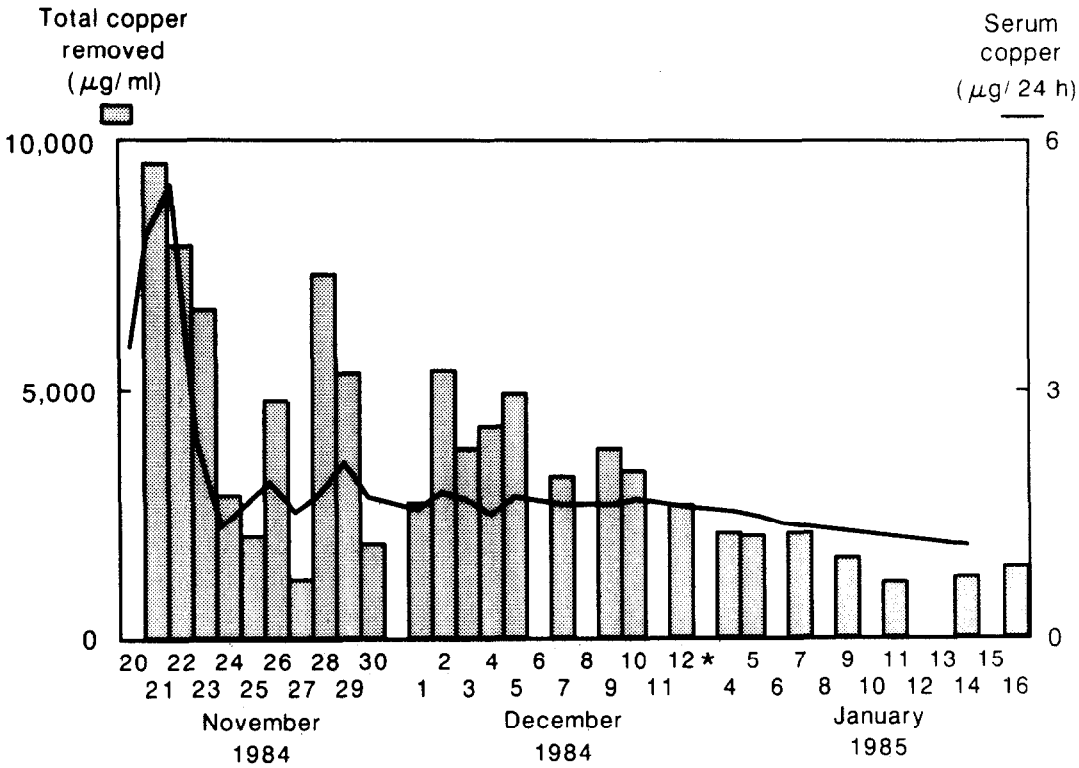

Figure 1. Copper removed by postdilution hemofiltration and continuous arteriovenous hemofiltration in a patient with fulminant Wilson's disease.

logic markers for hepatitis A virus, hepatitis B virus, cytomegalovirus, and Epstein–Barr virus were negative.

The presence of acute hepatic failure, hemolysis, renal failure, and moderately elevated aminotransferase levels prompted us to consider Wilson's disease as a possible diagnosis. Together with the serologic tests for hepatitis viruses, we requested an emergency serum copper determination which was completed that same day. The copper level was found to be 3.54 μg/ml (2.4 times the upper limit of the normal range, 0.75–1.45). This test result was considered confirmatory evidence for fulminant Wilson's disease.

After obtaining written informed consent, we included this patient in an institutionally approved clinical protocol (approved on July 22, 1983 at the Mayo Clinic) designed to assess the effectiveness of postdilution HF in the treatment of fulminant Wilson's disease. In using this treatment, we had three goals: (a) removal of excess copper from the circulation, (b) management of acute renal failure, and (c) provision of a treatment with the theoretical benefit of short-term extracorporeal hepatic support.

On the first day of hospitalization, treatment was initiated with postdilution HF and D-penicillamine, 500 mg per nasogastric tube twice a day. In the first 17 h, a total exchange of 64 L was carried out with HF. Thereafter, HF and continuous arteriovenous HF were alternatively utilized every 12 h over the next 15 days. Ultrafiltration rates of 60 ml/min and 10 ml/min, respectively, were achieved, and an average of 50.4 L were exchanged daily. We used a Gambro 202 hemofilter for standard HF and an Amicon 20 hemofilter (Amicon Corp., Danvers, Mass.) for continuous arteriovenous HF. Within 72 h of the start of treatment, the patient regained consciousness, her prothrombin time stabilized at 18 s, and her ceruloplasmin level dropped to 16 mg/dl. On November 30, 1984, one blood culture was positive for *Serratia liquefaciens*, and the patient was treated with gentamicin and mezlocillin. These antibiotics were discontinued 4 days later, and cefoxitin, 2 g intravenously every 24 h, was used for a total of 10 days. By December 5, 1984, her condition had stabilized to the point where HF therapy was changed to an alternate-day mode (average volume 30 L). On December 10, 1984, the patient developed a fever to 38.6°C and a skin rash appeared. D-Penicillamine was discontinued as a precautionary measure. Cultures of blood, urine, and sputum were negative. There was partial improvement of liver function during this period as evidenced by a prothrombin time that remained 18–19 s and serum aminotransferase levels that fluctuated between 150 and 250 U/L. Serum albumin consistently remained below 2 g%. The patient remained oliguric (urinary output <200 ml/day) throughout this hospital stay. In Figure 1, we have illustrated the amount of copper removal with both procedures and the changes in serum copper levels. We were able to remove a total of 95,700 μg of copper; 78,665 μg of this total were removed via HF alone. Abdominal ultrasound demonstrated hepatosplenomegaly and a patent portal vein. At this point, we concluded that further improvement was unlikely to occur, and on December 12, 1984, the patient was transferred to the University of Minnesota for consideration of orthotopic liver transplantation. Between December 13, 1984 and January 3, 1985, the patient underwent conven-