Acute Sin Nombre Hantavirus Infection Complicated by Renal Failure Requiring Hemodialysis

To the Editor: The hantavirus pulmonary syndrome (HPS), a zoonotic viral infection transmitted by rodents, is an unusual cause of acute respiratory failure and is rarely associated with renal insufficiency. We report a case of infection with Sin Nombre hantavirus complicated by acute respiratory failure and renal failure requiring hemodialysis.

Report of a Case. A 57-year-old man was transferred to Saint Marys Hospital in Rochester, Minn, because of respiratory insufficiency and altered mental status. He described a flulike illness beginning in late October and progressing over 1 week. Symptoms included headache, fever, chills, and difficulty thinking clearly. He had cleaned his garage several days before the onset of illness. He had no recent history of trauma, travel, or exposure to illness. He had donated his left kidney to his brother earlier in the year. A review of systems was otherwise unremarkable. His shortness of breath worsened, and he required supplemental oxygen.

On physical examination, the patient’s heart rate was 127 beats/min, and supine blood pressure was 100/63 mm Hg. His skin showed signs of dehydration without rash. Crackles were noted bilaterally on chest auscultation. Findings on abdominal examination were normal. Laboratory evaluation revealed a white blood cell count of 10.3 × 10^9/L with 85% neutrophils, a platelet count of 67 × 10^9/L, and a normal hemoglobin concentration. The serum creatinine level was 1.9 mg/dL. Urinalysis showed an elevated protein-osmolality ratio of 0.65 (normal, 0.12). Chest radiography revealed diffuse pulmonary infiltrates. Arterial blood gas studies yielded a PaO_2 of 65 mm Hg while the patient received 5 L of oxygen via nasal cannula. Computed tomography of the head showed normal findings, but computed tomography of the chest, abdomen, and pelvis revealed bilateral perihilar infiltrates in the mid and upper lung fields with stranding in the retroperitoneum bilaterally. Blood was withdrawn for cultures. Lumbar puncture revealed a cerebrospinal fluid protein level of 58 mg/dL and a glucose concentration of 80 mg/dL. Antibiotic therapy was initiated with levofloxacin, cefepime, metronidazole, and doxycycline.

Two days later, viral serologies sent to the Centers for Disease Control and Prevention were reported to be positive for Sin Nombre virus, with an IgM titer of 1:6400 and an IgG titer of 1:1600, both consistent with acute hantavirus infection. Supportive therapy was continued, and the patient remained in the MICU for 5 more days. He returned home 3 weeks later. At the time of discharge, his renal function had not fully recovered, but he did not require hemodialysis. Two months later, his renal function had returned to baseline.

Discussion. Hantavirus pulmonary syndrome was first recognized after an outbreak of severe respiratory illness in the southwestern United States in May 1993 that was traced to the Sin Nombre virus. Subsequently, other strains of hantaviruses were isolated in the United States, Canada, and South America. In the United States, the deer mouse (Peromyscus maniculatus) is the rodent host for Sin Nombre virus. Outside the United States, a common presentation of hantavirus infection is hemorrhagic fever with renal syndrome (HFRS), a group of similar illnesses that include Korean hemorrhagic fever, epidemic hemorrhagic fever, and nephropathia epidemica. Although hantavirus infection can occur without severe pulmonary symptoms, most patients with HPS experience pulmonary and hemodynamic compromise and require ICU admission and mechanical ventilation. In contrast to patients with septic shock, those with HPS reportedly have high vascular resistance and low cardiac output.

Laboratory findings commonly include thrombocytopenia, leukocytosis with myeloid precursors, increased hematocrit level, and coagulopathy. Typically, renal function is only mildly impaired. Only 20% of patients with HPS have serum creatinine values higher than 2.0 mg/dL. However, renal failure requiring dialysis has been described in patients infected with hantavirus strains other than Sin Nombre in the United States, and elsewhere renal impairment is a prominent feature of HFRS and HPS.

To our knowledge, this is the first report of an acute Sin Nombre infection complicated by renal failure requiring hemodialysis occurring in the United States. The presence of a solitary kidney due to organ donation 10 months previously likely played a role, although living kidney donors are not typically considered at increased risk for renal dysfunction. The pathophysiology of viral injury includes inflammation and increased vascular permeability, typically involving the pulmonary bed in HPS and the retroperitoneum in HFRS. The treatment of HPS is directed primarily toward management of hemodynamic and respiratory complications. Ribavirin is effective in treating patients with HFRS, but in an open-label study in patients with HPS, the drug had no appreciable effect. Limited case series of critically ill patients with HPS have shown increased survival with use of extracorporeal membrane oxygenation.
Conclusion. Hantavirus pulmonary syndrome due to Sin Nombre virus may be associated with renal insufficiency requiring dialysis. The presence of renal failure in the setting of other symptoms of HPS should not exclude this diagnosis.

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Use of the Internet for Medication Purchases and Health Information: Can We Make It Safer?

*To the Editor:* In the August 2004 issue of the *Mayo Clinic Proceedings*, Lineberry and Bostwick1 provided some excellent case studies of clinical problems associated with Internet purchases of medications. We concur with their comments and offer the following additional suggestions.

We propose that the US Food and Drug Administration (FDA) develop or recommend a reliable Web site for the purchase of drugs and for accurate drug information. The National Association of Boards of Pharmacy (NABP) developed the Verified Internet Pharmacy Practice Sites (VIPPS) program to help patients choose legitimate Internet pharmacy Web sites (www.nabp.net/vipps/intro.asp). Fung et al2 provided a detailed description of the VIPPS program in the February 2004 issue of the *Mayo Clinic Proceedings*. We recommend that all physicians be educated about purchasing medications via the Internet and share information about the VIPPS program Web site or an FDA-approved Web site with their patients. The system developed by the FDA to report unlawful sales of medical products on the Internet (www.fda.gov/oc/buynline/buynlineform.htm) should be used by physicians, other health care professionals, and consumers to report adverse events associated with Internet drug purchases. Once the FDA receives such information, it can investigate and shut down these sites. To aid in these investigations, the FDA can use the radiofrequency identification (RFID) technology that it recommended recently3 to trace counterfeit products to their source. It will be much easier to trace products that are sold illegally on the Internet when the RFID system is implemented universally. This system should serve as a deterrent to abusers of the Internet system, and pharmaceutical manufacturers should try to comply with this policy as soon as possible. Ultimately, the issue of medication purchases via the Internet may not be resolved until aggressive legal action is taken against rogue Internet pharmacies.

Another important consideration is the credibility of health information available on the Internet. Many sites provide such brief presentations on pharmaceuticals that it is difficult for physicians to determine if the information is evidence based. If highly trained physicians have such problems, how can the average patient evaluate the credibility and quality of the information on such sites?4 The FDA should develop guidelines to ensure the credibility of the information provided to physicians on the Internet. In addition, with such poor-quality information currently available for consumers, the FDA and the National Library of Medicine should develop a service that provides better criteria for rating information on Web sites. Examples from the DISCERN Project can be used effectively. DISCERN is an evaluative instrument developed in recognition of the need for a general set of quality criteria to evaluate written consumer health information on treatment choices.5

We hope that our suggestions help advance the safe and effective distribution of medications and drug information via the Internet.

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In reply: We agree with the concerns raised by Amrutkar and Sansgiry. The challenges for both patients and physicians in evaluating the safety of medications purchased through the Internet are profound. A June 2004 report by the US General Accounting Office1 cited problems with the handling, authenticity, and FDA approval status of medications obtained from Internet pharmacies. The General Accounting Office (the audit, evaluation, and investigative arm of the US Congress) purchased 11 different medications from 68 Internet pharmacy Web sites. It found fewer problems overall among pharmacies identified as being based in Canada or the United States (US) relative to pharmacies based in other countries. This report was published in the August 2004 issue of the *Mayo Clinic Proceedings*; it is available online at www.mayoclinicproceedings.com.

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States. However, 45 of the 68 sites did not require a patient-provided prescription. The medications often came without instructions or warning information, and those requiring special handling did not always receive it.

Congress continues to try to regulate the Internet pharmaceutical industry. First introduced on May 20, 2004, the Internet Pharmacy Consumer Protection Act was reintroduced on February 16, 2005. This legislation would “require internet pharmacies to identify their business, pharmacist and physician for consumers; prohibit internet pharmacies from distributing drugs to consumers with a prescription based solely on an online questionnaire; and give state Attorneys General the ability to shut down rogue websites nationwide, rather than just in their individual jurisdictions.” Amrutar and Sansgiry’s recommendations, combined with the proposed congressional legislation, could be important elements in improving safety. We continue to believe that proactively educating patients about the potential dangers of purchasing medications via the Internet is an essential first step.

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Prevention of Systemic Embolization Associated With Treatment of Gastric Fundal Varices

To the Editor: We read with great interest the article by Rickman et al1 about pulmonary and splenic embolization after endoscopic injection of 2-octyl cyanoacrylate into gastric fundal varices. We strongly agree with the use of diluted 2-octyl cyanoacrylate to prevent premature polymerization of the glue. Because most gastric fundal varices are associated with a gastrorenal shunt,2 blood flow is abundant, and injection of cyanoacrylate is likely to cause systemic embolization due to migration of the agent through a shunt. We speculate that the draining vein of the varices treated by Rickman et al was a gastrorenal shunt.

Injection of 2-octyl cyanoacrylate should be performed under fluoroscopic monitoring to avoid migration of the glue into the vena cava through a gastrorenal shunt and to confirm obliteration of the feeding vein.3 Irisawa et al4 found that such migration was more likely after dilution of cyanoacrylate to less than 40%. They proposed that gastric fundal varices larger than 12 mm in diameter be treated with a mixture of at least 62.5% cyanoacrylate or that another therapeutic modality be used to avoid migration of glue from the injection site. Therefore, it would be important to know the size of the varices treated by Rickman et al and why they chose a 1:1 mixture of 2-octyl cyanoacrylate and a lipid-based contrast agent. Did they inject the 2-octyl cyanoacrylate–contrast mixture under fluoroscopic monitoring? If so, leakage of some 2-octyl cyanoacrylate into a gastrorenal shunt or the splenic vein might have been revealed. Rengstorf and Binmoeller5 have stated that they are currently considering the use of radiopaque agents other than Lipiodol that allow fluoroscopic visualization without affecting polymerization. After the risk of early rebleeding is reduced with a small volume of highly concentrated 2-octyl cyanoacrylate–contrast mixture, portal hemodynamics should be evaluated to determine the most appropriate subsequent therapeutic strategy. Recently, multidetector row computed tomographic angiography has provided excellent visualization of varices as well as their feeding and draining veins.3 Although transjugular intrahepatic portosystemic shunting (TIPS) is considered a second-line treatment strategy for acute gastric fundal varices, the efficacy of TIPS alone for varices with a low portal pressure gradient (<12 mm Hg) seems doubtful.6

Balloon-occluded retrograde transvenous obliteration (B-RTO), a new radiologic technique, has been introduced to treat gastric fundal varices associated with a gastrorenal shunt.7 Ninoi et al8 showed that transcatheter sclerotherapy including B-RTO might provide better control of gastric variceal bleeding than TIPS, and they suggested that transcatheter sclerotherapy might contribute to a higher survival rate than that obtained with TIPS. Because B-RTO is less invasive and technically easier than TIPS, we recommend 2-octyl cyanoacrylate injection followed by B-RTO for the treatment of bleeding gastric fundal varices associated with a gastrorenal shunt.

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Editor’s note: When publishing a letter that comments on an article published previously in Mayo Clinic Proceedings, it is the journal’s policy to invite the author(s) of the reference article to publish a response. The corresponding author of the article by Rickman et al declined our invitation to respond in print.