Predominant Kidney Involvement in a Fatal Case of Hantavirus Pulmonary Syndrome Caused by Sin Nombre Virus

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A 27-year-old woman presented to a hospital with symptoms resembling pyelonephritis; respiratory distress did not develop until nearly a day after admission and she subsequently died. The Unexplained Deaths and Critical Illnesses Project of the Centers for Disease Control and Prevention confirmed Sin Nombre virus infection by the results of serological testing and sequencing of the viral genome; staining of Sin Nombre Virus antigen was performed to the pulmonary capillaries was relatively weak.

Sin Nombre virus (SNV) is the major cause of hantavirus pulmonary syndrome (HPS). HPS classically presents with a prodrome of headache, fever, and myalgia, followed by pulmonary capillary leakage and cardiorespiratory collapse [1]. Clinically, notable manifestations of renal involvement are rare [2]. The distribution of SNV infections mirrors that of its host, the deer mouse. In California, more than half of patients with cases of HPS resided in or visited the Sierra Nevada Mountains or the foothills of the eastern San Joaquin Valley. We report a case of HPS due to SNV infection in a woman who lived in California but had not traveled to these areas; the case initially resembled pyelonephritis, and only sparse hantavirus antigen was found in the lung.

Case report. In April 1999, a 27-year-old previously healthy woman developed left flank pain, chills, myalgia, and nausea. Two days later, the pain led her internist to make a tentative diagnosis of pyelonephritis (urinalysis was not performed). Intramuscular ceftriaxone was administered. The patient was hospitalized 4 days after the onset of symptoms because of increasing left flank pain, vomiting, and inability to drink fluids. She noted severe myalgias but denied having dysuria, hematuria, urinaly urgency, dyspnea, cough, headache, abdominal pain, and diarrhea. The patient had developed pyelonephritis several years earlier. She lived near San Francisco, denied having animal or outdoor exposures, and had not traveled during the previous 60 days.

In the emergency department, physical examination revealed the following: temperature, 38.9°C (103.1°F); pulse, 90 beats/min; blood pressure, 137/86 mm Hg; respiratory rate, 20 breaths/min; and left-side costovertebral angle tenderness. Her breath sounds were normal. A complete blood count revealed the following: hematocrit, 42%; WBC count, 5200 cells/mm3 (52% mature segmented neutrophils, 15% band forms, 11% lymphocytes, 8% monocytes, 4% eosinophils, and no metamyelocytes or reactive lymphocytes); and platelet count, 57,000 cells/mm3. Urinalysis demonstrated the following: specific gravity, 1.030; pH, 5.5; 3+ protein; but no WBCs, RBCs, nitrate, leukocyte esterase, bilirubin, or glucose. Findings of an iv pyelogram were normal. The patient was given a diagnosis of pyelonephritis and was hospitalized for administration of iv fluids and ciprofloxacin.

A chest radiograph was obtained after admission and revealed diffuse bilateral interstitial infiltrates with small pleural effusions. Twenty hours after admission, the patient noted progressive chest tightness that was not alleviated by oxygen. The patient developed acute respiratory distress syndrome and had recurrent cardiopulmonary arrests. She died 40 h after she was hospitalized. An autopsy disclosed neither pyelonephritis nor an underlying cause of death. Antemortem blood and urine cultures were sterile, and results of a battery of tests for respiratory pathogens were negative.

Because of the severe nature and undetermined cause of this illness, the case was referred to the Unexplained Deaths and Critical Illnesses Project (UNEX). UNEX is a surveillance network of the Emerging Infections Program of the Centers for Disease Control and Prevention and is designed to identify and evaluate life-threatening infectious diseases that occur among...
previously healthy persons. Surveillance through UNEX was begun in 1995 to detect emerging and difficult-to-diagnose pathogens that might not be reported through routine public health channels.

Testing of serum samples from the patient under the auspices of UNEX revealed IgM and IgG against recombinant SNV nucleocapsid and related antigens [3]. These results were confirmed by recovery of an SNV genetic sequence from the serum samples by use of nested reverse-transcription PCR [4]. Sequencing of complementary DNA demonstrated that the sequence was similar to SNV genomic variants previously found in California [4, 5].

Routine histologic examination revealed intra-alveolar edema with minimal inflammation in the lung and no inflammation in the kidney. Immunohistochemical staining for genus-specific hantaviral antigen demonstrated focal staining of renal and pulmonary capillary beds. However, the staining in the lung was very sparse, and the density of hantaviral antigen was much less than that seen in typical cases of HPS [6].

An investigation was initiated by the California Department of Health Services (Sacramento, Richmond, and Berkeley). None of the patient’s family or coworkers recalled that the patient had had a relevant exposure to rodents. Rodent feces were found near the patient’s cubicle at work, but no deer mice were caught in 290 traps placed in the patient’s home and workplace.

Discussion. Although hantavirus antigen can often be found in the lung, kidney, spleen and (rarely) liver, the comparative intensity of antigen staining generally reflects the clinical syndrome. In reported SNV infections in humans for which adequate tissue samples have been available, staining has been widespread and more intense in pulmonary than in renal capillaries [7].

This is the first reported case of HPS in which the detected burden of SNV was prominent in kidney tissue specimens but relatively sparse in lung tissue specimens. Although back pain is reported by ~25% of patients with HPS [8], this is the first case in which pulmonary symptoms were preceded by symptoms that were mistaken for pyelonephritis. Interestingly, significant renal dysfunction is seen in infections with other New World hantaviruses, but it is rarely a measurable component of SNV infection (i.e., hemorrhagic fever with renal syndrome, such as is caused by infection with Puumala virus or Dobrava virus) is associated with proteinuria, pyuria, microscopic hematuria, and renal dysfunction in 95% of cases and is accompanied by back pain in two-thirds of cases or more [10, 11]. In one series, pyelonephritis was the most common alternative diagnosis among persons for whom hemorrhagic fever with renal syndrome was ruled out [10].

Because of the unusual features of this case, its cause was identified only after the illness was reported to UNEX. Surveillance for such cases should help clinicians, pathologists, and public health officials identify the range of illnesses caused by emerging and difficult-to-diagnose pathogens.

References