Hantavirus pulmonary syndrome: Report of the first Canadian paediatric case

Bonita E Lee MD FRCPC, Ari R Joffe MD FRCPC, Wendy Vaudry MD FRCPC

Hantavirus pulmonary syndrome (HPS) was first characterized during an outbreak of severe respiratory illness in the southwestern United States in 1993 (1). The illness commonly begins with fever and myalgia with or without headache, cough and gastrointestinal complaints, and rapidly progresses to respiratory distress with noncardiogenic pulmonary edema. Other associated features include hypotension, leukocytosis, thrombocytopenia and hemococoncentration.

The etiological agent is a previously unknown hantavirus, an enveloped single stranded RNA virus of the Bunyaviridae family. At least three strains have been isolated to date: Sin Nombre (previously known as Muerto Canyon Virus) from the deer mouse (Peromyscus maniculatus) reservoir in the southwestern United States as well as Canada; the Black Creek Canal virus from the cotton rat (Sigmodon hispidus) reservoir in Florida and bayou virus from the rice rat (Oryzomys palustris) reservoir in Louisiana (2). Disease is transmitted by inhalation of infected rodent excreta. No human-to-human transmission has been reported in North America.

As of November 1997, there were 175 cases of HPS diagnosed in the United States (personal communication). Of the cases (94%) involved adults. Twenty-one cases have been recognized in Canada. This paper describes the first Canadian paediatric case and discusses some of the clinical features of this disease.

Key Words: Canada, Hantavirus pulmonary syndrome, Paediatric, Respiratory illness

Le syndrome pulmonaire causé par l’hantavirus : Rapport du premier cas pédiatrique canadien

RÉSUMÉ : Le syndrome pulmonaire causé par l’hantavirus a été reconnu comme une maladie respiratoire grave transmise par la voie d’excréments de rongeurs dans le sud-ouest des États-Unis en 1993. En date de novembre 1997, 175 cas ont été signalés aux États-Unis où l’on fait état d’un taux de mortalité imputable à cette maladie d’au moins 52% et qui, dans la majorité des cas (94%), touchent des adultes. Vingt et un cas ont été signalés au Canada. Le présent article décrit le premier cas pédiatrique identifié au Canada et traite des différents aspects cliniques de cette maladie.
those cases, 10 were children or adolescents 16 years of age or younger. The age of the children ranged from 11 to 16 years, with a mean and median age of 14 years. We describe the first Canadian paediatric case.

CASE PRESENTATION

A 16-year-old boy, who was previously healthy and an active participant in sports, presented to hospital in Westlock, Alberta in June 1997 with a three-day history of weakness, fever, chills, and generalized myalgia and arthragia. He also complained of nausea and a headache. After assessment at the hospital, he was admitted for dehydration. Initial blood work revealed mild leukopenia with a total white count of 2.7×10^9/L, platelet count of 141×10^9/L and hemoglobin of 136 g/L. Over the next 24 h, he progressed with more abdominal pain, vomiting, dizziness and mild cough. He was started on amantidine for possible influenza infection. He deteriorated over the next few hours, with tachypnea and oxygen saturation of 86% on room air, and hypotension with a blood pressure of 60/26 mmHg. He was given intravenous fluid bolus with Ringer's lactate while being transferred to the University of Alberta Hospital (UAH), Edmonton, Alberta. Before transfer, blood culture was completed, and a complete blood cell count was repeated, which showed a hemoglobin of 178 g/L, total white blood cell count of 11.2×10^9/L with 13% bands, and platelet count of 48×10^9/L.

On arrival at the UAH, temperature was 36.9°C, respiratory rate 44 breaths/min, heart rate 120 beats/min and blood pressure 110/70 mmHg. On 15 L/min oxygen by mask, oxygen saturation was 95%, and blood gases showed PO_2 of 65 mmHg, PCO_2 of 30 mmHg and pH of 7.46. Physical examination revealed moderate respiratory distress, diffuse inspiratory crepitations with decreased air entry and bronchial breath sounds in his left lower lobe. Chest x-ray was initially interpreted as interstitial abnormality in keeping with either adult respiratory distress syndrome, atypical pneumonia or pulmonary hemorrhage. He was later admitted to the paediatric intensive care unit (PICU) with a diagnosis of atypical pneumonia and sepsis, and HPS was considered.

He received supportive care with oxygen supplementation, and further fluid boluses were given to maintain his blood pressure. He was empirically treated with cefuroxime and erythromycin. Laboratory work continued to show thrombocytopenia (52 to 78×10^9/L). Aspartate aminotransferase was mildly elevated at 137 U/L and lactate dehydrogenase was 279 U/L. Prothrombin time international normalized ratio (INR) was normal at 1.1, and partial thromboplastin time was 45 s. Initial albumin was low at 26 g/L; electrolytes, calcium, magnesium, phosphorous and renal function were within normal limits. Repeated chest x-ray showed increased bilateral perihilar markings with airspace disease and a small left side effusion in keeping with pulmonary edema.

The patient improved in the PICU without requiring artificial ventilation, and his blood pressure remained stable without the need for inotropes. He was put on fluid restriction after his blood pressure was stabilized and was given several doses of furosemide. After a 29 h stay in the PICU, he was transferred to the general paediatric ward with a respiratory rate of 28 to 32 breaths/min and an oxygen saturation of 95% on 2.5 L/min oxygen via nasal prongs. Chest x-ray showed rapid improvement over the next few days. He was discharged home three days later in normal condition after a rapid recovery.

Nasal aspirate was negative by direct fluorescent antibody testing for influenza A and B, parainfluenza type 1, 2 and 3, and respiratory syncytial virus, and was negative for viral culture. Human immunodeficiency virus (HIV), mycoplasma, chlamydia and legionella serology, and monospot were all negative. One of the four blood cultures drawn grew coagulase-negative Staphylococcus species, which was considered as a contaminant. Hantavirus immunoglobulin (Ig) M serology was sent to Laboratory Centre for Disease Control (LCDC), Ottawa, Ontario on the day of the patient’s admission and was reported as positive at 1:1600 on the day of his discharge.

Further history revealed that the family lived by a grain field, and there were many mice in the area. The patient denied any known close contact to mice or working in any enclosed area. However, a few days before his illness started, he was helping with seeding in the fields, which created much dust in the air.

DISCUSSION

This boy presented with an illness typical of HPS. His febrile prodrome with myalgias and gastrointestinal symptoms, followed four days later by pulmonary edema, hypotension, thrombocytopenia and hemocoagulation, was as described in the literature (3). The confirmatory serological test for hantavirus IgM was done at LCDC. This is an ELISA test that was developed at the Centres for Disease Control and Prevention (CDC), Atlanta, Georgia; although no data are available regarding the sensitivity of the test, it is thought to be highly specific (5,6). Cases of HPS have been described in British Columbia (5) and Alberta (6,7), and seroprevalence of Sin Nombre antibodies in deer mice trapped in Alberta has ranged from 1.2% to 19.6% (6). What was unusual about this case was the patient’s age.

HPS is relatively uncommon in the paediatric population. Ninety-four per cent of the American cases were adults (personal communication). As of November 1997, 21 cases of HPS had been identified in Canada through serological testing at LCDC. The age of the 20 adult patients ranged from 27 to 62 years with a mean age of 45 years, and our patient is the only Canadian paediatric case known to date (personal communication). The reason for the increased incidence in adults is not known. In a recent review of the first one hundred cases of HPS in the United States, the majority of the cases (96%) had a history of peridomestic exposure, 17% of all cases had occupational exposure and only 4% had occupational exposure only (8). Children and adults would be expected to have similar exposure in a household environment. On the other hand, it is not known why the other family members who worked with our patient in the fields did not develop clinical illness; such family clustering of cases is known to be uncommon (2). Interestingly, HPS has not yet been reported in young children. The only case report of Sin Nombre hantavirus infection in a
young child was in a four-year-old Native American boy; his illness was recognized because of a case of HPS diagnosed in the same household (9). That boy had only very mild disease that did not meet the CDC or LCDC surveillance case definition for HPS (4,7).

It was remarkable that our patient had such a speedy recovery. The majority of the patients described in the United States were adults, with an overall case fatality of 52%; the median ages for the surviving and deceased case-patients were similar: 34 years (range 11 to 69) and 33.5 years (range 14 to 68), respectively (8). As of November 1997, the mortality rate was 40% (four of 10) in the 10 paediatric cases in the United States (16 years of age or younger) (personal communication).

In the cases in the United States, persons who survived were hospitalized for a median of 10 days (range two to 169), and those who died a median of one day (range none to 31), with death occurring within a median of five days (range one to 35) of disease onset (9). Eighty-four per cent of patients required intubation (8). Paediatric patients may have less severe infections, although data to determine this are not available. For hemorrhagic fever with renal syndrome, the data may suggest less severe infection in children, as discussed by Khan et al (10).

A large double-blind, placebo controlled trial to assess the efficacy of ribavirin in HPS is underway. Unfortunately, our patient could not be entered into the study because the placebo drug was not yet available in Edmonton at the time of his presentation. We were very fortunate that the natural progression of his illness was a favourable one.

In conclusion, we have presented the first Canadian paediatric case of HPS. This boy presented with a typical syndrome, and made a very rapid full recovery.

ADDENDUM

Since this report was submitted, a second paediatric case of HPS was diagnosed in a 15-year-old boy from Legal, Alberta. He presented to the emergency department with a four-day history of fever, headache, nausea, vomiting, diarrhea and dizziness. In the emergency room, he had a rapidly deteriorating course with shortness of breath and profound hypotension. Blood work showed a hemoglobin of 197 g/L, platelet count of $51 \times 10^9$/L, total white blood cell count of $59.2 \times 10^9$, with 50% lymphocytes, 15% monocytes, 2% eosinophils and 45% bands, creatinine of 345 mol/L, prothrombin time INR of 1.9 and partial thromboplastin time of 94 s. Chest radiograph showed diffuse air space consolidation in keeping with noncardiogenic pulmonary edema. He died of cardiac arrest in the PICU, despite aggressive resuscitation with intubation, fluids and high dose inotropes. Postmortem examination revealed diffuse pulmonary edema with no other cause of death found. Hantavirus IgM serology obtained from a postmortem blood sample was positive with a dilution of 1:400. This second paediatric case fulfils the diagnostic criteria of HPS.

REFERENCES
