A Case of Nephropathia Epidemica Associated with Panhypopituitarism and Nephrotic Syndrome

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Dear Sir,

Hemorrhagic fever with renal syndrome (HFRS) comprises a group of viral zoonoses with a worldwide distribution [1]. Nephropathia epidemica (NE) is the Scandinavian type of HFRS, and Puumala virus is the suggested causative agent [2]. Generally, NE has a benign course though severe complications have been reported [3]. We here report a case of NE complicated by nephrotic syndrome and panhypopituitarism. A previously healthy 62-year-old man was admitted on July 16, 1989, with a 2-day history of fever, vomiting, myalgia and severe headache. At admittance, the patient had a temperature of 40.3°C. Blood pressure was 130/90 mm Hg. Urinalysis was positive for protein, blood and glucose. Serum C3 and C4 levels were normal. On the 4th day of disease, hypotension (systolic blood pressure 90 mm Hg), oliguria, tachypnea and hypoxia developed. Pleuracentesis yielded 750 ml translucent fluid which contained a large number of inflammatory cells. Abdominal ultrasonography showed increased amounts of ascitic fluid, enlarged kidneys bilaterally and a swollen pancreas. Serum amylase level was 12.5 µkat/l (normal value < 4 µkat/l). In serum samples, specific IgM and IgG to Puumala virus could be demonstrated by use of the indirect immunofluorescence technique. On day 7, the patient had hematemesis (200 ml). Transfusions of packed red cells, fresh frozen plasma and platelet concentrates were given due to anemia (Hb 5.9 g/dl), low serum albumin (2.0 g/dl), and thrombocytopenia ($23 \times 10^9/l$). The patient then developed peripheral edema. Maximal urinary excretion of protein was 18.4 g/24 h. Serum levels of cholesterol and triglycerides were markedly elevated. Eighteen days after onset of disease, a percutaneous renal biopsy was performed. Microscopy revealed diffuse interstitial edema and infiltration of lymphocytes, plasma cells and granulocytes. Focal interstitial bleeding was noted in the medulla. Some distal tubuli were distended and contained granular casts. Immunofluorescence staining for IgG, IgA, IgM, C3 and Clq was negative. During the autumn of 1989, libido decreased and progressive fatigue, anorexia, vomiting, polydipsia, poly-

Table 1. Blood chemistry findings in a severe case of NE

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uria, weight loss and myalgia developed. His general condition was good, the skin was dry and scaling and body hair was reduced. Visual acuity was normal and there were no signs of chiasmal affection at perimetry. A computerized tomography of the sella was normal. The basal serum hormone levels 6 months after onset of disease were as follows (normal values in parentheses). TSH 0.51 arbitrary U/l (0.3-5.0), free thyroxine 2.8 pmol/l (7.4-15.9), growth hormone < 0.5 arbitrary U/l (> 10), prolactin < 2.0 µg/l (4-15), FSH 1.8 arbitrary U/l (3-28), LH 2.5 arbitrary U/l (4-22), and testosterone < 0.5 nmol/l (> 14). Tetracosactide tests indicated that the cortisol insufficiency was of hypo-thalamic-pituitary origin. At a TRH test, there were no increases of serum TSH, GH or prolactin concentrations. Urine osmolality after 8-hour thirst was 530 mosm/kg and after desmopressin administration 625 mosm/kg. He was treated with oral cortisone and thyroxine daily and monthly injections of testosterone and experienced a good clinical response.

To our knowledge, this is the first reported case of NE associated with panhypopituitarism and nephrotic syndrome. It is unclear why this NE patient had such a severe clinical course.

Hypothetically, this could be due to infection by a highly virulent Puumala virus strain, a high infective dose and/or host factors. A recent report of encephalitis in a NE patient suggested that Puumala virus might even replicate in the CNS [4]. In a NE-related disease in the Soviet Union, hemorrhage and necrosis of the anterior pituitary gland have been described [5]. Disseminated intravascular coagulation and prechoc in our patient might have resulted in hypothalamic-pituitary ischemia. Immunopathological mechanisms, which are known to occur in NE [6], might also have contributed to the severe course.

In summary, the reported NE case was complicated by gastrointestinal bleeding, pancreatitis, prechoc, disseminated intravascular coagulation, nephrotic syndrome, panhypopituitarism and possibly a partial diabetes insipidus. It clearly demonstrates the potential clinical severity of NE disease in Scandinavia.

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