Hantavirus infection in Europe - single centre experience

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Topic: Acute Kidney Injury, Clinical Epidemiology and outcome

INTRODUCTION

Acute kidney injury can be caused by infection with Hantavirus, a zoonosis transmitted by rodents (*Figure 1 and 2*). Hantaviruses, first described in Chinese writings 900 years ago, are enveloped RNA viruses, spherically shaped with diameter from 80 to 120 nm. They form separate genus within the Bunyaviridae family.

In contrast to other viruses from Bunyaviridae family, they are not transmitted by arthropod vector, but carried and transmitted to human by persistently infected natural rodent host reservoirs (mice, rats, voles). Most human infections occur by inhalation of contaminated aerolized rodent excreta. Viral glycoprotein is attached to the cell surface receptors of endothelial, epithelial, dendritic and lymphocyte cells. Like other enveloped viruses they are inactivated by heat (30 minutes at 60 °C), detergents, UV irradiation, organic solvents and hypochlorite solutions.

Hantavirus infection in human can cause two different clinical syndromes (*Figure 2*): haemorrhagic fever with renal syndrome (HFRS) and hantavirus cardiopulmonary syndrome (HCPS). Pathogenetic mechanisms of both HFRS and HCPS include increased vascular permeability and acute thrombocytopenia. The clinical presentation of HFRS varies from subclinical and mild to severe, depending on causative agent. In general, more severe disease courses are caused by Hantaan, Amur and Dobrava type of virus. HFRS is characterized by fever, acute kidney injury and haemorrhagic manifestations that can vary from petechiae to severe internal bleeding. The diagnosis is based on clinical and epidemiological data together with laboratory tests (serology). The treatment is primary supportive, vaccine is not available. Prevention is to avoid the exposure of rodent urine and droppings. Even though Hantavirus infection is rare in Europe, it should be considered in differential diagnosis of acute renal failure.

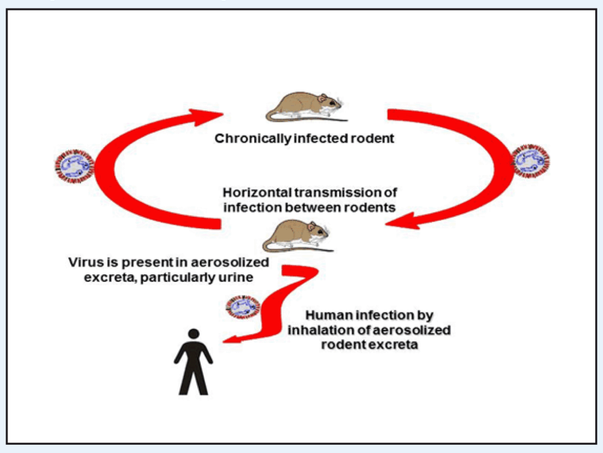

Figure 1: *Transmission of Hantavirus infection in human (adapted from www.phac-aspc.gc.ca/publicat/ccdr-rmtc/15vol41/dr-rm41-06/ar-02-eng.php)*

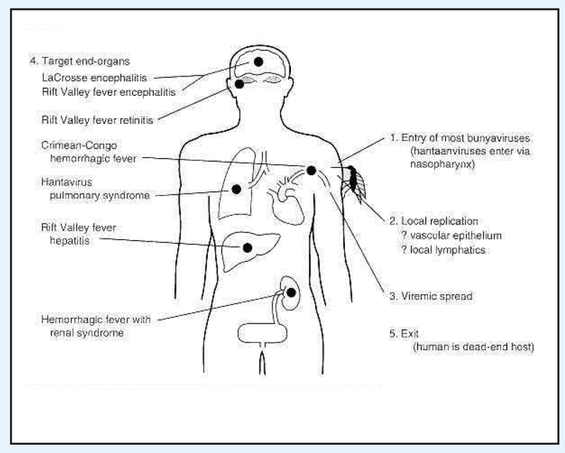

Figure 2: *Pathogenesis and target-end organs of infection of viruses of Bunyaviridae family (adapted from www.intranet.tdmu.edu.ua)*

AIM

The aim of this study was to analyse the characteristics and outcome of patients diagnosed with Hantavirus infection in our centre.

METHODS

- Retrospective analysis of medical records of patients with a positive test for Hantavirus infection
- Detection of antibodies against hantavirus with a commercially available ELISA kit (Euroimmun, Medizinische Labordiagnostik AG, Luebeck, Germany)
- Study period 2010 to 2016

RESULTS

- **59 patients** with clinically considered hantavirus infection included
- **10 (17%)** were **positive** (6x IgM positive, 1x IgM and IgG positive, 3x IgG positive), one of them (IgM positive) was excluded (concomitant ANCA-associated vasculitis)
- Patients with IgG positivity only but with clinically appropriate symptoms were included (*Table 1*)

Basic characteristics

Five of 9 patients were men (56%), the median age was 50 (range 24-75 years). No relation between contagion and season was found. Median CRP levels was 108 mg/L (ranging from 10 to 216). For further details see *Table 1*.

Patient	Age	Sex	Antibodies	Trombocytopenia	Anemia	CRP	Erytrocyturia	Leukocyturia	HD
1.	54	M	IgM - IgG +	+	+	107.9	+	+	+
2.	54	M	IgM + IgG -	+	+	208.6	+	+	+
3.	30	M	IgM + IgG -	+	+	110.9	+	+	+
4.	24	F	IgM+ IgG -	+	-	16.1	-	-	-
5.	49	M	IgM+ IgG +	+	+	49.6	+	+	-
6.	75	M	IgM - IgG +	-	+	127.5	+	+	-
7.	39	F	IgM + IgG -	-	+	10.2	-	+	-
8.	73	F	IgM - IgG +	-	+	216.1	+	+	-
9.	50	F	IgM+ IgG -	+	+	57.1	+	+	+

Table 1: *Basic clinical data of the patients*

Renal involvement

- Renal biopsy was performed in 3/9 patients (33%), acute tubular necrosis was found in 2 (67% of those undergoing biopsy).
- Median serum creatinine in non-dialysed ones was 345 µmol/L (range 87-533)
- 4/9 patients were oligo-anuric at presentation, proteinuria was usually negative or mild

Extra-renal involvement

- Glaucoma was found in 1/9 (11%) and 5/9 (55%) patients had internal bleeding diagnosed. No extra-renal involvement was observed in 3 (33%) - see *Figure 3*.

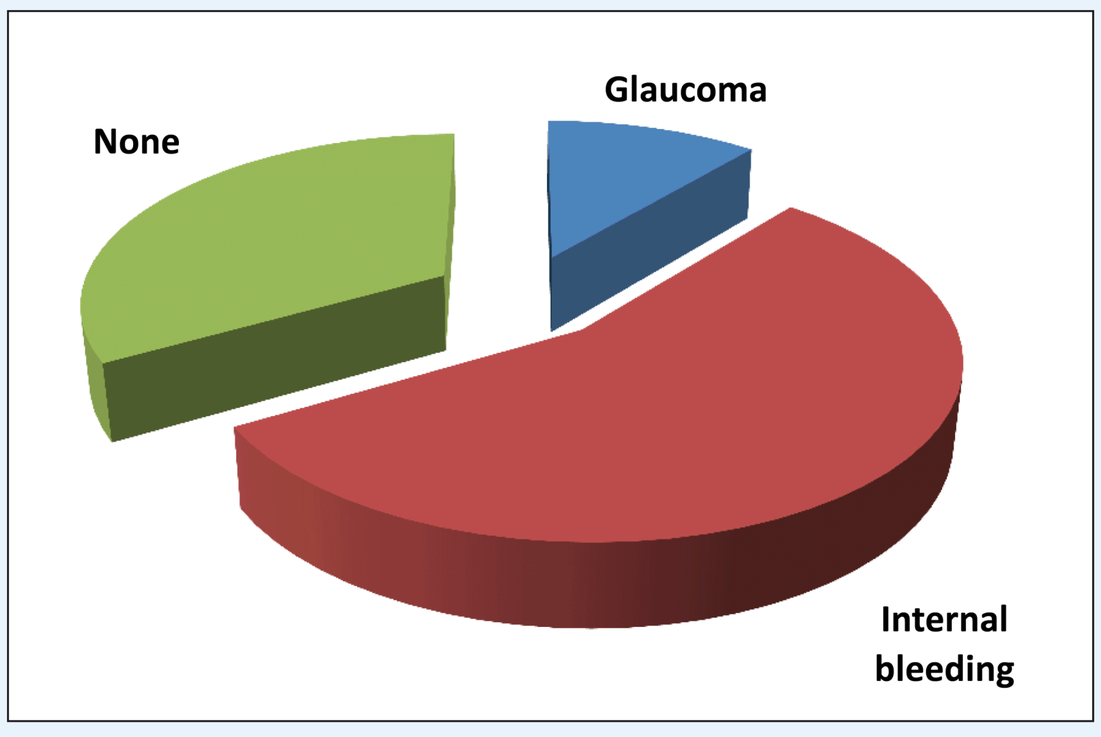

Figure 3: *Extra-renal involvement*

Disease course and long-term outcome

- 7/9 (77%) patients received antibiotics (the most commonly used was *Amoxicillin potentiated by clavulanic acid*)
- 5/9 (55%) patients received corticosteroids (mostly intravenously)
- 6/9 patients required ICU care
- All of the patients survived the acute infection, none remained on dialysis.
- At 3 months, 7/9 patients had normal or near-normal renal function, the remaining two had CKD stage 3 (*Figure 4*).

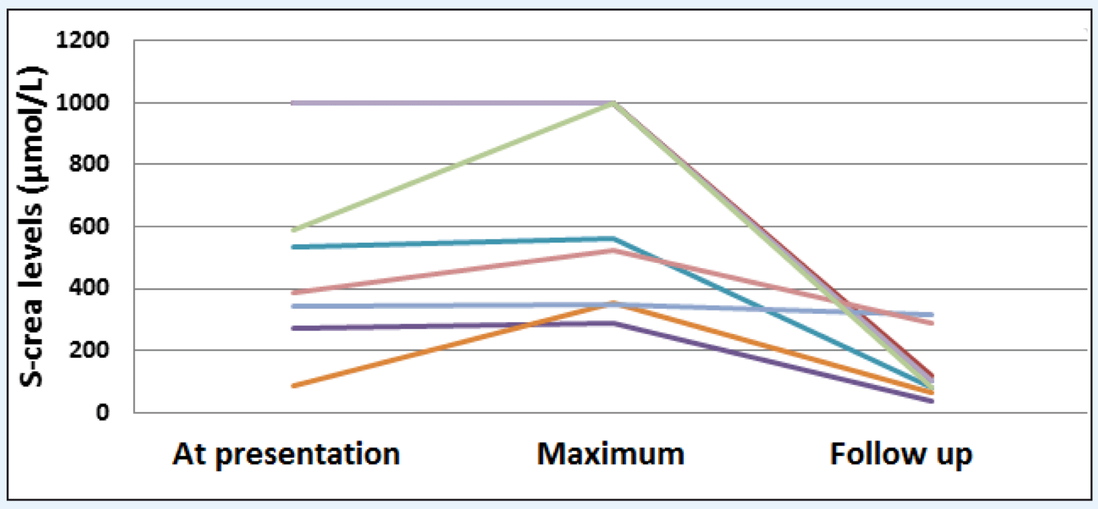

Figure 4: *S-creatinine levels in all patients at admission, maximum levels and at the long-term follow-up (in patients on HD S-creatinine=1000 was used).*

CONCLUSIONS

- Hantavirus infection in our centre was associated with quite a severe disease course in most patients
- Outcome was very good, none of the patients required long-term dialysis
- Although rare, Hantavirus infection should be considered as a potential cause of acute kidney injury, especially if there is history of fever and the cause is not completely clear

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