

*Nephroquiz*  
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## Viral haemorrhagic fever and a skin rash—what is the link?

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### Case

A 38-year-old, previously healthy woman was admitted with non-oliguric acute renal failure. Prior to admission she had a 2-week history of sudden fever with a peak of 40°C, lower back pain, severe headache, abdominal pain, emesis, increasing faintness and impaired vision. Initially she was admitted to a surgical unit, where the symptoms resolved within 3 days.

Physical examination showed a weight gain of 5 kg, oedema of the lower legs and a butterfly rash (Figure 1). She lived in a forest area and regularly collected firewood. Laboratory results are shown in Table 1. A kidney biopsy was performed, which showed the images in Figures 2 and 3a–c.

### Question

What is the most likely cause of the acute renal failure in this patient, and is this related to her skin rash?

### Answer

The cause of the acute renal failure was haemorrhagic fever with renal syndrome, due to an infection with the Hantavirus serotype Puumala (IgG and IgM positive). The kidney biopsy showed an interstitial lympho- and monocytic inflammatory infiltration, a typical finding in haemorrhagic fever with renal syndrome (Figure 2). A more thorough study of the renal biopsy including immunofluorescence revealed mild mesangial expansion with IgG and C3c de-

**Table 1.** Laboratory results

		Normal values
Serum creatinine	9.45 mg/dl	(0.1–1.3 mg/dl)
Urea	170 mg/dl	(<45 mg/dl)
Leukocytes	11.40/nl	(4–10/nl)
Eosinophilic granulocytes	0.7/nl	(<0.5/nl)
C3c	1.0 g/l	(0.9–1.8 g/l)
C4-complement	0.4 g/l	(0.1–0.4 g/l)
ANCA antibody titre	Negative	Negative
Hepatitis serology	Negative	Negative
Bence–Jones proteins	Negative	Negative

posits (Figures 3a–c), which were suggestive for mild lupus nephritis (class 1 ISN/RPS) [1] and a further laboratory work-up documented an increased ANA (antinuclear antibodies) titre of 1:160 (normal range <1:80) and the elevated Cardiolipin level of 18.5 mpl (normal range <10 mpl). The patient's history was re-evaluated and she was repeatedly seen by other physicians since her facial skin rash prompted a clinical and laboratory work-up for lupus erythematoses (Figure 1).

### Discussion

The genus Hantavirus includes the following serotypes:

- Hantaan virus (HTN), found in Asia
- Puumala virus (PUU), found in Scandinavia and Central Europe
- Dobrava virus (DOB), area of circulation similar to PUU
- Seoul virus (SEO), found in Korea and
- Sin-Nombre virus, prevalent in the United States.

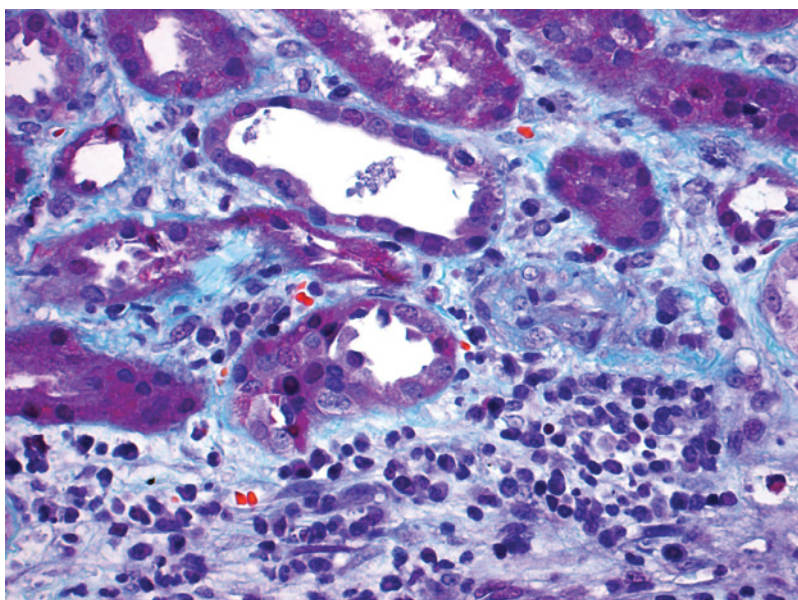
The serotype Puumala causes a mild to moderate haemorrhagic fever with renal syndrome (HFRS) and is also known as *Nephropathia epidemica* [2,3].

The viral agent is transmitted to humans from rodent reservoirs, especially from the red bank vole (*Clethrionomys glareolus*). The transmission occurs by inhaling aerosols of urine, saliva or faeces of infected rodents. The symptoms of HFRS are nausea, headache, vertigo as well

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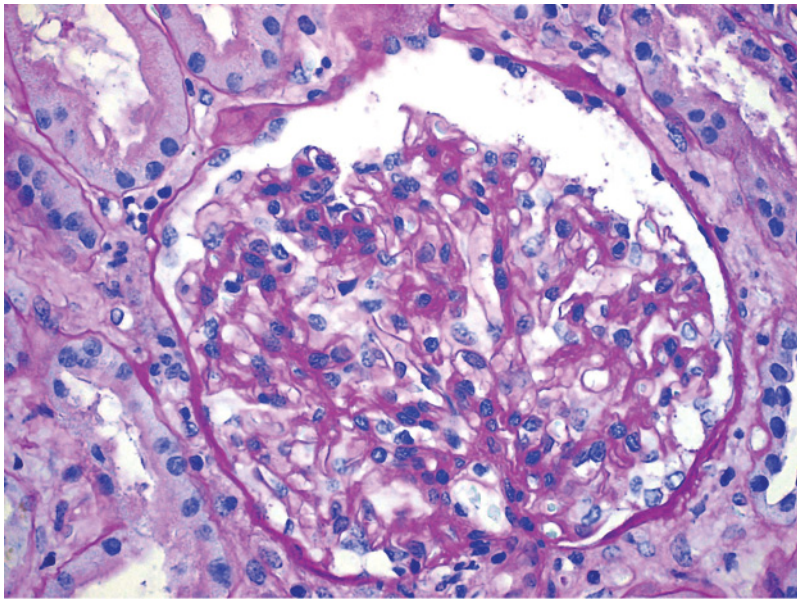


**Fig. 1.** Butterfly rash.

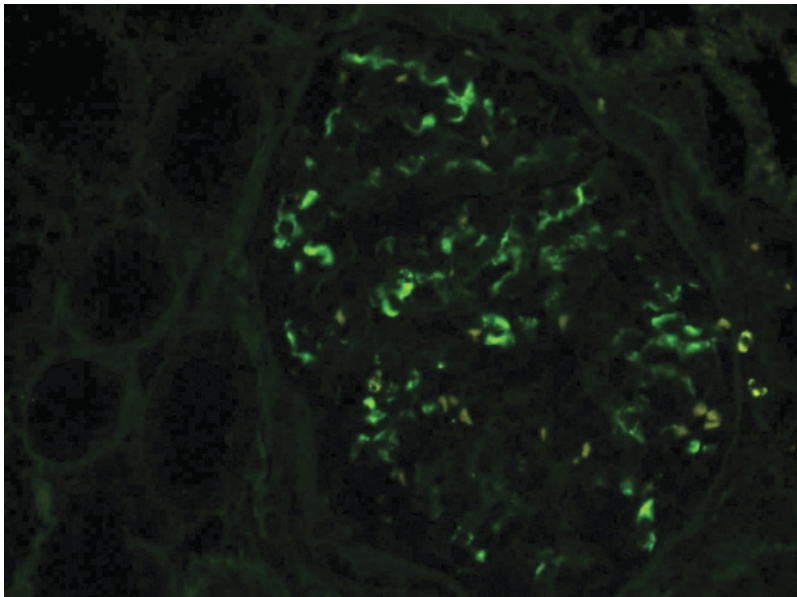


**Fig. 2.** Focal tubulointerstitial nephritis.





(a)



(b)

**Fig. 3.** (a) Glomerulus mild mesangial expansion. (b) Mesangial deposits of IgG. (c) Mesangial C3 deposits in the glomerulus.

as an acute renal failure with an increase of serum creatinine and proteinuria. In general, patients with HFRS due to Puumala serotype recover without persistent renal damage or hypertension, and the mortality during the course of the disease is very low [2–4].

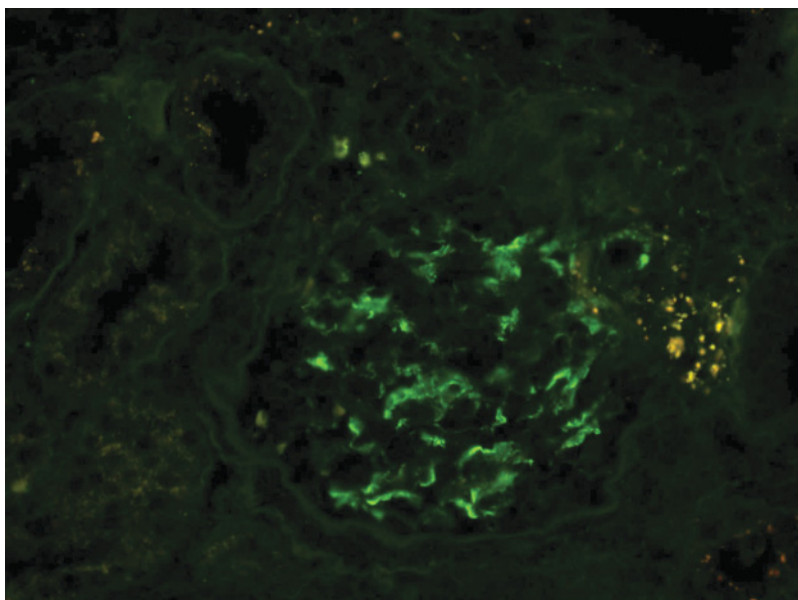
The diagnosis of Hantavirus infection is based on serology [2]. A renal biopsy usually shows an acute tubulointerstitial nephritis with interstitial oedema, mononuclear cell infiltrates and interstitial haemorrhage [5].

The therapy of HFRS is limited to supportive procedures to control the symptoms since there are no antiviral drugs

at present available. In 2007 the number of Hantavirus infections increased by <10-fold, possibly due to the mild winter and a rodent overpopulation due to beechnut mast which increased the number of rodent vectors [6].

The increased ANA titre, anticardiolipin IgM, the erythema (Figure 1) and the mild glomerulonephritis in this patient argue for concomitant pre-existing SLE.

In our patient, the serum creatinine decreased rapidly to normal values and at present the patient is doing well with a normal GFR. She has no immunosuppressive therapy and is seen by a nephrologist on a regular schedule.



(c)

Fig. 3. (Continued)

*Conflict of interest statement.* None declared.

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