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Clinical Characteristics of Ratborne Seoul Hantavirus Disease

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Although Seoul orthohantavirus is the only globally spread hantavirus pathogen, few confirmed human infections with this virus have been reported in Western countries, suggesting lower medical awareness of the milder, transient, and often chameleon-like symptoms of this zoonosis. We describe lesser known clinical and laboratory characteristics to help improve underreporting of this virus.

Recent reports from several Western countries, including the United States, have described an ill-known hantavirus disease, commonly called hemorrhagic fever with renal syndrome (HFRS), induced by Seoul orthohantavirus (SEOV) and spread by infected wild, laboratory, and pet rats. These reports might bring to an end the long-maintained concept that human hantavirus infections were limited to milder (case-fatality rate ≤1%), transient, and atypical hantavirus infections, some of which might represent SEOV infections.

HFRS and SEOV HFRS are characterized by the same prodromal symptoms for 3–5 days as for HCPS: fever, myalgia, malaise, and gastrointestinal discomfort (5). All HFRS forms show not only AKI, ranging from strictly normal to severely impeded renal function, but also rapidly changing degrees of proteinuria, microhematuria, and thrombocytopenia (5). However, established presence or absence of initial proteinuria and microhematuria has not been investigated so far in large-scale SNV HCPS studies.

Proteinuria and microhematuria, although transient, are considered severity indicators for HFRS (5,6). The rapidity of increasing/decreasing proteinuria is virtually pathognomonic for HFRS and was noted as early as 1964. Epidemics of a then ill-defined fever called epidemic hemorrhagic fever, which was later proven serologically to be a wild rat induced HFRS (7), was present principally in the back alleys of Osaka, Japan, and characterized by marked but transient proteinuria that peaked in 32 case-patients on day 6 postonset of symptoms and disappeared completely on day 7 in mild cases and on approximately day 12 in those with severe AKI (8). Moreover, severity of proteinuria was found to be predictive of overall epidemic hemorrhagic fever clinical severity, as confirmed 53 years later in 70 case-patients infected with Puumala orthohantavirus; proteinuria (30% of nephrotic range), which peaked on day 5 postonset of symptoms, decreased almost completely on day 11, whereas serum creatinine levels peaked on day 9 (6).

Until recently, sudden AKI with nephrotic-range proteinuria and microhematuria was considered a rare nephrologic triad in previously healthy young adults; these adults constituted most HFRS case-patients. AKI with proteinuria, after acute tubular necrosis, is sometimes ascribed to the effect of nonsteroidal anti inflammatory drugs (NSAIDs). Because NSAIDs are often prescribed for the influenza-like myalgia preceding HFRS, these drugs can obscure the real ensuing cause of AKI (5). However, NSAIDs do not induce thrombocytopenia or the other biochemical hallmarks...

In contrast to severe HCPS caused by SNV or Andes orthohantavirus (ANDV), HFRS cases can be a diagnostic puzzle involving several swollen organs and including the lungs (5). The 2 earliest documented hantavirus infections in Peru were 2 SEOV HFRS case-patients confirmed by reverse transcription PCR, but both case-patients had fatal HFRS with HCPS (9), thus further blurring the boundaries between the 2 syndromes. In Southeast Asia, where the wild rat was and is the major reservoir for pathogenic hantavirus-es, HFRS with liver involvement, imitating virus hepatitis, was moreover proposed as a new clinical entity (10).

Finally, laboratory confirmation of diagnosis, even by an expert clinician, can be confounded by use of current commercial serologic assays that use antigens having weak or no cross-reactivity with murine SEOVs, such as European arvicoline Puumala orthohantavirus or American sigmodontine SNV/Andes orthohantavirus. Close attention should be paid to the multifaceted diagnosis of SEOV infection (Appendix Table) in patients exposed to brown or black rat excreta, including pet rat owners.

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