A case report of crescentic glomerulonephritis associated with Hantaan virus infection

Soi Kim1, Sun Hee Sung2, Hye Rim An1, Yoon Hee Jun1, Mina Yu1, Dong-Ryeol Ryu1, Seung-Jung Kim1, Duk-Hee Kang1 and Kyu Bok Choi1

1Department of Internal Medicine and 2Department of Pathology, School of Medicine, Ewha Womans University, Seoul, Korea

Correspondence and offprint requests to: Dong-Ryeol Ryu; E-mail: drryu@ewha.ac.kr

Abstract

Although various glomerular diseases in hantavirus infection have been reported, an association between hantavirus infection and crescentic glomerulonephritis has not been described. Herein, we report a case of immune complex-mediated crescentic glomerulonephritis in a 70-year-old man with Hantaan virus infection.

Keywords: crescentic glomerulonephritis; Hantaan virus

Introduction

Hantaviruses comprise a genus of enveloped viruses within the family Bunyaviridae. Infection with hantavirus may induce haemorrhagic fever with renal syndrome (HFRS) or hantavirus cardiopulmonary syndrome. Hantaan virus, which is usually associated with HFRS in Korea, may lead to more severe HFRS than any other strain [1].

Acute renal failure (ARF) accompanied with hantavirus infection is closely linked to intrarenal events, such as endothelial and/or tubulointerstitial damage by various cytokines and other humoral factors [2]. The most prominent renal pathologic finding of hantavirus infection is reported to be an acute tubulointerstitial nephritis with infiltration of inflammatory cells [3]. Other common interstitial changes include hyperaemic medullary vessels, extravasated erythrocytes, interstitial oedema and tubular cell necrosis [3,4].

Although only a few cases of glomerulonephritis (GN), including diffuse proliferative and mesangiocapillary GN, have been reported [5–7], an association between hantavirus infection and crescentic GN has not been described. Herein, we report a case of immune complex-mediated crescentic GN in a patient with Hantaan virus infection.

Case report

A 70-year-old man was admitted to the hospital with a history of fevers, chills and oliguria for 4 days. On admission, his blood pressure was 190/110 mmHg, and the body temperature was 37.3°C. The physical examination revealed multiple petechiae on the skin and mild pretibial pitting oedema. The initial serum creatinine was 274.0 μmol/L (3.1 mg/dL). The blood cultures were negative. The urinalysis showed proteinuria, haematuria and granular casts, and the 24-h urine protein excretion was 3587 mg/day. The Hantaan virus titre, as measured by ELISA, was 1:2048. We diagnosed ARF with Hantaan virus infection, and haemodialysis was started.

However, he did not recover from oliguric ARF after 1 month. The serum C3 level was decreased to <0.17 g/L. The anti-neutrophil cytoplasmic antibody and anti-glomerular basement membrane antibody were negative. Cardiac echocardiography revealed no significant abnormalities. A renal biopsy was performed on Hospital Day 33. Light microscopy of a needle renal biopsy containing 25 glomeruli showed diffuse mesangial and endocapillary proliferative GN with frequent neutrophil infiltration. Cellular crescent formation was noted in 16 glomeruli. The tubules and interstitium showed a severe lymphoplasmocellular infiltration with marked interstitial oedema. On immunofluorescence (IF) staining, predominant C3 deposits (3+) and dominant IgA (2+) and mild IgM (1+) deposits were noted in the mesangium and capillary loops. Indirect IF using high-titre hantavirus serum revealed a positive reaction in the glomeruli. An electron microscopic examination showed frequent electron-dense deposits in the mesangium and both sides of the capillary loops (Figure 1). On the basis of these findings, the possibility of immune complex-mediated crescentic GN associated with Hantaan virus infection was highly suggested.

Three months after onset, the urine output gradually increased to 1400 mL/day, and the serum C3 level normalized (0.97 g/L), but the Hantaan virus titre increased to >1:4096, suggesting a recent infection. In the second renal biopsy, most glomeruli showed severe sclerotic changes, and fibrous crescents were frequently noted. Interstitial fibrosis and tubular atrophy were also noted (Figure 2). He discontinued haemodialysis and was followed up in the outpatient clinic. Fourteen months after onset, the serum creatinine level was stable at ~353.6 μmol/L (4.0 mg/dL) without haemodialysis.

© The Author 2010. Published by Oxford University Press on behalf of ERA-EDTA. All rights reserved.
For Permissions, please e-mail: journals.permissions@oxfordjournals.org
Discussion

In patients with hantavirus infection, renal disorders varying from mild-to-severe ARF are characteristic. Despite frequent renal involvement, however, crescentic GN has not been reported in these patients. Crescentic GN is the result of a non-specific response to severe injury to the glomerular capillary wall; thus, crescents may be seen in any form of severe glomerular disease including post-infectious GN. Post-infectious GN can be accompanied by various viral infections such as hepatitis viruses, human immunodeficiency virus and cytomegalovirus [8]. In addition, the associations between some viral infections and crescentic GN have been described [8,9].

Although it has been reported that serum C3 levels were decreased in some patients with interstitial nephritis associated with Hantaan virus infection [6], the hypocomplementaemia observed in our patient strongly suggested that crescent formation was mediated by an immune mechanism. This is the first report of a patient with immune complex-mediated crescentic GN associated with Hantaan virus infection.

In this patient, the causal relationship between Hantaan virus infection and crescentic GN is obscure. According to several findings, however, Hantaan virus infection was responsible for the development of crescentic GN. The first renal biopsy revealed increased cellularity and neutrophil infiltration within glomeruli as the characteristics of infectious GN. In addition, IF studies showed predominant C3, dominant IgA and mild IgG deposition in the mesangium and capillary loops indicative of immune complex-mediated GN. A positive reaction on indirect

Fig. 1. The first biopsy showed crescentic glomerulonephritis. (A) A cellular crescent is noted, and frequent inflammatory infiltration is accompanied in the collapsed glomerular tuft (periodic acid–Schiff, ×400). (B) Severe lymphoplasmocytic infiltration is noted in the tubulointerstitium (haematoxylin and eosin, ×200). (C) Indirect immunofluorescence using hantavirus-infected patient serum reveals a positive reaction in the glomeruli (fluorescein isothiocyanate, ×400). (D) Transmission electron microscopic examination shows marked mesangial proliferation with obliteration of the capillary lumen. Frequent electron-dense deposits are found in both the mesangium and subepithelial side of the capillary loops (×3000).

Fig. 2. The second biopsy findings 11 weeks after the first biopsy. Most glomeruli show sclerotic changes. Moderate interstitial fibrosis with tubular atrophy and diffuse mononuclear infiltration are accompanied (Masson trichrome, ×100).
IF using serum from a hantavirus-infected patient suggested that a significant amount of viral antigen existed on the glomeruli.

Due to the absence of other definite causes, infectious GN was the most likely diagnosis. Moreover, infective endocarditis, shunt nephritis and hepatitis C viral infection were easily excluded on the basis of clinical and laboratory results. Although it is possible that HFRS due to Hantaan virus infection and idiopathic rapidly progressive GN (RPGN) developed coincidently, idiopathic RPGN is now considered to be a rare disease, and it is recommended that such patients should be carefully evaluated for a possible underlying infection as the cause [10].

In addition, at the time of normalization of the complement level, the extent of glomerular inflammation and proliferation was also attenuated. Because Hantaan virus is known to be more virulent and usually induce more severe HFRS than Puumala virus, it is a possible hypothesis that the glomerular pathology of Hantaan virus is also more extreme than that of Puumala virus, such as diffuse proliferative or mesangiocapillary GN.

Taken together, we suggest that Hantaan virus infection-related immune complex-mediated GN was the most likely mechanism of deteriorating renal function in this patient.

Conflict of interest statement. None declared.

References