

Jovan DIMITRIJEVIĆ¹
Veselin ŠKATARIĆ²
Željka TATOMIROVIĆ¹
Ivana TUFEGDŽIĆ¹
Anastasia ALEKSIĆ²
Zoran KOVAČEVIĆ²
Ljubica ĐUKANOVIĆ⁴
Goran BRAJUŠKOVIĆ¹
Ana GLIGIĆ³

¹INSTITUTE OF PATHOLOGY MILITARY MEDICAL ACADEMY, BELGRADE, YUGOSLAVIA

²CLINIC OF NEPHROLOGY, MILITARY MEDICAL ACADEMY, BELGRADE, YUGOSLAVIA

³INSTITUTE OF IMMUNOLOGY AND VIROLOGY "TORLAK", BELGRADE, YUGOSLAVIA

⁴INSTITUTE OF UROLOGY AND NEPHROLOGY, UNIVERSITY CLINICAL CENTRE, BELGRADE, YUGOSLAVIA

Hemorrhagic fever in hantavirus infection: Histopathologic presentation

KEYWORDS: Hantavirus; Hemorrhagic fever; Renal syndrome; Pathology

INTRODUCTION

Hantaviral diseases in humans are caused by a group of closely related, trisegmented, negative-sense RNA viruses of the genus *Hantaanvirus*, of the family *Bunyaviridae*. The type and severity of the disease depends largely on the serotype of the virus involved. Two classes of hantavirus-associated illnesses have been described: HFRS for the disease in which the kidneys are primarily involved, and HPS for the disease in which the lungs are primarily affected. The recent data concerning the pathogenesis of Hantavirus infection (e.g. Sherif R. Zaki) confirm that the basic necroinflammatory changes in the infection develop in the blood vessels. The endothelium is the internal cover of the blood vessels and the largest endocrine and metabolic organ of the human body. Its role is to maintain the balance which has the fundamental importance in the life.

MATERIAL AND METHODS

We analyzed 34 renal biopsy specimens in patients infected by Hantavirus. In 6 cases the material was taken at autopsy. Reverse transcription-polymerase chain reaction (RT-PCR) was applied in 4 patients.

RESULTS

The most indicative findings demonstrate morphologic changes in the capillaries, arterioles and smaller arteries with segmental fibroendothelial proliferation and intimal lesions aggregates of the blood cellular elements (initial thrombosis). The finding of the preserved elastica externa seen in the arteries and recess generally limited to the intimal layer suggests the beginning of the

process in the arterial lumen. The remarkable histopathologic findings in the kidney tissue were slight glomerular congestion and mild hypercellularity, tubular dilatation and necrosis, vasculitis of intertubular vessels. Microscopic examination of the lungs reveals a mild to moderate interstitial pneumonitis with variable degrees of congestion, edema, and mononuclear cell infiltration. The cellular infiltrate is a mixture of small and enlarged mononuclear cells with the appearance of immunoblasts. There may be seen focal hyaline membranes, and also intraalveolar edema, fibrin, and polymorphic cellular infiltrates. Hantaviral antigens were founded in pulmonary microvasculature and in follicular dendritic cells within the lymphoid follicles of the spleen and lymph nodes, and in the kidney tissue the antigens were most frequently found within the epithelial tubular cells and endothelial cells.

CONCLUSION

We consider that the results presented in this paper provide important elements sufficient for pathologists presuming the presence of Hantavirus infection in the biopsy and autopsy specimens. Our results reveal that endothelium dysfunction is either the cause or the consequence of two different clinical syndromes. The differences or similarities of the observed lesions, in particular Belgrade Hantavirus (Ana Gligic) infections, could be the subject of future research.

REFERENCES

1. Passaro DJ, Shie WJ, Hacker JK, Fritz CL, Hogan Sr, Fischer M, Hendry RM, Vugia Dj. Predominant kidney involvement in fetal case of Hantaan virus pulmonary syndrome caused by Sin Nombre virus. *Clin Inf Dis* 2001; 33(2): 263-4.
2. Zaki SR, Peters CJ. Viral Hemorrhagic fevers. *Path Inf Dis* 1997;12:125-36.
3. Dimitrijevic J, Skataric V, Tomanovic S, et al Pathohistological findings in the kidney and liver in patients with hemorrhagic fever with renal syndrome(HFRS). 3rd International Conference on HFRS and Hantaviruses 1995;1:42.
4. Zaki SR, Gree PW, Coffield LM. Hantavirus pulmonary syndrome: pathogenesis of an emerging infectious disease. *Am J Path* 1995;146:552-79.

Address correspondence to:
Prof. Dr Jovan Dimitrijević, Institute of Pathology and Forensic Medicine, Military Medical Academy, Belgrade, Yugoslavia

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