Marburg and Ebola Hemorrhagic Fevers: Does the Primary Course of Infection Depend on the Accessibility of Organ-Specific Macrophages?

Viral hemorrhagic fevers (VHF) are prime examples of emerging/reemerging infectious diseases that have increased in frequency worldwide in the past. Of the human VHF, Marburg and Ebola hemorrhagic fever is characterized by extreme, severe courses and high case-fatality rates. After the onset of nonspecific symptoms (e.g., fever, headache, and asthenia), patients infected with filovirus (Marburg and Ebola viruses) display generalized fluid distribution problems, hypoproteinemia, coagulation disorders, and hemorrhages, finally resulting in fulminant shock and death [1, 2]. These symptoms are comparable to those of the cytokine-induced systemic inflammatory response syndrome that is a surplus reaction of the host triggered by pathogens or their products [3]. Since filoviruses do not produce substances comparable to the endotoxins or exotoxins of bacteria, the pathophysiology of these devastating infections remains unknown. Because filoviruses are classified as

Penicillin G is the antibiotic of choice for treatment of infections due to GBS, given that GBS are uniformly susceptible in vitro. High doses (10–12 million units q.d.) are recommended because MICs for GBS are higher than those for group A strains [1]. Quinolones have only moderate in vitro activity against GBS [1, 5].

Our patient developed a prostatic abscess. Diabetes mellitus, insertion of an urethral catheter, and inappropriate initial antibiotic treatment may have all contributed to the occurrence of this rare complication [6, 7]. Various drainage procedures have been described [6, 7]. Although transurethral interventions are preferred, due to the extent of the abscess in our patient, perineal drainage by means of incision was undertaken.

In conclusion, prostatitis, prostatic abscess, or infection due to an unusual pathogen like GBS should be a consideration for male patients with urinary-tract infections that do not respond to standard antimicrobial treatment.

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References

biohazard level 4 agents and thus must be studied in high-containment laboratories, the number of animal studies with filoviruses are limited. With the exception of different monkeys, which are suitable but ethically questionable models, other animal models are of limited value because of the different symptomatic courses of the disease.

We propose the following hypothesis: the primary organ tropism in filovirus infections is dependent on the accessibility of sessile macrophages to virus particles, which is mediated by the specific anatomical features of these organs.

Morphological studies on filovirus-infected humans and monkeys show that there is a predilection for the liver, spleen, and lymph nodes and that cells of the mononuclear phagocytic system are the primary replication sites during early stages of filovirus infection [4–6]. Cultured human monocytes/macrophages are highly susceptible to filovirus infections, resulting in cytolysis and
massive production of infectious particles [7]. These cells become activated early upon infection, indicated by a release of proinflammatory cytokines such as TNF-α [7]. Patients display increased cytokine levels, suggesting monocyte/macrophage activation in vivo as well [8]. Therefore, it seems reasonable to conclude that monocytes/macrophages are an important source of shock-inducing mediators during filovirus infections.

The main route of infection is person-to-person transmission by intimate contact through the skin and secretions. Virus enters through minute lesions of the skin and mucosae and might obtain either direct access to the vascular system or indirect access via the lymphatic system (figure 1). Common characteristics of primary target organs (lymph nodes, liver, and spleen) are large numbers of sessile macrophages, known to be primary sites for virus replication [4–7]. After entry via the lymph capillaries, virus particles are transported to the lymph nodes, where macrophages are bathed by lymphatic fluid in the sinuses. After primary infection, replication continues in secondary and tertiary lymph nodes, resulting in the release of particles into the venous vascular system (viremia) (figure 1). The subsequent step of infection seems to be mediated by macrophages in the liver sinuses and spleen, where macrophages are in close contact with circulating blood. This contact occurs in the spleen via open blood circulation, with sheathed capillaries (macrophages) and sessile macrophages present along the venous sinuses, and in the liver via Kupffer cells (sessile macrophages) located in the venous portal sinuses (figure 1). Thus, replication and activation may be initiated quickly in all these organs, since macrophages can be infected without penetration of cellular or tissue barriers.

Organ tropism may be determined further by specific structural characteristics of the endothelium. The portal liver sinuses are lined by a discontinuous endothelium that does not rest on a regular basement membrane. This endothelium contains transcellular gaps, allowing virus particles to directly enter the space of Disse from the blood [4, 6] and to infect hepatocytes without passing any barrier (figure 1). The endothelia of several other organs (e.g., the kidneys and circumventricular organs) are also discontinuous, but continuous basement membranes and the blood-liquid barrier may prevent efficient infection. The pantropism in late stages of filovirus disease seems to be due to extravasation of infected circulating monocytes/macrophages, resulting in spread of virus in extravascular tissues. Endothelial cells are also targeted by filoviruses, and cytolytic replication may further contribute to viremia and the spread of virus [4–6, 9, 10].

In conclusion, direct access of filoviruses to sessile macrophages present in the lymph nodes, liver, and spleen seems to be an important factor for replication and systemic release of shock-inducing mediators. Macrophage-derived mediators act on multiple organs, but mainly on the endothelium. The endothelium responds by an increase in permeability, dysregulation of vascular tone, expression of cell-adhesion molecules, and development of a procoagulable phenotype that together substantially contribute to the occurrence of shock.

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References

Capnocytophaga Sepsis in a Patient with Waldenström’s Macroglobulinemia

Capnocytophaga species are capnophilic, gram-negative, gliding bacilli that are commonly isolated from the oral cavity in humans with or without periodontal disease [1]. Although these organisms may cause a wide variety of infections in immunocompetent hosts, they have been increasingly recognized as a cause of sepsis in immunocompromised individuals, notably those with granulocytopenia [2]. We describe a case of capnocytophaga septicaemia in a patient with Waldenström’s macroglobulinemia.

A 79-year-old man presented to the emergency department with a 2-day history of fever, chills, shortness of breath, weakness, and confusion. Four days before presentation he had undergone plasmapheresis for Waldenström’s macroglobulinemia. In the past he had been treated with melphalan and prednisone, which had been discontinued several months earlier because there was no evidence of hyperviscosity syndrome.