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Emerging Nipah virus encephalitis and its modeling

Kum Thong Wong

Address: Department of Pathology, Faculty of Medicine, University of Malaya, 50603 Kuala Lumpur, Malaysia

Email: Kum Thong Wong - wongkt@um.edu.my

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The first known human Nipah virus (genus Henipavirus, family Paramyxoviridae) outbreak was from 1998–1999 in Malaysia and Singapore involving more than 350 people [1]. In Bangladesh and India there were several recurring Nipah virus (NiV) outbreaks starting 2001 affecting about 120 people so far. The incubation period was a few days to 2 weeks. Clinical manifestations ranged from fever, headache, drowsiness and cough to a fatal acute encephalitic syndrome with a mortality rate of 40% to 75% [1]. Human autopsy studies showed acute NiV infection to be a systemic infection [2]. Blood vessels and parenchymal cells in most major organs were affected. In blood vessels, the earliest lesion seemed to be the endothelial multinucleated syncytia, followed by endothelial ulceration, intramural inflammation and necrosis. Viral antigens and nucleocapsids were localized to endothelium, syncytia and tunica media. Associated thrombosis and vascular occlusion was often observed and gave rise to microinfarction. The brain was most severely involved by disseminated vascular lesions. Around vasculitic vessels with or without microinfarction, surviving neurons or other parenchymal cells may reveal viral inclusions, antigens/RNA and nucleocapsids. Vasculitis, parenchymal lesions and viral antigens could also be found in the lung, kidney, heart and other organs. In the lung, fibrinoid necrosis, vasculitis, alveolar multinucleated giant cells were observed. Kidney pathology was characterized mainly by vasculitis and glomerular lesions. Multinucleated syncytia probably arising from podocytes was occasionally noted.

The golden hamster was reported to be a good model for acute NiV infection [3]. Infected hamsters developed neurological features and evidence of systemic vasculitis, multi-organ parenchymal and central nervous system infection confirming findings in human autopsies. Like in human cases, viral antigens/RNA and nucleocapsids were demonstrable in blood vessels and susceptible parenchymal cells. This confirmed the unique double pathogenetic mechanism of tissue injury arising from infarction and direct parenchymal infection. Successful intranasal inoculation suggested that oral and/or respiratory tract could be a major route of infection in humans via contaminated pig or patient secretions.

In infections of the pig and cat, the main pathology was apparently in the respiratory system and meninges. There was evidence of pneumonia characterized by bronchial and alveolar inflammation, associated with multinucleated cells with viral inclusions and antigens. Vasculitis and meningitis was severe but encephalitis was rare or mild. In the pig, viral antigens were apparently more prominent in glial cells than neurons, and were also demonstrated in cranial nerves, olfactory bulb and cerebral cortex.

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