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Detection of HHV-6 and HHV-7 genomic sequences in autopsy specimens DNA from individuals with unspecified encephalopathy

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Encephalopathy is a term for any diffuse brain disease that alters brain function or structure. Various types of encephalopathy have been identified, however, the etiology of the disorder in most cases remains unknown. Human herpesvirus-6 and -7 (HHV-6 and HHV-7) are neurotropic viruses, associated with wide variety of neurologic disorders, including encephalitis, temporal lobe epilepsy, multiple sclerosis, Alzheimer's and Parkinson's disease.

The aim of this study was to examine the presence of HHV-6 and HHV-7 sequences in DNA samples isolated from autopsy specimens (peripheral blood, dura and pia mater, brain tissue) of individuals with and without signs of encephalopathy.

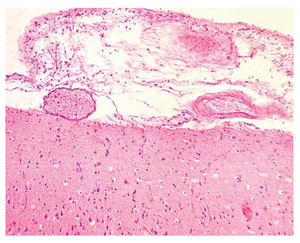
Materials and Methods

The specimens were obtained from 21 individuals with signs of encephalopathy and 23 individuals without signs of encephalopathy (control group). Nested polymerase chain reaction (nPCR) was used to detect HHV-6 and HHV-7 sequences and to define HHV-6 variant. The dura, pia mater and brain tissue samples were subject to histological examination.

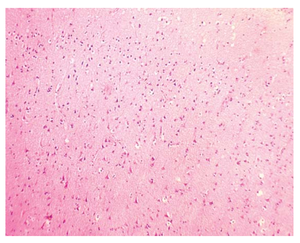
Results

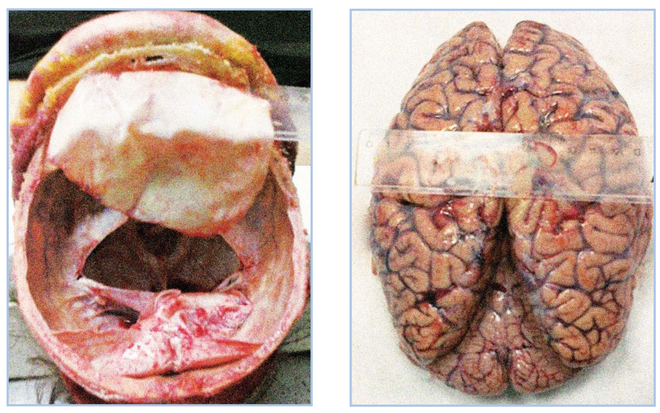
- Histological changes in pia mater of individuals with signs of encephalopathy were characterized by the presence of oedema and blood vessel full-bloodedness; brain tissue samples – by oedema, pericellular and perivascular oedema. (Figure 1)
- HHV-6 and/or HHV-7 sequences were revealed in 90.5% of samples from the individuals with encephalopathy and in 78.3% of samples from the control group individuals.
- Frequency of simultaneous detection of HHV-6 and HHV-7 sequences was significantly higher in the blood DNA samples from the individuals with encephalopathy (12/21 versus 6/23, p=0.029). (Figure 2)
- No difference was found between both groups regarding HHV-6 and/or HHV-7 sequences detection frequency in dura mater DNA samples. (Figure 3)
- Single HHV-6 sequence was detected only in pia mater DNA samples from the individuals with encephalopathy, but simultaneous HHV-6 and HHV-7 sequence detection rate was twice higher in these individuals in comparison to the control group (8/21 and 4/23, respectively). (Figure 4)
- Significantly higher frequency of single HHV-6 and HHV-7 sequence was revealed in the brain samples DNA of the individuals with encephalopathy in comparison to the control group (8/21 versus 3/23, p=0.047 and 7/21 versus 1/23, p=0.015, respectively). (Figure 5)
- In all cases HHV-6B variant was identified.

Figure 1. **Pia mater and brain microscopy: pia mater oedema, blood vessel full-bloodedness; brain oedema, pericellular and perivascular oedema**



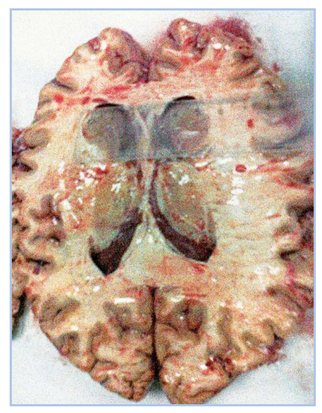
Hematoxylin-Eosin staining, x 100



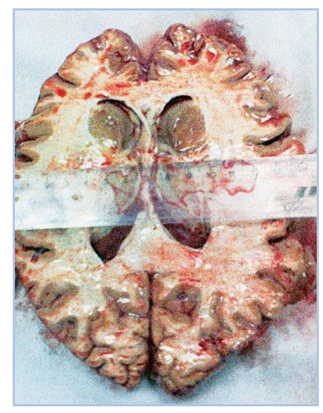


Dura mater macropreparation – oedema dura mater.

Brain macropreparation – sulci et gyri facies superolateralis cerberi et pia mater – oedema pia mater.



Brain macropreparation – horizontal cut. ventriculi lateralis, ventriculi tertius, substantia alba, substantia nigra,nuclei thalami, measurement of lateral ventricle for the diagnostics of encephalopathy (Evan's, Cella median index and Third ventricle cross section).



Criteria for taking materials of cerebral membrane – pia mater and dura mater and tissue-brain materials

Basic group. Turn-on mechanism: Dilation of side ventricles and the 3rd ventricle.

Turn-off mechanism: Haemorrhagic or ischemic changes (infarctions) in the cerebra-brain, haemorrhagic changes in cerebral membrane – pia mater and dura mater.

Control group. Turn-on mechanism: Macroscopically unchanged cerebra-brain, cerebral-brain oedema is permissible.

Turn-off mechanism: Dilation of side ventricles and the 3rd ventricle. Haemorrhagic or ischemic changes (infarctions) in the cerebra-brain, haemorrhagic changes in cerebral membrane – pia mater and dura mater.

The following criteria were used for the confirmation or refusal of macroscopic cerebral autoptat encephalopatia in the basic and the control group: Evans' index, Cella median index, Third ventricle cross section.

Figure 2. **HHV-6 and/or HHV-7 genomic sequences in whole blood DNA samples from individuals with unspecified encephalopathy and control group individuals**

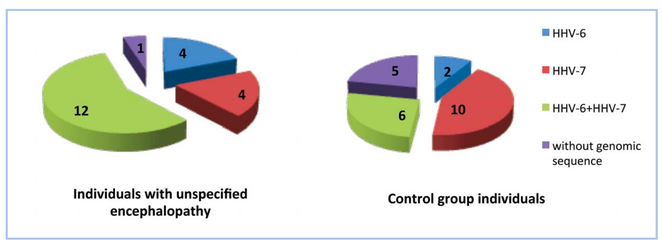


Figure 3. **HHV-6 and/or HHV-7 genomic sequences in dura mater DNA samples from individuals with unspecified encephalopathy and control group individuals**

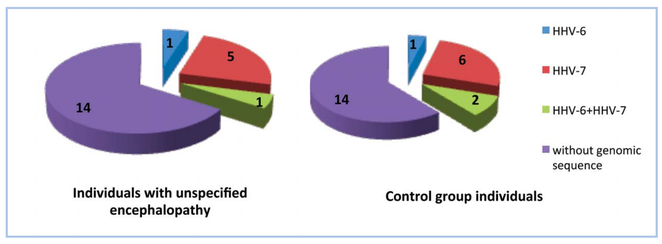


Figure 4. **HHV-6 and/or HHV-7 genomic sequences in pia mater DNA samples from individuals with unspecified encephalopathy and control group individuals**

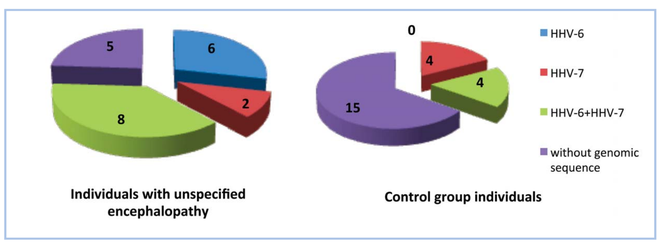
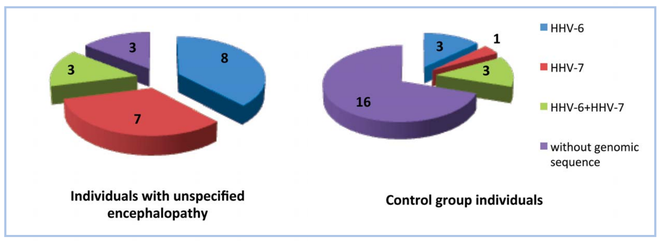


Figure 5. **HHV-6 and/or HHV-7 genomic sequences in brain DNA samples from individuals with unspecified encephalopathy and control group individuals**



Conclusion

The high detection rate of HHV-6 and HHV-7 sequences in pia mater and brain specimens DNA suggest a potential pathogenic role of these viruses in encephalopathy development.

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