MORPHOLOGY OF NON-SPECIFIED ENCEPHALOPATHY IN CASES OF POLYMERASE CHAIN REACTION PROVED PRESENCE OF HUMAN HERPESVIRUS-6

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BACKGROUND

The morphology of non-specified encephalopathy is a complex medical problem. Human herpesvirus-6 (HHV-6) infection can be discussed as a predisposing factor. Nearly 100% of us have been infected with the HHV-6 virus since early childhood and have antibodies to it, and at least 30% of us have small but detectable levels of latent virus in our blood (Alvarez-Lafuente 2002& Clark 1996), so the relevant questions are not *whether* you have the virus, but rather how *much* of the virus do you have, and is it *active* or *latent*? **The aim** of the present study was to investigate the presence of beta HHV-6 in non-specified adult encephalopathy cases.

METHODS

The blood, meninges and brain tissue were obtained in adult (aged 42-74 years) autopsies including 21 cases with encephalopathy and 23 cases in the control group. Tissues were submitted for routine histology including haematoxylin-eosin stain. The presence of HHV-6 genome (DNA) was analysed by nested polymerase chain reaction (nPCR), HHV-6 variants by restriction endonuclease analysis.

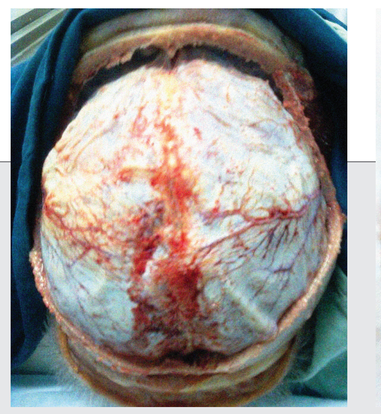
Criteria for taking materials of cerebral membrane – pia mater and dura mater and tissue – brain materials.

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

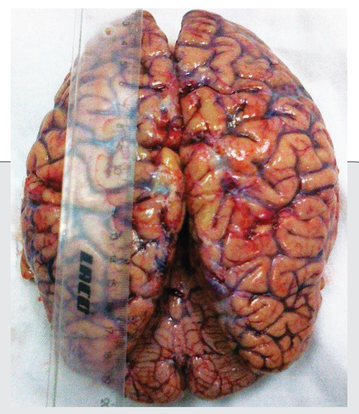
Turn-off mechanism: Haemorrhagic or ischemic changes (infarctions) in the cerebra, haemorrhagic changes in cerebral membrane.

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

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



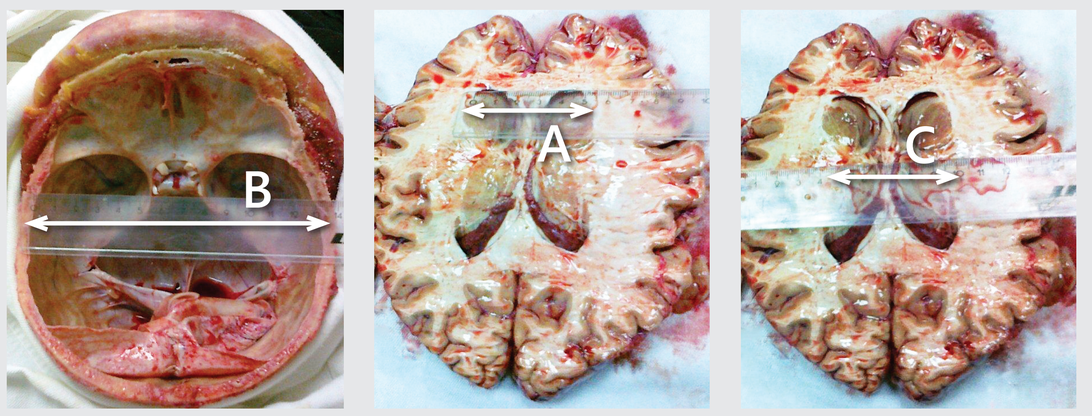
Dura mater macropreparation – oedema dura mater.



Brain macropreparation – sulci et gyri facies superolateralis cerberi et pia mater – oedema pia mater.
Brains sulcus with no greater than 3 mm.

The following criteria were used for the confirmation or refusal of macroscopic cerebral autoptat encephalopatia in the basic and the control group:

- Evans index (EI) – ratio of the transverse diameter of the anterior horns of the lateral ventricles to the greatest internal diameter of the skull, A/B no greater than 30%;
- Cella median index – ratio of the distance between the lateral ventricle to the greatest outer diameter of the skull, C/B no greater than 25%;
- Third ventricle cross section no greater than 8 mm;
- Brain sulcus width no greater than 3 mm;
- Brain ventricle norm variations no greater than 15%.



Measurement of Evans index calculated as the maximal width of the frontal horns (A) maximal width of the inner skull (B). Cella mediana index – ratio of the distance between the lateral ventricle (C) to the greatest outer diameter of the skull (B). Brain macropreparation – horizontal cut ventriculi lateralis, ventriculi tertius, substantia alba, substantia nigra,nuclei thalami, measurement of lateral ventricle for the diagnostics of encephalopathy (Evans, Cella median index and Third ventricle cross section).

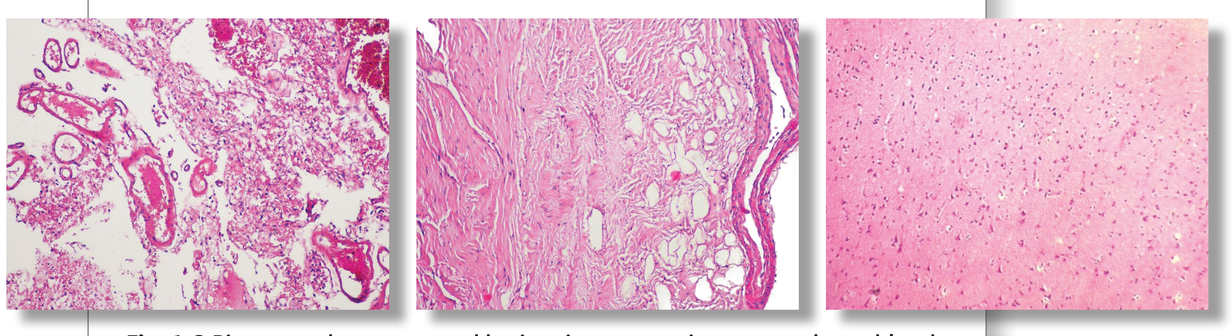


Fig. 1-3 Pia mater, dura mater and brain microscopy: pia mater oedema, blood vessel full-bloodedness; brain oedema, pericellular and perivascular oedema. Haematoxylin-Eosin staining, x 100.

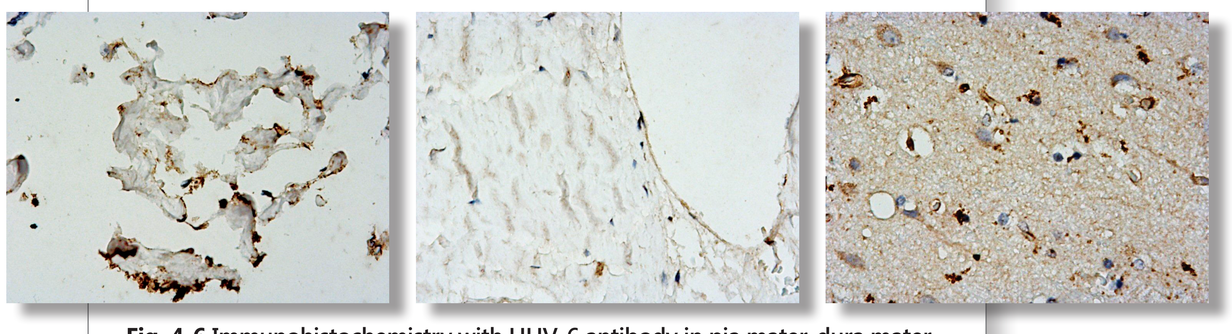


Fig. 4-6 Immunohistochemistry with HHV-6 antibody in pia mater, dura mater and brain. HHV-6 caused by pathogenic effect.
En vision method 400 x.

RESULTS

- The gross and microscopic structure did not reveal any specific changes.
- In the encephalopathy group, HHV-6 DNA sequence was found in meningeal tissues (16/21 cases; p=0.0036), in brain tissues (15/21 cases; p=0.0007), and both in brain and meningeal tissues (10/21 cases; p=0.0174).
- In the control group, the viral DNA was identified in meningeal tissues (7/23 cases), in brain tissues (4/23 cases), both in brain and meningeal tissues (3/23 cases).
- HHV-6B variant was detected in all cases.

* Comparison of group medians using Mann-Whitney U test resulted in a significant difference ($p<0.05$).

CONCLUSION

On the basis of the present study it can be concluded that HHV-6 is a pathogenic factor that can predispose to encephalopathy.

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