CASE 22: RABIES VIRAL ENCEPHALITIS: (Slide 22 A, B: H&E, IHC)

**Histology:**

The section from the cerebellum shows mild mononuclear inflammation in the meninges. In the cytoplasm of some of the Purkinje cells, intracytoplasmic, eosinophilic inclusions (single or multiple) are seen. They are sharply defined, round to oval and measure 1-8 µm across. Some of them are seen in the dendrites also. The nucleus of the neuron containing the inclusions is well preserved, indicating viable and normal metabolic state of the neuron. There is no evidence of neuronal necrosis, neuronophagia or microglial proliferation. The neurons containing the inclusions are usually clustered in groups. The Purkinje cells in other folia show anoxic changes, associated with proliferation of Bergmann glia in cerebellar folia. The histological features are characteristic of Rabies encephalitis.

The slide has been immunostained with polyclonal antibody prepared in-house (Department of Neurovirology, NIMHANS) to nuclear capsid protein of Rabies virus. The immunostaining highlights the viral nuclear capsid protein which has accumulated in the Negri bodies and spreading along the dendrites. Thus the viral protein visualized is many times more than the Negri bodies recognized by routine HE staining. The viral protein is seen in the Purkinje cells, their dendrites, small granule neurons and occasional glial cells in the cerebellar white matter.

**Diagnosis:** RABIES VIRAL ENCEPHALITIS

**Comment:**

Rabies is caused by a rhabdovirus, introduced from infected saliva following the bite by a rabid dog bite, or contact with abrasions or the mucous surfaces. The incubation period in man varies from 15 days to 1 year (mean 40 days). The incubation period is shorter in children and in patients with bites on the head. In the usual furious rabies (encephalitic form), the patient has fasciculations, convulsions, meningism and Cerebellar signs, progressing to death in 3-5 days. Hyperexcitability causing pharyngeal spasm in about half the patients is the cause for hydrophobia. Nearly 20% of patients manifest dumb (paralytic) rabies with paresis of a limb or ascending paralysis like in Guillain-Barre syndrome. In both forms of rabies, death is usually due to myocarditis or cardiopulmonary failure.

Macroscopic examination of the brain usually does not reveal any external abnormality. Histologically the changes are those of polioencephalomyelitis. The characteristic intracytoplasmic eosinophilic inclusions, Negri bodies are usually seen in the pyramidal cells of hippocampus, cerebral cortical neurons, Purkinje cells of the cerebellum and large motor neurons in the medulla oblongata and spinal cord. Immunofluorescence and ultrastructural studies reveal the presence of viral particles in the Negri bodies. Viral antigen is not just confined to Negri bodies but is found in many neurons and even in a few oligodendroglia. Another form of intracytoplasmic inclusions, Lyssa bodies are also seen to contain the viral particles on EM, and hence they are similar to Negri bodies. Therefore the term ‘Lyssa bodies’ is discarded. In some of the cases, the Negri bodies may be seen as vacuolated areas in the neuron and EM studies confirmed that these represent viral particles. The presence of inflammatory reaction to Rabies viral infection is usually scanty, but can be florid in rare cases. When florid, microglial nodules in the grey matter with neuronophagia and infiltration by acute and chronic inflammatory cells may be seen. In paralytic rabies, the pathological changes can be seen even in the spinal cord. Histology shows perivascular cuffing, lymphocytic leptomeningeal infiltration, neuronal degeneration in the spinal anterior horns admixed with microglial proliferation. The density of Negri
bodies is variable, and found in cerebellar Purkinje cells, hippocampal pyramidal cells and brainstem neurons and less in cerebral cortical neurons. Immunohistochemistry highlights many more labeled neurons with Negri bodies than recognized in routine histology.

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**Fig A:** Intra cytoplasmic round, eosinophilic viral inclusions in Purkinje cells – Negri bodies.  

**Fig B:** Immunohistochemical labeling of Rabies viral antigen by polyclonal antibody to viral nuclear capsid protein reveals densely stained intra-cytoplasmic Negri bodies in Purkinje neurons of cerebellum. In addition the viral antigen is seen extending along the dendritic branches.  

**Fig C:** Negri body inside a neuron- case of Rabies. The Negri body contains a granular matrix in which bullet shaped viral particles can be seen. (Inset: Higher magnification shows a transverse section of the Rabies viral particle inside rough endoplasmic reticulum in a neuron.  

(H&E Obj X 20)  

(IHC Obj X 40)  

(X12000; Inset: X30000)