

## Human Rabies Survivors in India: Epidemiological, Immunological and Virological Studies

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**Abstract :** Rabies is an acute encephalitis which is considered 100% fatal despite occasional reports of survivors. However, in recent times more cases of human rabies survivors are being reported. In the last 5 years, there are six laboratories confirmed human rabies survivors in India alone. All cases were children below 15 years and all contracted the disease by dog bites. All of them also had received the full or partial course of rabies vaccination and 4 out of 6 had also received rabies immunoglobulin. All cases were treated in intensive care units in hospitals at Bangalore, Mumbai, Chandigarh, Lucknow and Goa. We report here the results of immunological and virological studies conducted at our laboratory on these patients. The clinical samples that were obtained from these patients were Serum, CSF, nuchal skin biopsy and saliva. Serum and CSF samples were subjected to standard RFFIT for estimation of rabies neutralizing antibodies. Skin biopsy, CSF and saliva were processed by TaqMan real-time PCR for detection of viral RNA. CSF, saliva and skin homogenates were also processed for virus isolation by inoculation of suckling mice. The PBMCs isolated from fresh blood was subjected to ELISPOT assay to determine the type of immune response (Th1/Th2). Both CSF and serum were also investigated for selected cytokines by Luminex assay. The level of antibodies to virus G protein and N protein were determined by ELISA. All survivors had very high titers of RVNA in serum and CSF 100 fold higher than non-survivors and vaccine controls. A five-fold rise in titer could be demonstrated in 4 out of 6 patients. All survivors had a significant increase in antibodies to G protein in both CSF and serum when compared to non-survivors. There was a profound and robust Th1 response in all survivors indicating that interferon gamma could play an important factor in virus clearance. We could isolate viral RNA in only one patient four years after he had developed symptoms. The partial N gene sequencing revealed 99% homology to species I strain prevalent in India. Levels of selected cytokines in CSF and serum did not reveal any difference between survivors and non-survivors. To conclude, survival from rabies is mediated by virus-specific immune responses of the host and clearance of rabies virus from CNS may involve the participation of both Th2 and Th1 immune responses.

**Keywords :** rabies, rabies treatment, rabies survivors, immune response in rabies encephalitis

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