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Letters to the Editor: Published Article

Reported Case Report of Recovery From Rabies Using Intrathecal Rabies Immune Globulin was Flawed

Alan C. Jackson[1], Charles E. Rupprecht[2], Reeta S. Mani[3], Nidia Aréchiga-Ceballos[4] and Darryn L. Knobel[5]

[1]Department of Clinical Neurosciences, University of Calgary Cumming School of Medicine, Calgary, AB, Canada, [2]Auburn University, Auburn, AL, USA, [3]National Institute of Mental Health and Neurosciences, Bangalore, India, [4]Instituto de Diagnostico y Referencia Epidemiologicos, Direccion General de Epidemiologia, Secretaria de Salud, Ciudad de Mexico, Mexico and [5]Ross University School of Veterinary Medicine, St. Kitts and Nevis, West Indies

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We have read the recent report in BMJ Case Reports by Ing et al. that claims an adolescent girl developed rabies in Malaysia and had a complete recovery after successful treatment with four doses of intrathecal rabies immune globulin (RIG).[1] We are very concerned about numerous flaws in this report and recommend that it be disregarded when treatment options are considered for future patients with rabies.

Insufficient details are presented about the case and the post-exposure rabies prophylaxis to determine the extent of compliance with World Health Organization recommendations. The suspect dog was not available for diagnostic testing. Three doses of an unknown rabies vaccine were administered to the patient. It is unknown whether all wounds were infiltrated thoroughly with RIG (the report states "She received . . . a dose of RIG . . . ").

The symptoms of numbness, pain, and paraesthesias suggest the possibility of prodromal symptoms due to infection and inflammation in local dorsal root ganglia.[2] However, the documented sensory loss is a non-anatomical distribution (distal to the elbow) that is not helpful.

No symptoms or signs are reported suggesting clinical evidence of rabies encephalitis or myelitis, which would be expected to develop within a very short time after neurological prodromal symptoms. The first dose of intrathecal RIG was not given until the 4th hospital day and no clinical features of rabies encephalitis or myelitis were reported during this interval, which would be unusual if this was actually a case of rabies.

In order to have positive polymerase chain reaction (PCR) results for detection of rabies virus RNA, there must be centrifugal spread of the infection from the central nervous system to extraneural organs. Detection of rabies virus RNA in urine is not a sensitive diagnostic test for rabies. Saliva is a much more reliable fluid sample for detection of rabies virus RNA by a PCR assay.[3] In this report, saliva was negative on samples from 11 different days. Detection was positive only on day 1 in urine, but not in saliva or cerebrospinal fluid (CSF), at a time in which there were no clinical features of rabies encephalomyelitis, which raises serious concerns about potential problems with the PCR assay. Similarly, a positive assay in CSF only on day 6 is questionable. The PCR method was not presented or referenced and values for quantitative PCR were not given. PCR products should be sequenced to confirm the identity of the rabies virus variant, which was also not reported.

Patients that have rabies encephalomyelitis develop neutralizing anti-rabies virus antibodies in the CSF and patients that recover from rabies (or are successfully immunized) develop antibodies in their sera. No serology results were presented on sera or CSF. A skin biopsy was also not performed for detection of rabies virus antigen and/or RNA.

Administration of RIG by repeated lumbar intrathecal injections does not ensure good delivery to presumed infected CNS neurons. There is a good chance of development of a CSF leak, particularly with repeated injections, resulting in poor delivery to the intended targets. Theoretically intraventricular administration would be more favorable.

In summary, there is considerable uncertainty about whether the reported case actually had rabies because of the clinical features and laboratory evaluation. The delivery of intrathecal RIG via lumbar injections is questionable. We are also aware of unsuccessful attempts at therapy reported with both intravenous[4] and intrathecal infusion[5] of RIG in rabies patients. Hence, this report should not be considered a successful therapeutic outcome and we recommend that physicians should only embark on a similar approach with great caution and keeping our serious reservations in mind.

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Statement of authorship. ACJ, CER, RSM, NAC, and DLK each contributed to the writing of this manuscript.

Corresponding author: A. C. Jackson; Email: alan.jackson@ucalgary.ca

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