ORIGINAL RESEARCH PAPER
Volume - 9 | Issue - 7 | July - 2020 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

MULTIPLE SCLEROSIS PRECEDED BY RECURRENT HERPES LABIALIS (HSV 1): A RARE CASE

Neurology

Dr. Rahul Jain* Senior Resident, Department of Neurology, Atal Bihari Vajpayee Institute of Medical Sciences and Dr. Ram Manohar Lohia Hospital, New Delhi.*Corresponding Author

Dr. Kuljeet Singh Anand Professor and Head of the Department, Department of Neurology, Atal Bihari Vajpayee Institute of Medical Sciences and Dr. Ram Manohar Lohia Hospital, New Delhi

Dr. Abhishek Juneja Senior Resident, Department of Neurology, Atal Bihari Vajpayee Institute of Medical Sciences and Dr. Ram Manohar Lohia Hospital, New Delhi

Dr. Rakesh Kumar Mahajan Consultant and Professor, Department of Microbiology, Atal Bihari Vajpayee Institute of Medical Sciences and Dr. Ram Manohar Lohia Hospital, New Delhi

ABSTRACT

Multiple sclerosis is a common inflammatory demyelinating disorder of the central nervous system. It has multiple triggering factors that contribute to the pathogenesis of the disease. Amongst the viruses, Human Herpes Virus 6 and Epstein Barr Virus are most commonly implicated. However there are some studies suggesting association with Herpes Simplex Virus type 1 and 2, and Varicella Zoster Viruses too. We report a case of a young female, having recurrent herpes labialis (Herpes Simplex Virus type 1) presenting later on with multiple sclerosis, thus implying association of Herpes Simplex Virus type 1 in the pathogenesis of multiple sclerosis. To the best of our knowledge, this is one of the first cases reporting association of herpes labialis and multiple sclerosis.

KEYWORDS

Multiple Sclerosis, Herpes Simplex Virus, Herpes Labialis, Reactivation of Virus

Introduction:

Multiple sclerosis (MS) is a common inflammatory demyelinating disease of the central nervous system. The immune system plays a crucial role in the formation and maintenance of multiple sclerosis lesions.[1] There are many risk factors implicated in its development, like Vitamin D deficiency, smoking and genetic factors. Familial aggregation is well documented in MS.[2] Human Herpes Viruses (HHV) are also implicated in MS due to their neurotropism and ability to modulate human immune response.[3] Several herpes viruses like HHV-6, Epstein-Barr Virus, and less commonly Herpes Simplex Virus (HSV) 1 and 2, Varicella Zoster Virus (VZV), have been suggested as triggering factors for MS.

We report a case of a female suffering from recurrent herpes labialis (HSV 1) who later developed an acute attack of MS, thus contributing to the possible role of the virus in the pathogenesis of MS.

Case History:

A 16 year old girl, with history of 11 untreated episodes of multiple crops of vesicles on the upper lip in last 3 years, presented with numbness over the face mainly in the distribution of first (V1) and second (V2) division of trigeminal nerve for the last 4 months and abnormal sensations over the bilateral thumbs and right thigh for last 2 months. A month later, she developed sudden onset diminution of vision, drooping of eyelids, with downward and outward deviation of the left eye. She complained of pain on ocular movement. A week later, she developed asymmetric weakness of the bilateral lower limbs (right more than left). On inspection, she had multiple vesicles which were clustered together on an erythematous base, just above the right upper lip margin. **(Figure 1)**

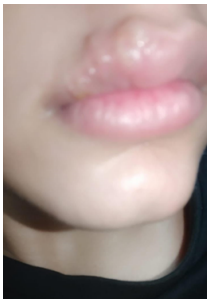

Figure 1 - Multiple vesicles clustered on an erythematous base over upper lip margin, suggestive of Herpes Labialis.

On neurological examination she was found to have reduced visual acuity 6/9 in the left eye, with relative afferent pupillary defect, left pupillary sparing third cranial nerve palsy, with left trigeminal nerve (V2) affection. She had predominantly distal weakness in bilateral lower limbs, right (Medical Research Council grade 3) more than left (Medical Research Council grade 4). Deep tendon reflexes were exaggerated in both upper and lower limbs. Plantar response was bilaterally extensor.

Magnetic resonance imaging (MRI) of brain revealed multiple, variable sized, hyper intense foci in bilateral periventricular and deep white matter, brainstem, bilateral cerebellar hemispheres with patchy predominantly nodular and peripheral enhancement with few lesions showing contrast enhancement and open ring sign, with no obvious restricted diffusion. **(Figure 2, Figure 3, Figure 4, Figure 5).**

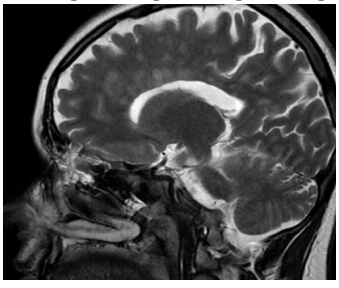

Figure 2 - Sagittal T2 image, showing multiple hyperintensities in the periventricular and subcortical regions.

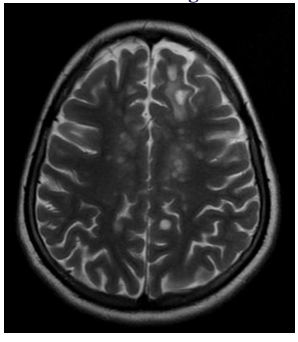

Figure 3 - Axial T2 image showing bilateral white matter hyperintensities, in cortical, subcortical and periventricular regions.

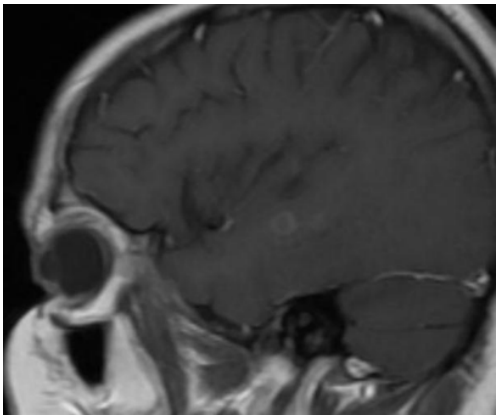

Figure 4 - Sagittal T1 post contrast image, showing a ring enhancing lesion.

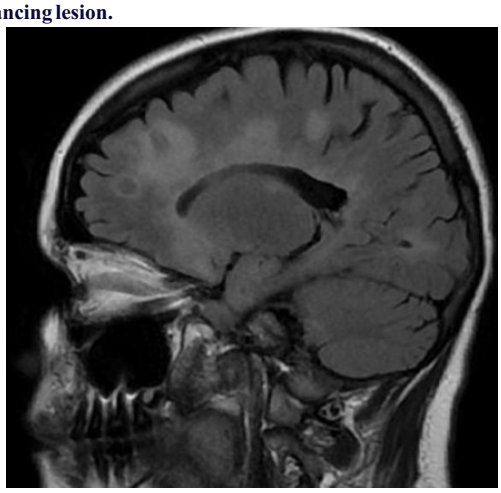

Figure 5 - Sagittal T2 FLAIR image showing open ring lesions in the subcortical region.

MRI of the spine was normal. P100 latencies were prolonged bilaterally (left more than right). Cerebro-Spinal fluid (CSF) viral panel for HSV 1, HSV 2, VZV, EBV, Cytomegalovirus, HHV 6, HHV 7, JC virus and Adenovirus by Polymerase Chain Reaction (PCR) was negative. CSF oligoclonal bands were positive. Also, serum HSV IgM antibody was positive. Routine laboratory tests including complete blood count, hepatic and renal function tests, thyroid profile and serum vitamin B12 levels were normal. Antinuclear antibody (ANA), Human immunodeficiency virus (HIV), Hepatitis B surface antigen and Hepatitis C antibody tests were negative by enzyme linked immunosorbent assay (ELISA).

She was started on pulse therapy of methylprednisolone 1gm intravenous daily for 5 days followed by oral prednisolone 50mg/day, and subsequently on disease modifying therapy Dimethyl Fumarate (240mg/day). She was also given oral tablet Valcyclovir 1 gm thrice a day.

Discussion:

This case projects a possible relationship between MS and HSV 1 virus infection, as the acute MS episode occurred in presence of preceding HSV 1 infection. In the past, many studies have been undertaken to establish an infectious cause of MS, out of which a few organisms like herpes virus - HHV 6 and EBV, Chlamydiae pneumoniae have been found to be the triggering factors.[4] The JC virus has also been found to multiply in the CSF of a few patients of MS in initial stages.[5] There are a few other case reports that have provided possible associations of HSV 1 and MS.[3,6] Experimental studies on mice, where in peripheral inoculation of HSV 1 leading to CNS demyelination at the root entry zone of the trigeminal nerve and other areas, have been described. [7] Many neurological diseases of humans have already been found to originate from immune mediated HSV 1 antigens, like Herpes Simplex Encephalitis, ADEM and Bell's palsy. [8,9]

The neurotropic viruses, can reach the central nervous system, by retrograde axonal transport through neurons (HSV and VZV) and the rest of the six HHV spread to the CNS through lymphocytes by hematogenous route, and then they can establish latency in sensory ganglions, B and T cells and multiple organs. [10] Reactivation of these viruses, may lead to a trigger of the autoimmune response leading to CNS demyelination. Theories suggesting infectious pathogenesis of MS, postulate that the IgG found with oligoclonal bands in the CSF of MS patients, are actually the antibodies directed against the infection responsible for MS, comparing to other diseases like subacute sclerosing panencephalitis, cryptococcal meningitis and neurosyphilis, where CSF oligoclonal IgG is directed against measles virus, cryptococcus and treponema pallidum, respectively. [4] IgG has also been found to occur at the periphery of the MS plaques.

Our patient, had recurrent episodes of herpes labialis for the last 3 years, and hence the HSV 1 would have become latent, and due to some trigger it was reactivated leading to cause brainstem demyelination in the form of unilateral trigeminal neuropathy, optic nerve and midbrain involvement, followed by cortical and subcortical CNS demyelination. Had the patient been treated with adequate antiviral therapy, it could have reduced the viral load, and prevented subsequent neuropathological injury. We excluded HSV encephalitis by absence of typical clinical, radiological and CSF findings.

Further studies are needed, to establish a cause and effect relationship between HSV 1 and MS, but this study does indicate an association between the two.

REFERENCES:

1. Neuhaus, O., Archelos, J. J., &Hartung, H. P. (2003). Immunomodulation in multiple sclerosis: from immunosuppression to neuroprotection. Trends in pharmacological sciences, 24(3), 131–138.
2. Ebers, G. C., Sadovnick, A. D., &Risch, N. J. (1995). A genetic basis for familial aggregation in multiple sclerosis. Canadian Collaborative Study Group. Nature, 377(6545), 150–151.
3. Buscarinu, M.C., Fornasiero, A., Romano, S. et al. (2017) Coincident onset of multiple sclerosis and Herpes simplex virus 1 encephalitis: a case report. MultScler Demyelinating Disord 2, 6.
4. Gilden D. H. (2005). Infectious causes of multiple sclerosis. The Lancet. Neurology, 4(3), 195–202.
5. Ribeiro, T., Fleury, M. J., Granieri, E., Castellazzi, M., Martini, F., Mazzoni, E., Coursaget, P., &Tognon, M. (2010). Investigation of the prevalence of antibodies against neurotropic polyomaviruses BK, JC and SV40 in serafrom patients affected by multiple sclerosis. Neurological sciences: official journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology, 31(4), 517–521.
6. Ferrò, M. T., Franciotta, D., Prelle, A., Bestetti, A., & Cinque, P. (2012). Active intrathecal herpes simplex virus type 1 (HSV-1) and human herpesvirus-6 (HHV-6) infection at onset of multiple sclerosis. Journal of neurovirology, 18(5), 437–440.
7. Kastrukoff, L.F., Lau, A.S. and Kim, S.U. (1987). Multifocal CNS demyelination following peripheral inoculation with herpes simplex virus type 1. AnnNeurol., 22: 52-59.
8. Sköldenberg, B., Aurelius, E., Hjalmarsson, A., Sabri, F., Forsgren, M., Andersson, B., Linde, A., Strannegård, O., Studahl, M., Hagberg, L., &Rosengren, L. (2006). Incidence and pathogenesis of clinical relapse after herpes simplex encephalitis in adults. Journal of neurology, 253(2), 163–170.
9. Kaji, M., Kusuhara, T., Ayabe, M., Hino, H., Shoji, H., & Nagao, T. (1996). Survey of herpes simplex virus infections of the central nervous system, including acute disseminated encephalomyelitis, in the Kyushu and Okinawa regions of Japan. Multiple sclerosis (Houndmills, Basingstoke, England), 2(2), 83–87.
10. Ludlow, M., Kortekaas, J., Herden, C., Hoffmann, B., Tappe, D., Trebst, C., Griffin, D. E., Brindle, H. E., Solomon, T., Brown, A. S., van Riel, D., Wolthers, K. C., Pajkrt, D., Wohlsein, P., Martina, B., Baumgärtner, W., Verjans, G. M., & Osterhaus, A. (2016). Neurotropic virus infections as the cause of immediate and delayed neuropathology. Actaneuropathologica, 131(2), 159–184.