

Parvovirus Encephalitis: Looking Through the Eyes

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ABSTRACT

Parvovirus B19 usually causes less severe symptomatic infections. Its severity depends upon the affected cells of a particular organ system. Whereas diseases affecting the skin and haematological systems tend to be milder, affection of CNS may turn serious. Direct invasion or NS1 toxicity of Parvo virus B19 has been postulated behind CNS tropism. Here we depict Parvovirus B19 causing acute encephalitis and ophthalmoplegia in an immunocompetent male child, taking an eventful course, responded with IVIG & steroids, reversed the symptoms except some VEP abnormalities. This explores the need for timely intervention with immunotherapy in such cases to prevent permanent sequelae.

Key words: encephalitis; immunotherapy; ophthalmoplegia; parvovirus B19; squint



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INTRODUCTION

Human Parvovirus, a member of Erythrovirus family is usually associated with asymptomatic infections or nonspecific febrile illness with or without skin eruptions.¹ Its pathogenicity does not require any helper cells as it has autonomous replicative property but because of selective tropism it is mainly cited as an agent to cause aplastic crisis in immune-compromised hosts.² However this virus is capable of infecting a variety of cells, as reflected by its isolation in forms of nucleic acids, viral proteins from different cells. Exact paediatric data is lacking regarding the extra-haematological manifestations of the parvovirus infection. When extrapolated from adult data most of the extra-hematological symptoms are joint and skin involvement followed by renal and nervous system involvement.³ Central nervous system involvement in immune-competent hosts is very rare. In this case, signs of encephalitis and resultant paresis of extra-ocular muscles were evidently attributed to none other than Parvovirus infection.

CASE REPORT

This 11 years old developmentally normal boy, presented in a confusional state with history of high grade fever of 10 days, one episode of tonic clonic seizure on third day of illness, with double vision followed by blurring of vision and vomiting on fifth day. There was no history of photophobia, trauma, bulging eyes or red eyes, sinusitis, ear discharge or rashes. On examination patient had features of raised intra cranial pressure, positive meningeal signs and Babinski sign. Fundoscopy showed presence of Grade 2 papilledema.

We noticed there was a serial fall of erythrocyte count not affecting other cell lines and progressive anaemia of normocytic normochromic type. Serum electrolytes, liver and renal function tests were within normal range. We performed bundle of blood tests to exclude infectious causes like malaria, dengue, chikungunya, rickettsia and typhoid, HIV, CMV and all were negative.

We conducted MRI brain including orbits which showed widening of cortical sulci suggestive of encephalitis and optic nerve edema. CSF study showed mild pleocytosis (6 cells/mm³) with

lymphocytic predominance and normal levels of sugar and protein, chloride and ADA (adenosine deaminase). In order to find out the etiology, pan neurotropic viral panel and autoimmune encephalitis profile of CSF were sent. Meanwhile tuberculosis was ruled out on the basis of negative Mantoux test, insignificant chest X-ray, absence of acid fast bacilli in sputum and CSF, negative CBNAAT status of those samples including negative RT-PCR for TB DNA from CSF. Tests for lupus profile and autoimmunity were also negative.

We started treating the child in the lines of acute encephalitis syndrome, with intravenous ceftriaxone, acyclovir, phenytoin and osmotherapy with mannitol followed by intravenous 3 % sodium chloride, but the child did not respond.

Pan-neurotropic virus panel of CSF came out to be positive for Human Parvovirus B19 and negative for others including herpes simplex virus. It is worthy to mention that the autoimmune encephalitis profile was inconclusive. Hence we stopped acyclovir. In view of persistent papilledema beyond two weeks along with impairment in visual fixation and persistent red cell aplasia, intravenous immunoglobulin (IVIG) was started at the dose of 1 gm/kg on day 15 after which the first symptom to disappear was diplopia and blurring of vision followed by papilledema. There was no history of blood transfusion in this case. Serum Parvovirus IgM came out to be positive too.

DISCUSSION

Reporting of neurological manifestations among children is on a rising trend over times. Approximately 39% cases of CNS manifestations due to Parvovirus B19 in children are linked to acute encephalitis and encephalopathy.⁴ More strikingly it has been observed in immunocompetent and otherwise normal children followed by the strata of paediatric patients suffering from sickle cell disease. Due to high concentration of P blood type antigen, receptor of B19 and $\alpha 5\beta 1$ integrin (the co-receptor for B19) the erythroid progenitor cells are permissive for B19 replication.⁵ P antigen is necessary for viral binding but not sufficient to permit entry of the virus inside the cell and this requires $\alpha 5\beta 1$ integrin as a cellular

co-receptor. Because non-erythroid progenitor cells with P antigen do not have $\alpha 5\beta 1$ integrin, Parvovirus B19 can bind, but cannot infect them. However, the NS1 protein exerts a cytotoxic effect on the cells, it binds without any B19 replication or virion accumulation.^{6,7} Interestingly though B19 DNA was detected in the brain of the affected paediatric patients, B19 virus itself has never been reported in children.⁸ Thus there is still controversy whether B19 itself by direct invasion or through its NS1 protein exerts its toxicity in CNS.

Wagner et al studied concentrations of IL 1 β and IL-6 and interferon (INF)- γ messenger RNA (mRNA) in peripheral blood mononuclear cells from patients with acute B19 infection and reported that these cytokine genes were activated in PBMC, suggesting systemic monocyte and T cell activation.⁹ Kerr et al reported that increased levels of TNF- α , IL-6, INF- γ , GM-CSF and MPC-1 in the serum and CSF of patients with B19 encephalitis and suggested that over-production of inflammatory cytokines might play a role in B19 encephalitis.¹⁰

Upon follow up with oral steroids for two weeks the child achieved complete recovery of the residual eye symptoms, with no decline in scholastic performance or social interactions and on repeat MRI, the optic nerve edema was resolved after three months and MRI brain was within normal limits except mild prominence of lateral ventricles.

As B19 infection is associated with cytokine dysregulation administering immunotherapy perhaps significantly improved the vision, diplopia and ophthalmoplegia. On follow up, VEP (Visual Evoked Potential) showed normal P₁₀₀ latency but decreased amplitude bilaterally.

CONCLUSIONS

Though serious Parvovirus infection has mostly been cited in immunocompromised patients, our case with no detectable immunodeficiency at this point of time had such a severe manifestation of meningoencephalitis attributed only to Parvovirus B19. Concomitant blood parameters (erythrocytopenia /pancytopenia) and CSF viral profile are needed in cases with high suspicion of viral etiologies. Besides the conventional treatment IVIG and steroids may be considered in resistant cases in order to prevent permanent damage to the nervous system due to Parvovirus infection where no specific and effective antiviral therapy is available.

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