Case Series

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Paediatrics Section

The Spectrum of Clinical Manifestations of Serious Human Parvovirus B19 Infection in Children without any Underlying Diseases- A Case Series

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ABSTRACT

Human Parvovirus B19 causes mild to life-threatening illnesses, especially in immunosuppressed individuals. In the immunocompetent individuals, the severe spectrum of clinical manifestations of the virus infection is not widely known. This case series presents the spectrum of clinical manifestations of serious Parvovirus B19 infection in children without any chronic haematological or immunodeficiency disease. This series is about a total of 12 children who were positive for Parvovirus Immunoglobulin M (IgM) antibody and the age range was between 1-12 years. Fever, fatigue, and arthritis were the most common manifestations. Pure red cell aplasia, the specific manifestation of Parvovirus infection, was seen only in one-third of patients. All the children were treated with Intravenous Immunoglobulin (IVIG) along with supportive therapy. All except one had a successful recovery.

Keywords: Hepatosplenomegaly, Immunocompetent, Paediatric, Tachypnoea

INTRODUCTION

Human Parvovirus B19 (B19V) is a single-stranded Deoxyribose Nucleic Acid (DNA) virus of the family Parvoviridae. The virus was first discovered in 1975 and first linked to human disease in 1981 [1]. Infection with B19V is very common and occurs worldwide without ethnic or geographical boundaries and range from mild to life-threatening illnesses, especially in people with underlying haematological disorders or in immunosuppressed individuals. Infection in immunocompetent children usually manifested as mild upper respiratory tract illness, rash, etc., with rare incidences of severe clinical syndromes [2]. B19V infection causes several clinical syndromes like fifth disease, transient aplastic crisis and pure red cell aplasia [3,4].

Traditionally, laboratory diagnosis of B19V infection is confirmed by serologic and DNA tests. IgM antibodies appear one week post-infection and persist for two to three months and are most widely used for the diagnosis of Parvovirus infection [5-7].

Specific antiviral therapy is not available to treat B19V infection. As most of the infections in immunocompetent hosts is mild, treatment is symptomatic. Severe diseases are treated with IVIG [8]. There are several regimens, but a single dose of 1 gm/kg of IVIG is commonly practiced [9]. In case of IVIG failure, immune modulators like prednisolone and cyclosporine remains the treatment option.

While patients with pre-existing chronic haematological or immunodeficiency disorders are known to suffer more severe diseases, the severe spectrum of disease manifestations, especially which requires inpatient admission, is unclear in immunocompetent children and data is scarce in published literature [10].

CASE SERIES

This series presents 12 children who reported to the Department of Paediatrics Medicine, IPGMER and SSKM Hospital, Kolkata, West Bengal, India. All of them tested positive for Parvovirus IgM antibody detected by enzyme immunoassay method, but had no pre-existing co-morbidities or immunodeficiency disorders. Immunocompetency was confirmed based on clinical history, i.e., no history of recurrent infection, examination, haematological parameters including absolute neutrophil count, immunoglobulin assay in comparison with age; and Human Immunodeficiency Virus (HIV) seronegative status. All the children were treated with IVIG @1 gm/kg, followed by prednisolone, if required. The median hospital stay was 13 days. Most of the children reported between 1st January 2019 and 31st December 2020.

Fever was the most common clinical sign (n=9) with a median duration of fever of 10 days. The next common symptoms were fatigue (n=6), joint pain (n=4), and rash (n=3). Two children presented with cough and respiratory distress. Almost half of the children had arthritis, mainly monoarthritis (n=3). Hepatosplenomegaly and lymphadenopathy were present in a majority of cases [Table/Fig-1].

While waiting for the parvovirus serology result, a provisional diagnosis was made in each of the children for the initiation of treatment. Four children were provisionally diagnosed with systemic onset juvenile idiopathic arthritis, three with fever with monoarthritis, two with lower respiratory tract infection, and two with Haemophagocytic Lymphohistiocytosis (HLH). One child was diagnosed with Pyrexia of Unknown Origin (PUO) [Table/Fig-2].

S.No.	Age (years)/gender	Presented symptom	Clinical signs	Haematological findings	No. of hospital stay (days)	Outcome
1.	1/M	Cough	Tachypnoea	Anaemia	10	Recovered
2.	2/F	Fever	Hepatosplenomegaly	Anaemia	14	Recovered
3.	4/M	Arthralgia	Hepatosplenomegaly	Pure red cell aplasia	12	Recovered
4.	6/M	Fever	Lymphadenopathy	Pure red cell aplasia	16	Recovered
5	6/M	Fever	Hepatosplenomegaly	HLH	19	Death
6	7/F	Arthralgia	Lymphadenopathy	Pancytopenia	15	Recovered
7	8/M	Fever	Lymphadenopathy	Anaemia	18	Recovered
8	9/F	Fever	Hepatosplenomegaly	Pure red cell aplasia	11	Recovered

9	9.5/M	Fever	Hepatosplenomegaly	Anaemia	17	Recovered
10	10/M	Fever	Lymphadenopathy	Pancytopenia	12	Recovered
11.	11.5/F	Fever	Hepatosplenomegaly	Hypereosinophilia	12	Recovered
12.	12/F	Fever	Lymphadenopathy	Pure red cell aplasia	10	Recovered

[Table/Fig-1]: Case representation of all the patients.
M: Male; F: Female; HLH: Haemophagocytic lymphohistiocytosis

Haematological abnormalities were present in more than ninety percent of the children. Isolated anaemia was present in the majority (n=8), whereas, two of the children had pancytopenia. One child presented with hypereosinophilic syndrome. Reticulocytopenia (defined as reticulocyte count <50,000/mm^3) was found in five children. Anaemia was attributable to iron deficiency in four children. There was pure red cell aplasia in three children. In the children who presented with pancytopenia, there was trilineage suppression in the bone marrow.

Diagnosis	n
Haemophagocytic Lymphohistiocytosis (HLH)	2
Respiratory tract infection	2
Systemic onset JIA	4
Pyrexia of Unknown Origin (PUO)	1
Monoarthritis	3

[Table/Fig-2]: Provisional diagnosis prior to confirmation (N=12).

After treatment with IVIG and supportive therapy, all children improved gradually, except one with HLH who succumbed to the disease. One child presented with hypereosinophilic syndrome and required additional treatment with prednisolone for four weeks with gradual dose tapering.

DISCUSSION

This case series documented the profile of Parvovirus B19 infection in immunocompetent children. The majority of Parvovirus B19 infection in immunocompetent children is mild or self-limiting [10]. Severe clinical manifestation is rare. This series describes the serious clinical spectrum of Parvovirus B19 infection, which required hospitalisation.

Fever, rash, arthritis and particularly monoarthritis were the most common clinical symptoms as described in this case series. Cough and respiratory distress were present in a handful of cases. Kishore J and Singh J reported B19V infection in a nine-year-old girl, who had fever, rash, myalgia, arthralgia and mild anaemia with haemoglobin ranging around 9 gm% [11]. A study done by Sim JY et al., showed a similar result with fever and rash were common, but arthritis was not described [3]. Lymphadenopathy and hepatosplenomegaly were present in most of the children. A majority of children had anaemia, while pure red cell aplasia was present in one-third of them. A retrospective case control study done in Kenyan children showed high B19 IgM levels were significantly associated with severe anaemia [12]. One of the previous study also described thrombocytopenia as the most common haematological abnormality in contrast to finding of this study [4]. Hypereosinophilic syndrome is also reported in one child.

All the children were treated with IVIG. Recovery was uneventful in all except one, who developed HLH. He was treated as per HLH-2004 protocol. Despite best of authors efforts, the child succumbed to death. There are several case reports of Parvovirus induced HLH in adults, often reported as having increased mortality compared to other HLH aetiologies [13]. Multiorgan dysfunction was commonly reported [14].

CONCLUSION(S)

Parvovirus B19 infection can cause serious clinical manifestations even in children without co-morbidities. Fever, rash, and arthritis with anaemia were the most common clinical manifestation. Awareness of the clinical symptoms can lead to prompt evaluation and management. Early initiation of treatment can save the lives of many children.

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