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Case Report

Aplastic anemia induced by human parvovirus B19 infection in an immunocompetent adult male without prior hematological disorders: A case report

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ABSTRACT

Introduction and importance: Parvovirus B19 (B19V) is a human pathogenic virus of clinical relevance. Human parvovirus B19 infection can be asymptomatic or frequently associated with erythema infectiosum, or joint symptoms in healthy adults. Aplastic anemia as a complication of human parvovirus infection is rare in healthy adults without prior hematological disorders.

Case presentation: We report a case of severe aplastic anemia in a 22-years-old immunocompetent adult male without any hematological dysfunction who presented with periumbilical pain, loose watery stools, and fever with chills and rigor. General examination, laboratory investigation, and peripheral blood smear revealed anemia with leucopenia and relative lymphocytosis, thrombocytopenia, and severe neutropenia. Bone marrow biopsy revealed hypocellular bone marrow with maturation arrest at the proerythroblast stage with intranuclear inclusions and no blast and hematopoietic cells replaced by mature adipocytes in marrow spaces. Parvovirus B19 infection was confirmed by viral serology and polymerase chain reaction.

Clinical discussion: Asymptomatic or mild infection occurs most often when B19 affects immunocompetent adults. However, this is the fourth case reporting severe aplastic anemia in immunocompetent adults and the first case reported in immunocompetent adult males. The patient was admitted for close monitoring and supportive management, which effectively improved the patient's clinical condition, and discharged with a strict follow-up schedule in an outpatient setting.

Conclusion: Thus, acute infection with this virus must be considered a cause of acquired aplastic anemia even in individuals without underlying disease.

1. Introduction

Human Parvovirus, from the Parvoviridae family, is a non-enveloped single-stranded virus [1,2]. The common clinical manifestations of Parvovirus B19 infection in immunocompromised patients are fever, arthralgia, and rash [1]. Infection is usually asymptomatic or mild in immunocompetent individuals. Human Parvovirus B19 can cause hydrops fetalis and fetal death in utero, erythema infectiosum in children, an arthritis-like syndrome in adults, and hematological disorders such as leukopenia, thrombocytopenia, and transient aplastic crisis in immunocompromised patients [2–4]. However, in individuals with acute infection with Parvovirus B 19 without underlying diseases, severe cases of transient aplastic anemia with or without thrombocytopenia have been reported [3,5]. We present the case of a previously healthy adult male who developed severe aplastic anemia with serologically proven acute parvovirus B19 infection. We hereby declare that this work

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has been prepared and edited in line with the SCARE 2020 guidelines [6].

2. Presentation of case

A 22-year-old male with no known comorbidities, presented to the emergency department at Shree Birendra Hospital with periumbilical pain for one week, multiple episodes of loose watery stools for two days, and fever with chills and rigor for one day. The patient also complained of generalized fatigue and weakness. There was no history of joint pain and rashes over the body. The vital parameters were stable and his general examination showed the presence of pallor in the lower palpebral conjunctiva.

On systemic examination, periumbilical tenderness was noted during superficial palpation. There was no organomegaly. The laboratory investigations are shown below in Table 1.

The basic laboratory investigation of complete blood count revealed pancytopenia. The peripheral blood smear revealed normocytic normochromic anemia with leucopenia and relative lymphocytosis with thrombocytopenia. There were no atypical cells and hemiparasites. He had normal liver and renal function tests, LDH, serum albumin, serum vitamin B12, and serum folic acid. The serology for HIV, Hepatitis A, B, and C was non-reactive. The chest X-ray and ultrasonography of the mediastinum and abdomen were unremarkable.

The absolute neutrophil count (ANC) was 184 cells/microliter which signified severe neutropenia (<500 cells/microliter). For further evaluation of pancytopenia, a bone marrow biopsy was performed. The bone marrow biopsy revealed hypocellular for that age (cellularity of 10–20%) as shown in Fig. 1. The marrow spaces showed hematopoietic cells replaced by mature adipocytes. Serological analysis for Cytomegalovirus, Epstein Barr virus, and Parvovirus B19 was performe to determine the cause of hypocellular marrow. The analysis revealed parvovirus B19 IgM antibodies of 1.55 i.e., positive (reference range <0.9) but the IgG antibodies were negative. This was indicative of a recent infection with Parvovirus B19. Similarly, the serology of all the other viruses was negative. Enzyme Immunosorbent Assay (EIA) technique was used to detect the IgM antibodies. The patient had no prior history of any exposure to radiation (therapeutic or radiation), drug,and no family history with a similar illness.

Table 1
Laboratory investigations.

Laboratory tests	Result	Unit	Reference range
Total Leukocytes Count (TLC)	19	10^3/μL	4–11
Neutrophil	14	%	40–80
Lymphocyte	80	%	20–40
Hemoglobin (Hb)	9.6	g/dl	13–17
Hematocrit/Packed Cell Volume	28.8	%	40–50
Mean Cell Volume (MCV)	88	fL	80–100
Mean Cell Hemoglobin Concentration	34.9	g/dL	31–35
Mean Cell Hemoglobin	30.7	pg	26–34
Platelet Count	55	10^3/μL	150–450
Red Blood Cell Count (RBC Count)	3.27	10^6/μL	4.5–5.5
Urea	31	mg/dl	17–43
Creatinine	1.2	mg/dl	0.7–1.3
Sodium	142	mEq/L	135–145
Potassium	4.1	mEq/L	3.5–5.5
Bilirubin Total	0.8	mg/dl	0.1–1.2
Bilirubin Direct	0.2	mg/dl	0.0–0.2
Alkaline Phosphatase (ALP)	48	U/L	53–128
Alanine Transferase (ALT)	27	U/L	0–35
Aspartate Transferase (AST)	32.7	U/L	0–35
Reticulocyte count	1.8	%	0.5–2.5
Prothrombin time (PT)	10.9	seconds	11–13.5
Serum Calcium	10.05	mg/dL	8–10
Serum Iron	268.04	μg/dL	50–100
Serum Ferritin	804.8	μg/dL	20–250
Total Iron Binding Capacity	289	mcg/dL	228–428
Serum Albumin	4.60	g/dL	3.5–5.2
Serum Lactate Dehydrogenase (LDH)	166	U/L	140–280
Vitamin B12 (Serum/Blood)	274.10	pg/ml	197–771
Folic Acid (Serum/Blood)	11.33	ng/ml	4.6–34.8

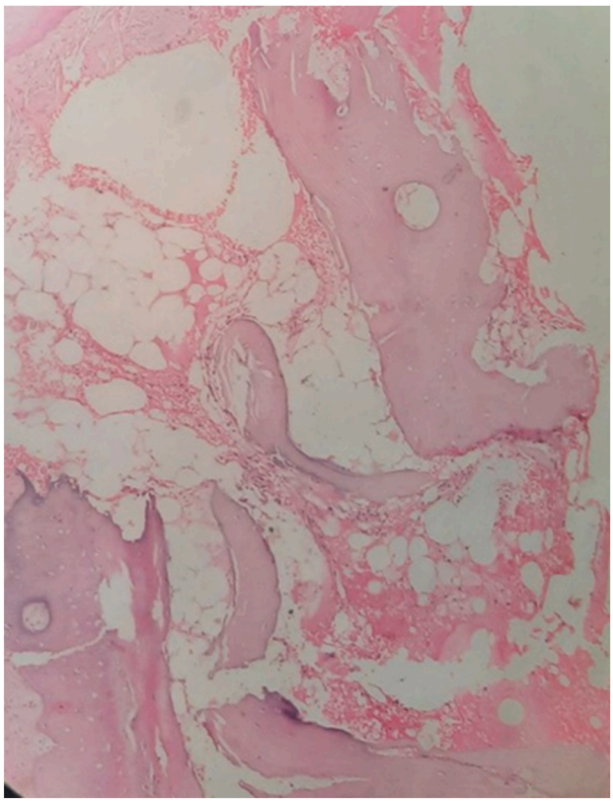

Fig. 1. Bone marrow Aspirate showing hypocellularity. The marrow spaces show hematopoietic cells replaced by mature adipocytes. Only scattered hematopoietic cells were seen and comprised of a few myeloid and erythroid series mostly in later stages of development: hematoxylin-eosin staining.

After these investigations, he was considered to have developed transient aplastic crisis (TAC) secondary to acute Parvovirus B19 infection. But as the red cell production did not return to baseline even after 2 weeks, he was diagnosed with aplastic anemia secondary to Parvovirus B19 infection. The patient complained of blurry vision during illness. The ophthalmologic consultation revealed retinal hemorrhages on direct ophthalmoscopy.

Empirically, the symptoms of abdominal pain, diarrhea, and fever were managed with antibiotics, paracetamol, and fluid supplements. Packed red cells and platelets rich plasma were transfused for the declining hematological parameters. The patient got symptomatically better over the weeks but hematological parameters were not improving as shown: hemoglobin: 10.1 g/dl, TLC: 2.5 $\times$ 10^3/μL with neutrophil 20% and lymphocyte 80%; RBC count: 3.27 $\times$ 10^6/μL; platelet count: 10 $\times$ 10^3/μL.

The patient was kept under observation to prevent any risk of bleeding. Due to the unavailability of HLA matched donor, he was kept in hospital under evaluation. He was planned for immunosuppressive therapy consisting of eltrombopag, anti-thymocyte globulin, and cyclosporine or hematopoietic cell transplantation for refractory immunosuppressive therapy. Over a course of a few weeks, his condition improved and was discharged with a strict follow-up schedule.

3. Discussion

Erythema infectiosum, often known as the fifth disease is the most common manifestation in children, whereas, in healthy adults, most cases of infection are asymptomatic [7] or associated with arthritis and myalgia [8]. The virus causes infections worldwide that vary in severity

depending on the age as well as the immunologic and hematologic status of the host [4]. When immunocompromised hosts are exposed to parvovirus B19, the common clinical manifestations are fever, arthralgia, and rash and they develop chronic viremia and RBC aplasia [1,9]. Rajput et al. suggest that parvovirus B19 can have significant marrow aplastic effects even in immunocompetent individuals [10]. Previously, only three cases of aplastic anemia in immunocompetent adult women had been reported [8,10,11]. This is the fourth case reporting severe aplastic anemia in immunocompetent adults and the first case reported in an immunocompetent adult male. Aplastic anemia has also been documented in immunocompetent children by Osaki et al. [12]. According to Rogo et al., adults have more severe cases of parvovirus disease than children, and fatigue, depression, and malaise can be more severe in women than in males, who are more likely to have a flu-like illness [1]. Despite being an adult male, our patient's condition was severe. The course of our patient's illness differed slightly from that of previously described cases in immunocompetent patients [8,10,11]. Fever with chills and rigor was present in our patient, as in prior reported cases [10]. However, our patient did not have rash or arthralgia.

Clinical diagnosis of parvovirus infection is usually made without laboratory confirmation if typical presentations like erythema infectiosum are present. If laboratory confirmation is required, serum immunoglobulin M testing is recommended for immunocompetent patients; viral DNA testing is recommended for aplastic crisis patients and those who are immunocompromised [13,14]. Since erythema infectiosum was not present, the diagnosis was suspected through bone marrow biopsy, which revealed hypocellular bone marrow, pure erythrocyte aplasia, and adipocytes replacing hematopoietic cells in marrow spaces.

A blood smear revealed normocytic normochromic anemia with leukopenia with relative lymphocytosis with thrombocytopenia similar to previously reported cases. Cases of thrombocytopenia, neutropenia, pancytopenia, and even aplastic anemia have also been reported in non-immunocompromised, presumably healthy subjects [8,10,12]. The diagnosis of aplastic anemia in parvo virus-infected individuals is usually made by bone marrow biopsy, which often reveals the pure erythrocyte aplasia with giant and dysplastic pronormoblasts. Bone marrow smear typically showed hypocellular bone marrow, adipocytes replacing hematopoietic cells in marrow space. The findings were similar in our case to previous cases [10]. Both parvovirus B19 specific IgM antibody and viral DNA detection have been recommended in the literature due to the limited diagnostic efficacy of each method [15]. Hence, serological analysis was performed which revealed a recent infection by parvovirus B19 (parvovirus B19 IgM antibodies). Viral serology and polymerase chain reaction were positive for parvovirus B19 infection.

At present, there is no particular therapy for this illness. Intravenous immunoglobulin is often used in patients with severe parvovirus B19 viremia and clinical complications [16]. If the patient's condition is not addressed, he or she may become critically ill. Sometimes the patient's condition deteriorates to the point where blood transfusion is necessary as in our patient [10,13,17]. Hence, the patient was admitted for close monitoring and supportive management (intravenous immunoglobulin and blood transfusion) was provided which was effective in improving the patient's clinical condition, and discharged with a strict follow-up schedule in the outpatient setting.

4. Conclusion

The severity of the infection is influenced by the patient's age and hematological and immunological status. However, we report this fourth case of severe aplastic anemia in an immunocompetent adult and the first case in an immunocompetent adult male, to emphasize that, while most severe and well-documented in fetal infections, parvovirus B19 can also cause thrombocytopenia, anemia, leukopenia or pancytopenia in children and adults. As a result, more research into the mechanisms involved in the pathogenesis of parvovirus B19-associated aplastic anemia is required. Furthermore, it is highly suggestive to consider Parvovirus infection as one of the causes of sudden and severe aplastic anemia in previously hematologically normal individuals with intact immunity. Patients should be treated symptomatically until their hematopoiesis restores, and regular follow-up is critical for detecting chronic anemia or recurrence and treating it promptly.

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Ethical approval

This is a case report, therefore, it did not require ethical approval from ethics committee.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editor-in-chief of this journal on request.

Author contribution

Author 1: Led data collection, follow-up of case, contributed to writing the case information and discussion. Supervised the study. Author 2: Contributed to literature review, data collection, follow-up of case, writing case details. Author 3: Involved in literature review, prepared initial draft of introduction and discussion. Author 4: Resident in internal medicine, informed about the case, involved in the conceptualization of the study, contributed to review and editing. Author 5: Involved in Literature review, involved in conceptualization of the study. Author 6: Involved in Literature review, prepared the final draft after revising and editing the initial draftAll authors read and approved the final version of the manuscript.

Registration of research studies

Not applicable

Guarantor

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Declaration of competing interest

The authors report no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2022.103998.

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