Myocarditis Associated with Human Parvovirus B-19 Infection in Children: A Case Series of Three Patients During the 2024 European Epidemic and a Brief Literature Review

Emanuele Filice[1,*], Arianna Gobbato[2], Laura Luppi[2], Nunzia Lisanti[2], Giulia Menconi[2], Elena Moccia[2], Emma Modena[2], Mattia De Agostini[1], Francesca Di Florio[1], Francesca Lombardi[1], Giacomo Stera[1] and Chiara Ghizzi[1]

[1]*Pediatric Unit, AUSL Bologna, Ospedale Maggiore, Bologna, Italy*

[2]*School of Pediatrics, Alma Mater Studiorum - University of Bologna, Italy*

Abstract: *Background:* Human Parvovirus B19 (PVB19) is a globally distributed virus associated with a wide range of clinical manifestations, from mild erythema infectiosum to severe, life-threatening complications including myocarditis. Epidemiological data from early 2024 indicate an increasing prevalence of PVB19 infections in Europe, raising concerns regarding its potential complications in pediatric populations.

Objective: This study describes three pediatric cases of severe PVB19 infection.

Cases presentation: We retrospectively analyzed three cases of PVB19 infection diagnosed at a tertiary care hospital in Bologna, Italy, between March and June 2024 who presented with viral myocarditis. They all required intensive care management, with one patient experiencing cardiac arrest and requiring mechanical ventilation. Despite the severity of their conditions, all three recovered following inotropic support and immunoglobulin therapy. All patients tested positive for PVB19 DNA, and no alternative viral causes were identified.

Conclusions: This case series underscores the wide clinical spectrum of PVB19 infection and its potential for severe, life-threatening complications in pediatric patients. Considering the recent rise in PVB19 cases, clinicians should maintain a high index of suspicion for myocarditis in children presenting with severe symptoms. Early recognition and prompt supportive management are crucial in improving outcomes. Further research may help to better understand PVB19 pathogenesis and develop targeted preventive strategies.

Keywords: Myocarditis, Parvovirus, b19, pvb19, Children, Erythema infectiosum.

INTRODUCTION

Human Parvovirus B19 (PVB19) is a common, globally distributed, non-enveloped, single-stranded DNA virus that exclusively infects humans by binding to the P blood group antigen on red blood cells and their precursors [1, 2].

PVB19 infection manifests in a wide spectrum of clinical presentations, depending on the patient's immunological and hematological status [2, 3] usually on a biphasic basis with more severe manifestations taking place in the second phase [4] likely with a pathological role of immune system.

Immunocompetent individuals may be asymptomatic whereas immunocompromised patients may develop severe clinical conditions involving the brain, joints, heart, and bone marrow [2].

Due to its widespread prevalence, PVB19 is the most common viral cause of myocarditis in the pediatric population [5].

Unlike other viruses known to infect cardiomyocytes, PVB19 primarily targets coronary endothelium, leading to myocardial ischemia and dysfunction. Its biphasic tendency is observed also in heart damage: following the primary infection the virus appears to enter in a latent phase waiting for favorable factors (such as transitory immune system debilitation) to reactivate and exert its pathogenic activity by strongly eliciting local inflammation leading to myocardial damage [6].

As long as viral load is high in myocardial cells, inflammation progresses, potentially causing long-term dilated cardiomyopathy (DCM) and subsequent chronic heart failure. In adult patients, suppressing PVB19 viral load in DCM may lead to better prognosis even after a huge amount of time from the primary infection [7].

Compared to other forms of fulminant viral myocarditis, PVB19-associated myocarditis in children has been associated with worse outcomes, including higher rates of cardiac transplantation and mortality [8].

Very recently, a cluster of seven previously health children who suffered from myocarditis due to PVB19 infection, with one dying from cardiac shock and two requiring heart transplantation [9] was reported from Rome, Italy.

*Address correspondence to this author at the UOC Pediatria, Ospedale Maggiore, Largo Bartolo Nigrisoli, 40133 Bologna (BO), Italy;
E-mail: emanuele.filice@ausl.bologna.it

Received on 03-08-2025 Accepted on 19-09-2025 Published on 27-09-2025

E-ISSN: 2311-8687/25

Despite encouraging data from *in vitro* Brincidofovir, a novel drug active against dsDNA viruses, whose use seems to inhibit PVB19 replication [10], no specific antiviral therapy is currently available for PVB19. Similarly, no specific vaccine strategy, despite being studied, has been appointed [10] yet.

The absence of specific therapy leaves clinicians with very few opportunities, sometimes controversial, such as intravenous immunoglobulin (IVIG). IVIG is an immunotherapy, derived from healthy blood donors, mostly containing IgG.

Its low-dose use is well-established in immunodeficiencies as a replacement therapy while its use on high doses is known to exert an immunomodulating effect in conditions characterized by an uncontrolled immune system activation such as Kawasaki Disease (KD) [11].

IVIG is widely used in presumed myocarditis both in children and adults, the rational being the combination of the direct virus neutralization by specific antibodies, when present, with a modulation of the immune system [12].

At the beginning of 2024 epidemiological data indicated a significant increase in PVB19 infections in children [13] and healthy adult blood donors in France, where prevalence has reached nearly 7% [14] raising concerns about its implications, particularly for vulnerable populations [15].

Among the bigger concerns are pregnant women, in whom frightening data indicated an increase of PVB19 infection both in Germany [16] and Italy [17] leading clinicians to suggest a PVB19 screening in pregnancy to prevent major in-womb complications. Similar data emerged also from Japan, where PVB19 has been indicated as the only virus whose seroprevalence is not decreasing throughout the years among pregnant women [18].

Here, we report three cases of PVB19-associated myocarditis diagnosed at a tertiary care hospital (Ospedale Maggiore-Pizzardi, Bologna, Emilia-Romagna, Italy) located in a metropolitan area where post-COVID PVB19 upsurge has been described [4]. The reported cases were diagnosed between March and June 2024.

MATERIALS AND METHODS

This is a case series describing three cases of myocarditis attributable to PVB19 in Bologna, Italy in 2024. All consecutive cases diagnosed between March and June 2024 were included.

Diagnostic criteria for myocarditis were not predefined and remained at the discretion of clinicians.

A review of medical records was conducted to detail the cases retrospectively.

Each patient had been previously informed that clinical-biological information could be used for research, without oral opposition. Informed consent was obtained by parents or legal tutors.

CASE SERIES PRESENTATION

Patient 1.

A 21-month-old girl, with unsignificant previous medical history, was admitted for a sudden onset of respiratory distress and tachycardia without three weeks after being diagnosed with Fifth disease/erythema infectiosum. She was afebrile. Clinical examination revealed liver enlargement, tachycardia and tachypnea. Elevated troponin I (TnI) on blood tests, ventricular dysfunction on point-of-care ultrasound (PoCUS), pulmonary congestion on chest X-Ray (CXR) and antero-septal repolarization abnormalities on EKG led to hypothesize a diagnosis of myocarditis.

Inotrope support with dobutamine and dopamine was started. 12 hours after admission, due to the worsening of her condition, inotrope support was upscaled and mechanical ventilatory support was started. High-dose (2g/Kg) intravenous immunoglobulins (IVIG) treatment was administered on day 2 on a 48-hours infusion.

After a failed extubation attempt resulting in cardiac arrest on day 4, promptly managed with cardiopulmonary resuscitation obtaining return of spontaneous circulation (ROSC) after 2 minutes, her conditions improved over the following days allowing progressive descaling of inotrope support and weaning from ventilatory support after 8 days of mechanical ventilation.

She was discharged home 19 days following admission on ACE inhibitors (ACE-i), beta-blockers (BB), loop-diuretics (LD) and potassium-sparing diuretics (PSD) with a normalized EKG and echocardiogram.

Serologic tests showed positivity of PVB19 IgM and IgG and viral load of PVB19 DNA was 150636 copies/mL.

Investigations aimed at finding alternative viral etiologies, including Epstein–Barr virus (EBV), Cytomegalovirus (CMV), SARS-CoV-2, rubella,

coxsackie, adenovirus, enteroviruses on blood, throat swab, feces and urines) tested negative.

Patient 2.

A 25-month-old girl was admitted for mild respiratory distress, vomiting and loss of appetite for one week, without ongoing fever. Vital parameters were stable. Clinical examination revealed hepatomegaly, confirmed on ultrasound. CXR showed diffused bilateral consolidations. Routine blood tests were unconclusive except for an elevation of aspartate transaminase (AST) (96 U/l). Empiric antimicrobial therapy and IV fluids were started.

18 hours later, she developed a severe respiratory distress with RR 100 BPM, Oxygen Saturation (SpO2) 81% on room air and circulatory impairment (HR 160 bpm, weak peripheral pulses and central cyanosis).

She was put on oxygen support with high-flow nasal cannula. Gas analysis revealed metabolic acidosis, TnI and BNP were elevated. Hypokinetic left ventricle and massive mitral insufficiency on cardiac ultrasound led to diagnose acute heart failure in presumed myocarditis.

Inotrope support was started. She received ACE-i, LD and PSD. Two doses of IVIG were administered on day 2 and day 9. PVB19 DNA was isolated on blood. No other virus was found.

The child fully recovered by the time of hospital discharge.

Patient 3.

A 26-month-old male was admitted for fatigue and progressive shortness of breath. Recent personal history included a 7-day history of fever, loss of appetite and vomiting and recent diagnosis of erythema infectiosum (three weeks earlier).

On clinical evaluation he appeared pale and asthenic, afebrile, with tachycardia and tachypnea. An examination revealed reduction of basal vesicular sounds and hepatomegaly.

CXR showed lung congestion and right pleural effusion. Lab reported elevated TnI and BNP.

The echocardiogram showed dilation and poor contraction of left ventricle with moderate systolic dysfunction; EF being estimated to 40-45%.

Table 1: Clinical Features of Patients

	Pt1	Pt2	Pt3
Age (months)	21	25	26
Sex (M/F)	F	F	M
Symptoms at onset	Respiratory distress	Respiratory distress and vomit	Respiratory distress and fatigue
Fever at onset (yes/no)	No	No	No
RR at onset (BPM)	70	50	70
HR at onset (bpm)	170	140	140
SpO2 on room air at onset	99	97	99
FE at onset (%)	35-40	30	40-45
TnI at onset (ng/L)	2671.1	1092.2	721
BNP at onset (pg/mL)	Unavailable	4256	5691
X-Ray at onset	Diffuse pulmonary congestion	Diffused bilateral consolidations	Patchy opacities in the lower right lung field with right pleural effusion and cardiomegaly
Previous history of infection	Yes (3 weeks earlier)	Yes (3 weeks earlier)	Yes (1 week earlier)
Need for inotropic support (yes/no)	Yes	Yes	No
Need for mechanical ventilation (yes/no)	Yes	No	No
IVIG administration	Single administration (2g/Kg)	Two administrations (2g/Kg each) on day 2 and 9	Two administrations (2g/Kg each) on day 2 and 12
Other therapies	ACEi, BB, LD, PSD	ACEi, LD, PSD	ACEi, Ivabradine, LD, PSD
FE on discharge (%)	>55	>55	45
PVB19 viral load on peripheral blood (copies/mL)	150636	34315	135738

ACEi: ACE-inhibitors; BB: Beta-blockers; LD: Loops Diuretics; PSD: Potassium-Sparing Diuretics

Therapeutic management of acute heart failure included LD, PSD, ACE-i and ivabradine. Two doses of IVIG were administered on day 2 and 12 from hospital admission.

PVB19 DNA was isolated on blood. On hospital discharge, cardiac function remained mildly impaired.

DISCUSSION, BRIEF LITERATURE REVIEW AND CONCLUSION

PVB19 is widely distributed all over the world, affects previously healthy young children with a huge heterogeneity of manifestations, ranging from asymptomatic cases to life-threatening patterns such as myocarditis. Myocarditis may be a real medical emergency especially due to its highly unspecific clinical manifestations, ranging from fatigue to vomiting and respiratory distress, often masquerading as fewer worrying diseases until being lately hypothesized for otherwise unexplained global worsening of general conditions.

The entity of myocardial damage itself is variable, ranging from acute heart failure requiring circulation support to wilder forms leading to chronic heart failure. American Heart Association recommends a prompt clinical recognition to improve patients' outcome [19] therefore a heightened clinical suspicion in pediatric patients is crucial.

Considering the clinical patterns of presentation, none of the three patients required medical attention for strikingly heart-associated symptoms. While older patients may help the physician reporting chest pain or palpitations, younger patients represent a real diagnostic challenge.

Usually in the Emergency Room (ER), a patient is presented to the physician by their vital signs, even before the chance to have a quick look at them. Markedly elevated RR and HR in afebrile patients should appear as disproportional and may lead both the triage nurse and the physician to increase the level of suspicion for potentially serious conditions since they may testify an overworking heart trying to compensate for a defective situation. Medical history must be thoroughly collected, despite the urgency of ER evaluation, and include recent infections.

The present paper focuses on PVB19 but it is extremely important to keep in mind that many other viruses, enteroviruses above all, may lead to a delayed myocardial involvement making the finding of a recent infection a potential key to unfolding the current pattern.

One of the presented cases (Patient 2), despite afebrile, was at first labeled as pneumonia with subsequent feeding difficulties because of respiratory distress and consolidation on XR. The diagnosis was questioned due to the worsening of general conditions despite being on antibiotics. This is a perfect example of how myocarditis may be hidden under conditions physicians are way more familiar with, such as respiratory or gastrointestinal infections.

In addition to circulatory support, all three patients received timely administration of IVIG. IVIG therapy in myocarditis is discussed for its uncertain evidence in terms of benefit, as stated in 2021 Cochrane [12], but despite the scarcity of reliable data (the only available RCT compares IVIG to placebo in a relatively small number of patients, 86, and with a "*very low"* grade of evidence), the cost/benefit ratio (low to none serious adverse events) and the wide experience about its use in children with immune-dysregulation disease such as KD, makes it still play a key role as an adjunctive therapy.

Authors are aware that IVIG-therapy alone cannot be considered as a resolutive therapy and that its role may be overestmated due to the concurrent use of supportive care without considering, moreover, the natural course of viral myocarditis.

PVB19-associated myocarditis, in particular, is hypothesized to benefit differently than other virus-associated myocarditis from IVIG therapy. While in myocarditis associated with CMV and adenovirus immunoglobulins show both a decrease in heart inflammation and an eradication of the viruses, PVB19 appears to resist to the eradication, the only benefit of IVIG therapy seemingly being related to its huge anti-inflammatory effect [12]. Heymans and colleagues conducted an RCT on IVIG in adult patients suffering from cardiomyopathies with PVB19 persistence showing no benefit compared to placebo, adding further doubts about IVIG chance of eradicating PVB19 [20].

Early identification of myocarditis and prompt supportive treatment can significantly improve patient outcomes. Increasing awareness among pediatricians and emergency physicians, especially those working in peripheral centers without the availability of a pediatrician skilled in emergency care, can lead to more timely interventions, reducing morbidity such as long-term heart failure, and improving survival rates.

Ultimately, this study emphasizes the importance of ongoing surveillance and research into the pathogenic mechanisms of PVB19. On a purely speculative basis, future clinical trials and real-world studies could assess the potential usefulness of preventive strategies, particularly for at-risk populations such as children and their mothers in fertile age. Focus should be given on

developing cellular and innate immunity and for that vaccine development may be a desirable option [21].

AUTHORS' CONTRIBUTION

AG, NL, EIM, LL, GM, EmM all equally contributed to collect data and describe the cases.

MdA, FdF, FL and CG critically revised the manuscript.

LIMITATIONS OF THE STUDY

The current study is a case series so, by its intrinsic nature, it is purely intended to describe a limited number of clinical cases. Every therapeutic hypothesis or speculation is to be verified in more robustly designed studies.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

REFERENCES

[1] Parvoviruses - PubMed. https://pubmed.ncbi.nlm.nih.gov/29489222/.

[2] Rogo, L. D., Mokhtari-Azad, T., Kabir, M. H. & Rezaei, F. Human parvovirus B19: a review. Acta Virol 58, 199-213 (2014). https://doi.org/10.4149/av_2014_03_199

[3] Landry, M. L. Parvovirus B19. Microbiol Spectr 4, (2016). https://doi.org/10.1128/microbiolspec.DMIH2-0008-2015

[4] Venturoli, S., Bertoldi, A., Manaresi, E., Lazzarotto, T. & Gallinella, G. Epidemiology of Parvovirus B19 Infection In an Italian Metropolitan Area, 2012-2024: COVID-19 Pre-Pandemic, Pandemic and Post-Pandemic Trends. J Med Virol 97, (2025). https://doi.org/10.1002/jmv.70296

[5] Schultz, J. C., Hilliard, A. A., Cooper, L. T. & Rihal, C. S. Diagnosis and treatment of viral myocarditis. Mayo Clin Proc 84, 1001–1009 (2009). https://doi.org/10.1016/S0025-6196(11)60670-8

[6] Krych, S. *et al*. Viral Myocarditis as a Factor Leading to the Development of Heart Failure Symptoms, Including the Role of Parvovirus B19 Infection—Systematic Review. International Journal of Molecular Sciences 2024, Vol. 25, Page 8127 25, 8127 (2024). https://doi.org/10.3390/ijms25158127

[7] Dennert, R. *et al*. Intravenous immunoglobulin therapy for patients with idiopathic cardiomyopathy and endomyocardial biopsy-proven high PVB19 viral load. Antivir Ther 15, 193-201 (2010). https://doi.org/10.3851/IMP1516

[8] Molina, K. M. *et al*. Parvovirus B19 myocarditis causes significant morbidity and mortality in children. Pediatr Cardiol 34, 390-397 (2013). https://doi.org/10.1007/s00246-012-0468-4

[9] Ferro, V. *et al*. Severe Outcomes From Suspected Human Parvovirus B19 Infection in Immunocompetent Children: The Need for Timely Recognition. J Med Virol 97, (2025). https://doi.org/10.1002/jmv.70324

[10] Bua, G. *et al*. Antiviral activity of brincidofovir on parvovirus B19. Antiviral Res 162, 22-29 (2019). https://doi.org/10.1016/j.antiviral.2018.12.003

[11] McCrindle, B. W. *et al*. Diagnosis, treatment, and long-term management of Kawasaki disease: A scientific statement for health professionals from the American Heart Association. Circulation 135, e927-e999 (2017). https://doi.org/10.1161/CIR.0000000000000484

[12] Robinson, J., Hartling, L., Vandermeer, B., Sebastianski, M. & Klassen, T. P. Intravenous immunoglobulin for presumed viral myocarditis in children and adults. Cochrane Database Syst Rev 2020, CD004370 (2020). https://doi.org/10.1002/14651858.CD004370.pub4

[13] d'Humières, C. *et al*. An unusual outbreak of parvovirus B19 infections, France, 2023 to 2024. Euro Surveill 29, (2024). https://doi.org/10.2807/1560-7917.ES.2024.29.25.2400339

[14] Guillet, M. *et al*. New atypical epidemiological profile of parvovirus B19 revealed by molecular screening of blood donations, France, winter 2023/24. Eurosurveillance 29, 2400253 (2024). https://doi.org/10.2807/1560-7917.ES.2024.29.21.2400253

[15] Risks posed by reported increased circulation of human parvovirus B19 in the EU/EEA. https://www.ecdc.europa.eu/en/publications-data/risks-posed-reported-increased-circulation-human-parvovirus-b19-eueea.

[16] Jiménez Cruz, J. *et al*. Ongoing outbreak of maternal parvovirus B19 infections in Germany since end of 2023: consequence of COVID-19 pandemic? Ultrasound Obstet Gynecol 65, (2025). https://doi.org/10.1002/uog.29197

[17] Saffioti, C. *et al*. Outbreak of parvovirus-B19 infection in pregnant women: Is it time to rethink a preconception or first trimester screening? Int J Gynaecol Obstet (2025). https://doi.org/10.1002/ijgo.70057

[18] Takemoto, K. *et al*. Seroprevalence of eight viruses and pertussis in pregnant women at a regional hospital in Japan in 2022: Comparison with previous studies. Jpn J Infect Dis JJID.2024.307 (2025). https://doi.org/10.7883/yoken.JJID.2024.307

[19] Kociol, R. D. *et al*. Recognition and Initial Management of Fulminant Myocarditis: A Scientific Statement from the American Heart Association. Circulation 141, E69-E92 (2020). https://doi.org/10.1161/CIR.0000000000000745

[20] Hazebroek, M. R. *et al*. Intravenous immunoglobulin therapy in adult patients with idiopathic chronic cardiomyopathy and cardiac parvovirus B19 persistence: a prospective, double-blind, randomized, placebo-controlled clinical trial. Eur J Heart Fail 23, 302-309 (2021) https://doi.org/10.1002/ejhf.2082

[21] Burton DR. Antibodies, viruses and vaccines. Nat Rev Immunol. 2002; 2(9): 706-713. https://doi.org/10.1038/nri891

[22] Corcoran A, Doyle S. Advances in the biology, diagnosis and host-pathogen interactions of parvovirus B19. J Med Microbiol. 2004; 53(Pt 6): 459-475. https://doi.org/10.1099/jmm.0.05485-0

https://doi.org/10.12974/2311-8687.2025.13.04