PARVOVIRUS B19 MYOCARDITIS WITH ACUTE HEART FAILURE REVEALING ASYMPTOMATIC ATRIAL SEPTAL DEFECT

Myokarditída spôsobená parvovírusom B19 s akútnym srdcovým zlyhaním v teréne asymptomatického defektu predsieňového septa

Stefan PORUBCIN[1,2], Alena ROVNAKOVA[1,2], Pavol ZENUCH[3], Pavol JARCUSKA[1,2], Ondrej ZAHORNACKY[1,2]

[1]The Department of Infectious Diseases and Travel Medicine, Louis Pasteur University Hospital, Kosice, Slovakia, head Dr.h.c. prof. MUDr. P. Jarčuška, PhD.
[2]Pavol Jozef Safarik University in Kosice Faculty of Medicine, Kosice, Slovakia, rector prof. MUDr. D. Pella, PhD.
[3]2nd Department of Cardiology, East Slovak Institute of Cardiovascular Diseases, Kosice, Slovakia, head prof. MUDr. D. Pella, PhD.

Abstrakt
Prezentujeme prípad 23-ročného muža s negatívnym predchorobím, ktorý bol hospitalizovaný na Klinike infektológie a cestovnej medicíny UNLP v Košiciach s horúčkou, bolesťami hlavy, myalgiami a nevoľnosťou. Pri úvodnom vyšetrení boli zistené iba zvýšené zápalové parametre. PCR test z nazofaryngového výteru následne potvrdil akútnu infekciu parvovírusom B19 (PVB19). Počas hospitalizácie sa u pacienta rozvinul difúzny celotelový makulopapulózny exantém a príznaky pravostranného srdcového zlyhania s námahovou dýchavičnosťou. Transtorakálna echokardiografia (TTE) odhalila veľký defekt predsieňového septa (DPS), dilatáciu a hypertrofiu pravej komory. CT vyšetrenie hrudníka a brucha potvrdilo prítomnosť kongestívneho srdcového zlyhania s pleurálnymi a perikardiálnymi výpotkami, kongesciou pečene a ascitom. Katetrizácia srdca preukázala výrazný ľavo-pravý skrat bez prítomnosti pľúcnej hypertenzie. Tento prípad zdôrazňuje zriedkavú prezentáciu infekcie PVB19 vedúcu k myokarditíde a srdcovému zlyhaniu, pričom bol odhalený dovtedy asymptomatický DPS. Chceme týmto prípadom poukázať na dôležitosť vysokého klinického podozrenia a význam TTE a CT vyšetrení pri diagnostike štruktúrnych srdcových defektov a plánovaní liečby *(tab. 1, obr. 2, lit. 24). Text v PDF www.lekarsky.herba.sk.*
KĽÚČOVÉ SLOVÁ: parvovírus B19, myokarditída, defekt predsieňového septa, zlyhanie srdca.
Lek Obz 2025, 74 (2): 85-90

Abstract
We present a case report of a 23-year-old male with no medical history, who was admitted to the Department of Infectious diseases and Travel Medicine with fever, headache, myalgias, and nausea. Initial evaluation showed elevated inflammatory parameters. PCR testing confirmed acute parvovirus B19 (PVB19) infection. The patient developed a diffuse maculopapular rash and signs of right heart failure, including exertional dyspnea and pleural effusions. Transthoracic echocardiography (TTE) revealed a large atrial septal defect (ASD), right ventricular dilation, and hypertrophy. Chest and abdominal CT showed congestive heart failure with pleural and pericardial effusions, liver congestion, and ascites. Cardiac catheterization confirmed a significant left-to-right shunting without pulmonary hypertension. This case highlights the rare presentation of PVB19 infection leading to myocarditis and heart failure, emphasizing the need for high clinical suspicion and the critical role of TTE and CT in identifying structural heart defects and guiding management *(Tab. 1, Fig. 2, Ref. 24). Text in PDF www.lekarsky.herba.sk.*
KEY WORDS: Parvovirus B19, myocarditis, atrial septal defect, heart failure.

Lek Obz 2025, 74 (2): 85-90

Introduction

Parvovirus B19 (PVB19) is a small, non-enveloped, single-strand DNA virus from the *Erythrovirus* genus. It is primarily transmitted via respiratory droplets, close contacts, and vertical transmission from mother to fetus (1). While infection often results in asymptomatic or mild illness such as erythema infectiosum, it can also manifest in other clinical syndromes (2). These include transient aplastic crises in patients with underlying hematologic disorders, chronic anemia in immunocompromised patients, and arthropathies in adults (3, 4). Occasionally, PVB19 infection has been associated with severe complications such as myocarditis - a potentially life-threatening inflammation of cardiac tissue.

Furthermore, myocarditis can lead to acute heart failure (5). Septal defects may further complicate the clinical picture. We present a case report of a patient with PVB19-induced myocarditis, complicated by acute heart failure and the incidental finding of asymptomatic atrial septal defect.

Case Presentation

A 23-year-old patient without a history of any medical condition was admitted to The Department of Infectology and Travel Medicine in Kosice, Slovakia with symptoms of fever, headache, myalgias and arthralgias, nausea, and vomiting. Upon admission, the patient had a fever (39.7 °C), was eupneic, and had borderline positive lower meningeal signs. The patient's initial vital signs were - heart rate of 80 bpm, blood pressure of 124/68 mmHg, respiratory rate of 17 breaths/min, and oxygen saturation of 97%. Laboratory tests showed a moderate elevation of inflammatory markers, lymphopenia, and prolonged prothrombin time (Tab. 1). A computerized tomography (CT) scan of the brain was normal.

After an unsuccessful lumbar puncture, the patient was treated empirically for suspected aseptic meningitis. Further evaluation, including lung and abdominal ultrasound, was unremarkable. However, PCR testing of a nasopharyngeal swab was positive for PVB19 with a low Ct (Cycle threshold) value of 18.32, leading to a diagnosis of acute PVB19 infection. On the 3rd day, the patient developed a diffuse maculopapular rash. Due to persistent fever and lack of clinical improvement, additional testing revealed bilateral B-lines on lung ultrasound, few subpleural nodules, and pleural effusions. Empiric antibiotic treatment (cefotaxime and azithromycin) for suspected secondary bacterial pneumonia was initiated. During the hospital stay the patient displayed laboratory evidence of liver dysfunction, as well as elevated concentrations of N-terminal pro-B-type Natriuretic Peptide (NTproBNP) and troponin. Clinical deterioration with signs of exertional dyspnea and dry cough ensued. The relevant laboratory parameters during hospitalization are summarized in table 1. Chest and abdominal CT confirmed congestive heart failure, bilateral pleural effusions, pericardial effusion, liver congestion, hepa-

Table 1. Laboratory parameters.

Parameters	Reference range, Adults	On admission	2nd result	On discharge
Hematocrit (%)	36–46	0.33	0.38	0.42
Hemoglobin (g/dL)	12–16	14.03	10.1	11.7
White-cell count (x10^9/L)	4.0–10	4.36	8.51	7.97
Differential count (x10^9/L)				
Neutrophils	1.4–6.5	3.45	2.99	2.89
Lymphocytes	1.5–4.0	**0.31**	1.37	3.93
Monocytes	0.25–0.6	0.59	**0.81**	**0.93**
Eosinophils	0.05–0.25	0.1	0.12	0.1
Platelet count (x10^9/L)	150–400	**93**	**106**	324
Prothrombin-time international normalized ratio	0.85 –1.15	**1.26**	**1.20**	0.99
D-dimer (mg/L)	<0.5	0.37	**1.17**	**1.9**
C-reactive protein (mg/L)	<5	**32**	**86**	**26**
Urea (mmol/L)	2.8 –7.2	4.11	5.7	6.29
Creatinine (mmol/L)	64 –104	103	67.9	83.6
Bilirubin (μmol/L)	5 –21	**21.7**	19	18.8
Aspartate aminotransferase (μkat/L)	0.05 –0.6	**0.94**	**1.13**	**1.96**
Alanine aminotransferase (μkat/L)	0.05 –0.6	**1.45**	**2.74**	**3.9**
Gamma glutamyl transpeptidase (μkat/L)	0.05 –0.63	**1.78**	**5.68**	**4.2**
Alkaline phosphatase (μkat/L)	0.5 –2	0.92	0.91	1.33
Procalcitonin (μg/L)	< 0.5	0.145	0.205	0.148
Lactate (mmol/L)	0.5 –2.2	1.93	1.8	**2.7**
Interleukin 6 (ng/L)	1.5 –7	**19.3**	–	3.19
Troponin (μg/L)	0.003 –0.014	0.012	**0.123**	**0.096**
N-terminal pro B-type Natriuretic Peptide (pg/mL)	< 125	**1038**	**2486**	**3020**
Parvovirus B19 PCR	negative	positive *(Ct 18.32)	positive (Ct 23.51)	positive (Ct 29.9)

* Ct – cycle threshold

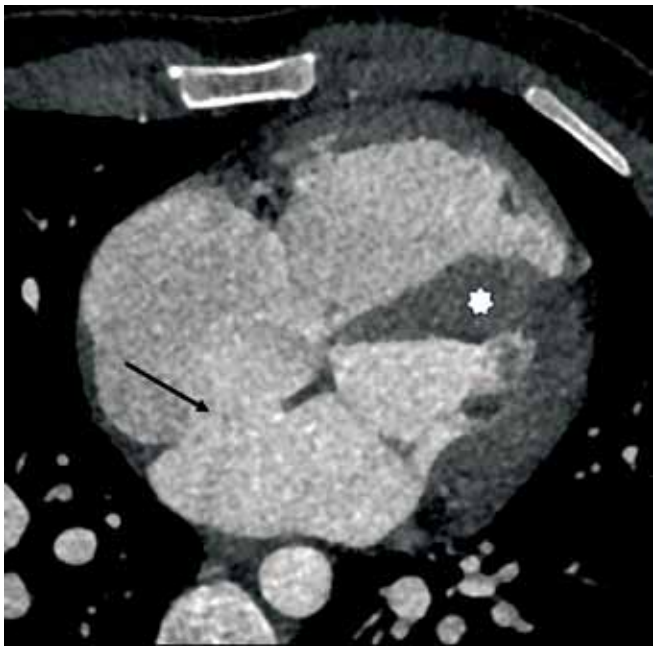
tosplenomegaly, and ascites. Diuretic therapy was initiated. Transthoracic echocardiography (TTE) revealed a large atrial septal defect (ASD) with left-to-right shunting, marked right ventricular dilation, and right ventricular hypertrophy, consistent with right-sided decompensation (Fig. 1). A small, asymmetric pericardial effusion without tamponade and small bilateral pleural effusions were also noted.

After a 7-day hospitalization, the patient was transferred to the 2nd Department of Cardiology at the Eastern Slovak Institute of Cardiovascular Diseases, Kosice. A comprehensive diagnostic evaluation was conducted to determine the underlying cause of heart failure.

A follow-up transesophageal echocardiography (TEE) was performed, which confirmed the presence of a large secundum-type ASD, measuring approximately 38x20 mm, which resulted in a substantial left-to-right shunting. The septal defect had a minimal aortic rim and only a small posterior rim, making catheter-based closure challenging. The examination also revealed dilation of the right heart chambers, while the systolic function of the left ventricle remained preserved, with an ejection fraction of approximately 60%. The left atrium and ventricle had normal dimensions, and mild tricuspid regurgitation was present, with a pulmonary artery pressure of 30.88 mmHg. A minimal pericardial effusion was also detected.

Subsequent cardiac CT imaging was conducted, with a precise width measurement of the ASD (21 mm). The examination also showed dilation of the right-sided heart chambers, with the right atrium measuring 62.3 mm and the right ventricle 37 mm (Fig. 2). An interesting finding was the presence of five pulmonary veins draining into the left atrium, without any apparent anomalous pulmonary venous return. The CT scan further revealed a pericardial effusion in the area of the right heart chambers, up to 13 mm in width. There was also suspicion of a small ventricular septal defect (VSD) measuring 6 mm at the level of the pars membranacea, which required further evaluation.

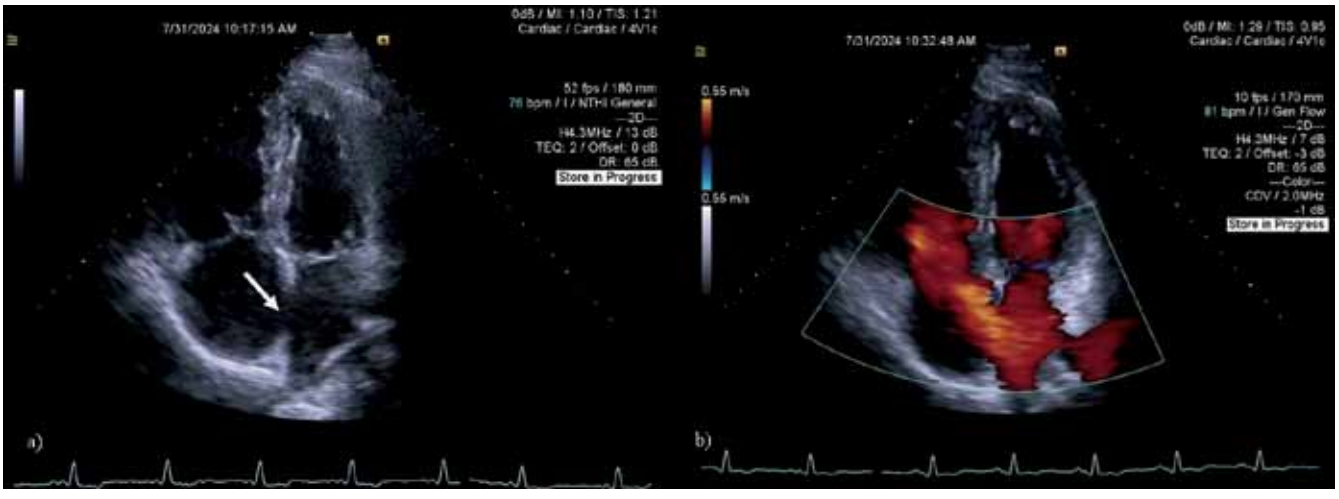
Figure 2. Cardiac computerized tomography of the heart, showing atrial septal defect (arrow) **and marked hypertrophy of the right ventricle wall** (asterixis).



On the same day, the patient underwent a right-sided cardiac catheterization, which aimed to quantify the shunt size and assess the presence of pulmonary hypertension. The examination confirmed the presence of a significant left-to-right shunt, with a QP/QS ratio of 3.25, but without evidence of pulmonary hypertension. The patient's cardiac output was normal, and the pulmonary arterial pressure was within the normal range, supporting the conclusion that pulmonary hypertension was absent. These findings led to the decision that the patient was not a suitable candidate for catheter-based closure of the atrial septal defect, and surgical intervention would need to be considered.

A few days later, another TTE was performed, which confirmed the persistent dilation of the right heart chambers. The left ventricular ejection fraction was

Figure 1. Transthoracic echocardiography. a) Apical four chamber view showing atrial septa l defect (arrow). b) Color flow mapping of the atrial septal defect.



again measured at 60%, without any signs of kinetic disorders. Given the persistent suspicion of a ventricular septal defect, an MRI examination was recommended.

Based on these results, the patient was included in a cardiothoracic surgery evaluation meeting, where the option of surgical closure of the atrial septal defect was discussed.

The patient consented to the proposed surgical plan, and following clinical stabilization, was discharged to outpatient management.

Discussion

This case presents a complex interplay of parvovirus B19 infection, myocarditis and pre-existing structural heart defect, leading to acute heart failure.

PVB19 is known to cause a wide range of clinical manifestations, from mild erythema infectiosum to severe complications like myocarditis, particularly in susceptible populations (2). The patient's initial clinical presentation, which included fever, headache, and cytopenias, was highly suggestive of acute PVB19 infection. It is well recognized that the virus interferes with DNA replication and causes apoptosis in erythroid progenitor cells, contributing to anemia. In addition to the primary effect on erythroid progenitor cells, PVB19 infection may also result in thrombocytopenia and leukopenia, likely due to disruption in the bone marrow microenvironment and alterations in cytokine production. The severity of these cytopenias can vary depending on the individual's immune status and underlying hematological conditions (6).

Furthermore, the development of a generalized maculopapular rash during hospitalization is a well-recognized manifestation of PVB19 infection, also supporting this diagnosis as the underlying etiology of the patient's myocarditis and subsequent heart failure (7). The positive PCR test with a low Ct value confirmed the diagnosis and indicated a high viral load, potentially contributing to the severity of the illness. Early diagnosis through PCR enables timely intervention, which can significantly impact patient outcomes, particularly in high-risk individuals such as pregnant women, immunocompromised patients, and those with underlying cardiac conditions (8).

While the initial workup did not reveal specific signs of myocarditis, the subsequent development of exertional dyspnea, dry cough, elevated NT-proBNP levels, and evidence of right heart dilation and dysfunction on echocardiography strongly suggests myocardial involvement.

The elevation of troponin in this patient further strengthens the diagnosis of myocarditis. Cardiac troponin is a highly sensitive and specific marker of myocardial injury. Its elevation indicates damage to myocardial cells, a key feature of myocarditis (9). While other conditions, such as acute coronary syndrome, can also cause troponin elevation, the overall clinical picture, including the presence of PVB19 infection, right heart dysfunction, and young age, points towards myocarditis as the primary cause of myocardial damage in our case.

The pathogenesis of myocarditis caused by PVB19 is thought to be triggered by an inflammatory cascade that can lead to myocardial damage. The virus initially binds to the P antigen receptor, expressed on the surface of erythroid progenitor cells, endothelial cells, and cardiomyocytes, enabling viral entry and replication (10).

Additionally, the direct cytopathic effects of the virus on cardiomyocytes may contribute to myocardial dysfunction. The combination of these pathogenic mechanisms likely explains the myocardial involvement observed in our patient. Cases of PVB19-associated myocarditis mimicking acute myocardial infarction in adults have been reported (11, 12).

Diagnosing myocarditis can be challenging because its symptoms can vary widely, and there is no single definitive test for the condition. Although the endomyocardial biopsy (EMB) is considered the gold standard for diagnosis, its invasive nature often restricts its use, particularly in stable patients. Non-invasive markers like cardiac magnetic resonance imaging (MRI), NT-proBNP, and troponin play a crucial role in assessing the syndrome. In this case, the combination of elevated troponin, NT-proBNP, the distinct clinical picture of right heart failure, and PVB19 infection provided sufficient evidence for a clinical diagnosis of myocarditis, thus precluding the need for EMB. This approach reflects the emerging trend of relying on a combination of non-invasive diagnostic tools, such as biomarkers and clinical assessments, to diagnose myocarditis. EMB is now reserved for cases with diagnostic uncertainty (13).

The discovery of a large secundum-type ASD introduces additional complexity to the situation. While the ASD might have been asymptomatic previously, the added stress of myocarditis and right heart failure likely exacerbated the left-to-right shunt, contributing to the hemodynamic instability. The significant shunt fraction (QP/QS ratio of 3.25), observed during cardiac catheterization, confirms the hemodynamic significance of the ASD.

The initial positive lung ultrasound findings, while suggestive of pulmonary involvement, likely represented early signs of heart failure rather than primary pneumonia. Although B-lines, subpleural nodules, and pleural effusions can occur in both conditions, several factors point towards heart failure as the primary driver in this clinical case. The echocardiographic evidence of right heart dilation and dysfunction correlates with the lung ultrasound findings, as right heart failure increases pulmonary capillary pressure, causing fluid leakage into the interstitial and pleural spaces, resulting in B-lines and pleural effusion (14, 15, 16). Subpleural nodules can also develop due to fluid accumulation and interstitial thickening (17).

The various imaging modalities employed in this case provided valuable insights on the patient's condition. CT confirmed congestive heart failure, pleural effusions, pericardial effusion, passive liver congestion, and ascites, supporting the diagnosis of right heart failure. TTE played a crucial role in identifying ASD, asses-

sing right heart function, and raising a suspicion of VSD. Cardiac catheterization quantified the shunt fraction and ruled out pulmonary hypertension, guiding the decision for surgical intervention.

The suspicion of a small VSD, based on TTE and CT scan findings, warrants further evaluation with cardiac MRI. While small VSDs are often asymptomatic, their presence in the context of myocarditis and right heart failure may further compromise cardiac function. Cardiac MRI is crucial for confirming the presence of VSD and guiding further management (18).

The patient's management involved a multidisciplinary approach, including an infectious disease specialist, a cardiologist, and a cardiothoracic surgeon. Initial treatment focused on managing the PVB19 infection and suspected secondary bacterial pneumonia. Diuretic therapy was initiated to address heart failure. Treatment of PVB19-associated myocarditis often focuses on managing the symptoms and supporting cardiac function while the immune system clears the virus (13). For patients with acute heart failure, standard treatment with diuretics, ACE inhibitors, and beta-blockers, is typically administered. Intravenous immunoglobulin (IVIG) has shown promise in some studies, by modulating the immune response and reducing inflammation. However, the efficacy of IVIG remains debated, and further research is required to establish its role in the treatment of parvovirus B19 myocarditis (19). In severe cases, mechanical circulatory support, such as extracorporeal membrane oxygenation, may be necessary to stabilize the patient while awaiting recovery. Immunosuppressive therapies, like corticosteroids, are generally not recommended unless there is evidence of persistent viral replication or autoimmune myocarditis (20). The prognosis for parvovirus B19 myocarditis is generally favorable, with most patients achieving complete recovery. However, some individuals may develop chronic dilated cardiomyopathy (DCM), requiring long-term management (21). Factors influencing this progression include viral persistence causing chronic inflammation, immune-mediated damage via dysregulated inflammation, host factors such as genetic predisposition, and the severity of the initial myocarditis. Although DCM is not inevitable, monitoring for ventricular dilation and systolic dysfunction is crucial for early detection and management to improve outcomes (8, 9, 22, 23).

The decision to pursue surgical closure of the ASD is warranted given its size and hemodynamic significance. Further evaluation with cardiac MRI is essential to confirm the presence and characterize the VSD before proceeding with surgery (24).

Finally, the patient's prognosis depends on the outcome of the surgical closure of the ASD and the suspected VSD. The patient is expected to recover with appropriate treatment and close monitoring.

Conclusion

This case highlights the complexity and severity of parvovirus B19 infection, particularly its ability to cause myocarditis and induce acute heart failure, even in previously healthy patients. The incidental finding of a hemodynamically significant ASD complicated the clinical picture and emphasized the importance of a thorough cardiac examination in patients with suspected myocarditis. This case addresses the need for a multidisciplinary approach, involving infectious disease specialists, cardiologists, and cardiac surgeons to ensure optimal patient care. Although the patient's prognosis is generally favorable with appropriate treatment and close monitoring, the potential for long-term complications such as DCM requires continuous follow-up. Various clinical manifestations of PVB19 infection underscore the need for early clinical suspicion, timely diagnostic and treatment management to reduce potential adverse outcomes.*

***Declaration of Human Rights:** The authors declare that all procedures used were in compliance with the ethical standards of the relevant ethics committee for clinical work with humans, and the work was conducted in accordance with the Declaration of Helsinki.

Informed Consent: The authors of the publication declare that informed consent was obtained from the patient.

Conflict of Interest: The authors declare that they have no conflicts of interest.

References

1. WEIR E. Parvovirus B19 infection: fifth disease and more. CMAJ 2005, 172 (6): 743.
2. BROLIDEN K, TOLFVENSTAM T, NORBECK O. Clinical aspects of parvovirus B19 infection. J Intern Med 2006, 260 (4): 285 – 304.
3. MEYER O. Parvovirus B19 and autoimmune diseases. Joint Bone Spine 2003, 70 (1): 6 – 11.
4. COLMEGNA I, ALBERTS-GRILL N. Parvovirus B19: its role in chronic arthritis. Rheum Dis Clin North Am 2009, 35 (1): 95 – 110.
5. BUGGEY J, ELAMM CA. Myocarditis and cardiomyopathy. Curr Opin Cardiol 2018, 33 (3): 341 – 346.
6. BHATTARAI AM, DHAKAL B, ROKAYA P, et al. Aplastic anemia induced by human parvovirus B19 infection in an immunocompetent adult male without prior hematological disorders: A case report. Ann Med Surg (Lond) 2022, 79: 103998.
7. CHINSKY JM, KALYANI RR. Fever and petechial rash associated with parvovirus B19 infection. Clin Pediatr (Phila) 2006, 45 (3): 275 – 280.
8. ESMEL-VILOMARA R, DOLADER P, IZQUIERDO-BLASCO J, et al. Parvovirus B19 myocarditis in children: a diagnostic and therapeutic approach. Eur J Pediatr 2022, 181(5): 2045 – 2053.
9. SOZZI FB, GHERBESI E, FAGGIANO A, et al. Viral Myocarditis: Classification, Diagnosis, and Clinical Implications. Front Cardiovasc Med 2022, 20 (9): 908663.
10. LAMPARTER S, SCHOPPET M, PANKUWEIT S, et al. Acute parvovirus B19 infection associated with myocarditis in an immunocompetent adult. Hum Pathol 2003, 34 (7): 725 – 728.
11. KÜHL U, PAUSCHINGER M, BOCK T, et al. Parvovirus B19 infection mimicking acute myocardial infarction. Circulation 2003, 108 (8): 945 – 950.
12. BÜLTMANN BD, KLINGEL K, SOTLAR K, et al. Fatal parvovirus B19-associated myocarditis clinically mimicking ischemic heart disease:

an endothelial cell-mediated disease. Hum Pathol 2003, 34 (1): 92 – 95.
13. MAISCH B, ALTER P. Treatment options in myocarditis and inflammatory cardiomyopathy: Focus on i. v. immunoglobulins. Herz 2018, 43 (5): 423 – 430.
14. DOERSCHUG KC, SCHMIDT GA. Intensive care ultrasound: III. Lung and pleural ultrasound for the intensivist. Ann Am Thorac Soc 2013, 10 (6): 708 – 712.
15. LUI JK, BANAUCH GI. Diagnostic Bedside Ultrasonography for Acute Respiratory Failure and Severe Hypoxemia in the Medical Intensive Care Unit: Basics and Comprehensive Approaches. J Intensive Care Med 2017, 32 (6): 355 – 372.
16. MOJOLI F, BOUHEMAD B, MONGODI S, et al. Lung Ultrasound for Critically Ill Patients. Am J Respir Crit Care Med 2019, 199 (6): 701 – 714.
17. LICHTENSTEIN DA. Lung ultrasound in the critically ill. Ann Intensive Care 2014, 9, 4 (1): 1.
18. ROJAS CA, JAIMES C, ABBARA S. Ventricular septal defects: embryology and imaging findings. J Thorac Imaging 2013, 28 (2): W28 – 34.
19. ROBINSON J, HARTLING L, VANDERMEER B, et al. Intravenous immunoglobulin for presumed viral myocarditis in children and adults. Cochrane Database Syst Rev 2020, 19, 8 (8): CD004370.
20. POLLACK A, KONTOROVICH AR, FUSTER V, et al. Viral myocarditis – diagnosis, treatment options, and current controversies. Nat Rev Cardiol 2015, 12 (11): 670 – 6 80.
21. COOPER LT Jr. Myocarditis. N Engl J Med 2009, 360 (15): 1526 – 1538.
22. MICHAEL L. RENO, CHRISTINA R. COX, ELEANOR A. POWELL. Parvovirus B19: Clinical and Diagnostic Review. Clinical Microbiology Newsletter 2022, 44 (12): 107 – 114.
23. KRYCH S, JĘCZMYK A, JURKIEWICZ M, et al. Viral Myocarditis as a Factor Leading to the Development of Heart Failure Symptoms, Including the Role of Parvovirus B19 Infection-Systematic Review. Int J Mol Sci 2024, 25 (15): 8127.
24. MCKINSEY DS, RATTS TE, BISNO AL. Underlying cardiac lesions in adults with infective endocarditis. The changing spectrum. Am J Med 1987, 82 (4): 681 – 688.

Accepted for publication November 7, 2024.

Address for correspondence:
O. Zahornacký, MD, PhD.
The Department of Infectious Diseases and Travel Medicine
Louis Pasteur University Hospital
Rastislavova 43
040 11 Kosice
E-mail: *ondrejzahornacky@gmail.com*