



## Lower extremity thrombosis and myocarditis due to Human PVB19 infection

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### ABSTRACT

This is a case report of a six years old boy who presented with seizure to the emergency department and was admitted for further evaluation. The following day he developed fever and ventricular tachycardia requiring cardioversion. Echocardiography revealed myocarditis and viral PCR was positive for PVB19. During his ICU stay he developed right lower extremity pallor and poikilothermia attributed to DVT and arterial thrombosis found on duplex. Despite IV heparin and therapeutic PTT levels, his lower extremity didn't improve and therefore he underwent thrombectomy. He was discharged six days postoperatively. At three month follow up, he was in good health.

### 1. Introduction

Human parvovirus B19 (PVB19) is a non-enveloped, widespread, small, single-strand DNA virus that can present with a wide range of symptoms. The most commonly disorder associated with PVB19 infection is Erythema Infectiosum also known as fifth disease. There is increasing evidence that parvovirus may present as an independent risk factor for myocarditis and hyper-coagulation events [1,2].

Here a case of myocarditis and lower limb thrombosis in a 6-year old boy with PVB19 infection is reported.

### 2. Case presentation

A 6-year old boy presented to the American University of Beirut (AUBMC) emergency department after a drop attack followed by a tonic-clonic seizure for 20 min. The boy had no developmental problems except for delayed speech. He also had recurrent tonsillitis with the last episode occurring one month prior to this presentation. Computerized tomography (CT) scan of the brain showed no abnormalities, and lab studies were also normal except for mild WBCs elevation  $12.49 \times 10^9/L$ . The patient was discharged with a plan to work up his seizure on an outside basis.

However, the next day he had another episode lasting 3 min, after which he was admitted to the Pediatric Intensive Care Unit (PICU), where he developed ventricular tachycardia (rate = 240 bpm). He required cardioversion by DC shock (25 J) and was started on Amiodaron (5 mcg/kg/min) to control his heart rate. The patient was intubated on

synchronized mandatory minute ventilation (SMMV) for 8 days. Upon follow up, he did not have any similar episodes and his heart rate remained within normal with occasional premature ventricular contractions (PVCs). Echocardiography was done and was compatible with myocarditis with ejection fraction 36–38% and moderate left ventricular dilation. The patient developed one episode of high-grade fever (38). His laboratory tests revealed a high increase in myocardial infarction markers CK-MB index of 8.4 (normal 0.0–2.6) and Troponin T of 0.873 (normal 0.00–0.03). Viral infection laboratory testing was performed. The patient was positive for PVB19 IgM, IgG and PCR but not for cytomegalovirus and Epstein-Barr virus. Therefore, PVB19 infection was proposed as the potential cause of the cardiomyopathy.

Two days after, he developed pallor and poikilothermia in the right foot. Venous duplex scan showed deep vein thrombosis in the right common femoral, femoral, popliteal and posterior tibial veins. The arterial duplex scan revealed a thrombosed right common femoral artery with a patent right external iliac artery, and reduced sluggish flow in right superficial femoral, popliteal and tibial arteries. He was started on continuous intravenous (IV) heparin drip to keep his Activated PTT between 60 and 80 s. His overall course and especially his cardio pulmonary system improved over the following eight days however without any significant improvement in his lower extremity; thus, he underwent thromboembolectomy of the right common femoral profunda and superficial femoral arteries. The arteriotomy was repaired with saphenous vein patch angioplasty. Intraoperative, there were strong palpable pulses in the common femoral, superficial femoral and profunda arteries. Doppler signals were restored over the posterior

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**Abbreviation key**

PCR	Polymerase chain reaction
PVB19	Parvovirus B19
ICU	Intensive care unit
DVT	Deep vein thrombosis
PTT	Partial thromboplastin time
IV	Intravenous
DNA	Deoxyribonucleic acid
AUBMC	American University of Beirut Medical Center
CT	Computerized tomography

WBC	White blood cell
PICU	Pediatric intensive care unit
DC	Direct current
SMMV	Synchronized mandatory minute ventilation
PVC	Premature ventricular contractions
CK-MB	Creatine Kinase-MB
MTHFR	Methylene tetrahydrofolate reductase
HIV	Human immunodeficiency virus
CMV	Cytomegalovirus
HSV	Herpes simplex virus

tibial and the dorsalis pedis arteries.

In the next day, the patient developed a drop in his platelet count  $81 \times 10^3/\mu\text{L}$ . The patient was then diagnosed with Heparin-Induced Thrombocytopenia (HIT) type II, and the heparin was replaced by Sodium Fondaparinux. Subsequently, there was continued improvement in the blood flow of the right superficial femoral, popliteal, posterior tibial and anterior tibial arteries where the waveform became triphasic. Molecular laboratory tests for Factor V Leiden (61691A), Factor II (Prothrombin), and Methylene tetrahydrofolate reductase (MTHFR) gene mutations were normal. Anti-thrombin III = 105% (normal 83–128), protein C = 46% (normal 69–134), protein S = 69.9% (normal 65–140), and lupus anticoagulant was negative. Therefore, PVB19 infection was postulated to have played a significant role in causing the lower limb ischemia and venous thrombosis. The patient was discharged six days postoperatively. At three month follow up, he was in good health.

### 3. Discussion

PVB19 has been connected with variant diseases in children, extending from subclinical illness and Erythema Infectiosum (fifth disease) to more severe illnesses such as hydrops fetalis, polyarthropathy, transient aplastic crisis in patients with hemolytic anemia, chronic infection and anemia in immunocompromised hosts [3,4]. Immunoglobulin G (IgG) antibodies can be discovered in 5–10% among young children (aged 2–5 years), increasing to 50% by age 15 years and 85% of individuals older than 70 years [5].

Myocarditis is a rare presentation of PVB19. Although most of the exposures to PVB19 are without serious sequel, the medical literature has increasingly identified PVB19 as a leading cause of myocarditis, which may cause significant mortality and morbidity in children [6,7]. The exact pathophysiology of PVB19 in myocarditis, whether incidental or pathogenic, is still uncertain [8]. However, two mechanisms were suggested to interpret the causation of myocarditis with PVB19 [1]. First, PVB19 can directly cause myocarditis through viral cytotoxicity. Second, PVB19 can indirectly induce cell injury through immune targeting of infected cardiomyocytes. In this case, we report a PVB19-induced fulminant viral myocarditis in a young patient, which lead him to ventricular dysfunction. The diagnosis has been established through virology studies.

In addition, several reports have implicated PV B19 in hypercoagulable conditions, related to the antiphospholipid syndrome, which cause multiple small pulmonary emboli and microvascular thrombosis with multi organ involvement including renal insufficiency and hypertension, heart failure, and Coombs positive anemia [9,10]. PVB19 was also linked with middle cerebral artery thrombosis and thrombotic microangiopathy after renal transplant [11,12]. Here we present a case of an ischemic lower extremity with deep venous thrombosis, which to our knowledge, is the first case of lower extremity mixed arterial and venous thrombosis after PVB19 infection.

Many viral infection including HIV, CMV and HSV have been

implicated in the pathogenesis of hyper-coagulation events [2]. Pathogens may induce a pro-coagulant state by the restraining the anticoagulant system (proteins C and S) and by increasing fibrinogen levels, fibrin generation, thromboplastin expression, and Cardiolipin immunoreactivity. In our case, the patient may have experienced occasional vein puncture to the groin which could have served as a trigger for his lower extremity thrombotic event. PVB19 had decreased the protein c, which led to increase the risk of thrombosis and exert right leg ischemic; thus, PVB19 was proposed the potential cause of the leg ischemia.

We conclude that the clinician should keep in mind the possibility of PVB19 in myocarditis presenting in immune-competent patients. Furthermore, PVB19 should be considered as a potential risk factor for lower limb arterial or venous thrombosis in young people.

### Conflicts of interest

The authors declared that there was no conflict of interest.

### Declarations of interest

None.

### Appendix A. Supplementary data

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.epsc.2018.01.014>.

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