Case Report

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Adult with Coxsackie B virus-induced cardiomyopathy presents rare case of complicated acute embolic ischaemic stroke

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Introduction and importance: Stroke, a global health concern, often results from embolic events of cardiac origin. Coxsackie B virus (CBV) myocarditis, a common cause of viral heart infections, can lead to cardiac thrombi formation, subsequently causing devastating complications such as embolic stroke. The authors present a rare case of a 26-year-old male who experienced an embolic stroke following CBV myocarditis and cardiomyopathy.

Case presentation: The patient exhibited left-sided weakness, facial droop, and respiratory distress. Laboratory findings indicated leukocytosis, hyponatremia, and elevated troponin I. Imaging revealed an acute right basal ganglia infarct and multifocal pulmonary embolism. The diagnosis involved positive CBV serology, severely reduced left ventricular function, and a large apical thrombus.

Discussion: Cardioembolic strokes, often attributable to atrial fibrillation, can also result from intracardiac thrombosis associated with myocarditis. CBV, implicated in up to 40% of acute myocarditis cases, binds to cardiac myocytes, triggering inflammation and potential thrombus formation. Myocarditis-induced hypercoagulability increases the risk of thromboembolic events, complicating the clinical course.

Conclusion: CBV myocarditis poses a risk of heart failure, cardiomyopathy, and thromboembolic complications such as embolic stroke. Vigilant monitoring for complications and prompt management is crucial, as primary disease treatment remains primarily supportive. This case highlights the need for increased awareness and further studies to understand the intricate relationship between viral myocarditis and embolic strokes.

Keywords: coxsackie B virus, embolic stroke, viral myocarditis

Introduction

Stroke is a significant cause of morbidity and mortality worldwide[1]. Among ischaemic strokes, a fraction is of embolic aetiology, mostly of cardiac origin. Myocarditis in itself, as well as the resultant heart failure and arrhythmias, lead to the formation of cardiac thrombi, which can in turn embolize, resulting in devastating complications such as pulmonary embolism and embolic stroke[2,3]. The Coxsackie B virus (CBV) is the most common virus to affect the human heart. It primarily affects young children; however, sporadic cases are noticed among the adult population as well[3]. Here, we present a rare case of a 26-year-old male who presented to the emergency with an embolic stroke subsequent to a CBV myocarditis and cardiomyopathy.

HIGHLIGHTS

- In this case a 26-year-old with Coxsackie B virus-induced cardiomyopathy suffers embolic stroke, emphasizing the link between viral myocarditis and devastating complications.
- Complicated acute embolic stroke in young adults highlights the need for increased awareness of Coxsackie B virus myocarditis as a potential precursor to thromboembolic events.
- The case underscores the intricate relationship between viral myocarditis, dilated cardiomyopathy, and severe complications like embolic stroke.
- Coxsackie B virus myocarditis poses risks of heart failure, cardiomyopathy, and thromboembolic complications, emphasizing the importance of vigilant monitoring and prompt management.

Case presentation

A 26-year-old male presented to our emergency department with left-sided weakness and left-sided facial droop. The weakness was

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acute in onset, more in the lower extremity, and was associated with slurring of speech. There was no history of alteration or loss of consciousness, abnormal body movements, incontinence, headache, blurring of vision, or trauma of any sort. His mother revealed that he had been sick for about a week before presenting with the acute event. He had a cough with clear to green-coloured phlegm, nasal congestion, and a mild fever for the past week. Along with this, he had also developed palpitations, shortness of breath, reduced tolerance for activity, bilateral lower limb oedema, features of paroxysmal nocturnal dyspnoea, and orthopnea necessitating the use of more pillows than usual while lying flat over the past week. He had not sought any medical attention for this and was resorting to over-the-counter medications, with progressive worsening of symptoms. There was no history of travel or of long flights. He did not have any significant past medical or surgical history and there were no known allergies to any medications or otherwise. He had a family history of myocardial infarction in his grandfather at the age of 44 years and Guillain–Barre syndrome (GBS) in his father 1 year ago.

At presentation, his blood pressure was 148/116 mmHg, was tachycardic with a heart rate of 137 beats/min, and he was hypoxic, requiring 2 l of oxygen via nasal cannula to maintain a saturation of 96%. Systemic examination revealed left-sided upper extremity grip strength was mildly reduced in comparison to right, left-sided shrug strength was weaker in comparison to right, and bilateral lower extremity strength was 1/5 on the left side and 5/5 on the right side.

Significant laboratory findings include leukocytosis with a white blood cell (WBC) count of 13 900/cu mm, 126 mEq/l sodium, 20 mEq/l bicarbonate, 0.116 ng/ml troponin I, 15.9/1.6 prothrombin time/international normalized ratio (PT/INR). Additional pertinent details are provided in Table 1. The initial computed tomography (CT) scan of the head and computed tomography angiography (CTA) of the head were unremarkable. With neurology consultation, tissue plasminogen activator (tPA) was started within 2 h of hospital admission, following which he was subsequently transferred to the ICU for further evaluation and management. Aspirin, deep vein thrombosis (DVT) prophylaxis, or any other anticoagulation were held initially, and blood pressure (BP) was closely monitored. A repeat CT scan of the head done in 24 h following tPA administration was also unremarkable. Aspirin, along with warfarin, was resumed 24–48 h post tPA administration. MRI of the brain showed an acute infarct involving nearly the entire right basal ganglia, as shown in Figure 1. The CTA of the chest revealed multiple areas of consolidation, along with scattered bilateral subsegmental filling defects pointing towards multifocal pneumonia and multifocal pulmonary embolism. The patient was managed with the IV antibiotics ceftriaxone and azithromycin for a total duration of five days. Septic workup, including blood culture, streptococcus, and legionella antigens, was negative. The bilateral lower extremity DVT screen was negative. For pulmonary embolism, he was given Heparin, followed by a transition to full-dose anticoagulation. Hypercoagulability workups with protein C, protein S, antithrombin III activity, factor V Leiden activity, and antiphospholipid antibody levels were ordered. Protein C was found to be lower than the reference range and could have been a contributory factor in hypercoagulability in this case, but there was no confirmatory evidence for this in our case. The patient needed 2 l of oxygen via nasal cannula for acute hypoxic respiratory failure due to community-acquired pneumonia and/or pulmonary vascular congestion, and furosemide was given for hypervolemic hyponatremia.

Table 1

List of investigation of a 26-year-old male.

Investigations	Result	Reference range
Haemoglobin	15.2 g/dl	12–18 gm/dl
Leucocyte count	11 200 cells/mm^3	4000–11 000 cells/mm^3
Neutrophil percentage	55%	40–75%
Lymphocyte percentage	36%	20–45%
Platelet count	2 750 000 cells/mm^3	150 000–450 000 cells/mm^3
Prothrombin time	12.3 S	9.4–12.5 S
International normalized ratio	1.2	0.8–1.2
Random blood sugar level	130 mg/dl	70–125 mg/dl
HBA1C	6.2%	< 5.7%
Sodium	134 mEq/l	135–145 mEq/l
Potassium	5 mEq/l	3.5–5 mEq/l
Serum creatinine	0.84 mg/dl	0.6–1.2 mg/dl
Blood urea nitrogen	35 mg/dl	6–20 mg/dl
C-reactive protein	7 mg/l	< 10 mg/l
Erythrocyte sedimentation rate	10 mm/h	Men:0–15 mm/h Women:0–20 mm/h
Total cholesterol	214 mg/dl	< 200 mg/dl
Serum triglyceride	142 mg/dl	< 150 mg/dl
HDL	34 mg/dl	> 40 mg/dl
Total bilirubin	0.8 mg/dl	0.2–1.2 mg/dl
Direct bilirubin	0.28 mg/dl	0–0.3 mg/dl
SGOT (AST)	28.32 U/l	5–34 U/l
SGPT (ALT)	42.23 U/l	7–55 U/l
Urine routine microscopy	Moderate glycosuria without proteinuria	
Stool routine microscopy	2–4 pus cells without ova and parasites	
Coxsackie Type B (1) Ab	1:8	
Coxsackie Type B (2) Ab	1:8	
Coxsackie Type B (3) Ab	Negative	
Coxsackie Type B (4) Ab	1:16	
Coxsackie Type B (5) Ab	1:16	
Coxsackie Type B (6) Ab	1:16	

ALT, alanine transaminase; AST, aspartate transaminase; HBA1C, hemoglobin A1C; HDL, high density lipoprotein; SGOT, serum glutamic oxaloacetic transaminase; SGPT, serum glutamic pyruvic transaminase.

A transthoracic echocardiogram was ordered that showed an enlarged left ventricle and severely decreased left ventricular systolic function, as shown in Figure 2. There was global hypokinesia of the left ventricle, with an ejection fraction (LVEF) of 15%, and this pattern was suggestive of dilated cardiomyopathy. There was a large mobile apical thrombus present. Bi-atrial enlargement suggestive of mild pulmonary hypertension was also seen. Antibodies against the CBV came back positive on serology. Viral myocarditis was suspected, but given his new dilated cardiomyopathy on echocardiography, the patient was brought for coronary angiography to exclude underlying coronary disease, which revealed normal coronaries.

Subsequent CT head without contrast showed maturation of acute infarction within the right basal ganglia, as shown in Figure 3. There was no new area of acute infarction, haemorrhage, or any evidence of midline shift, despite a slight mass effect on the anterior horn of the right lateral ventricle on follow-up CT scans of the head. A repeat CTA of the head and neck with contrast showed right M1, M2, middle cerebral artery (MCA) occlusions. A chest X-ray during hospitalization showed

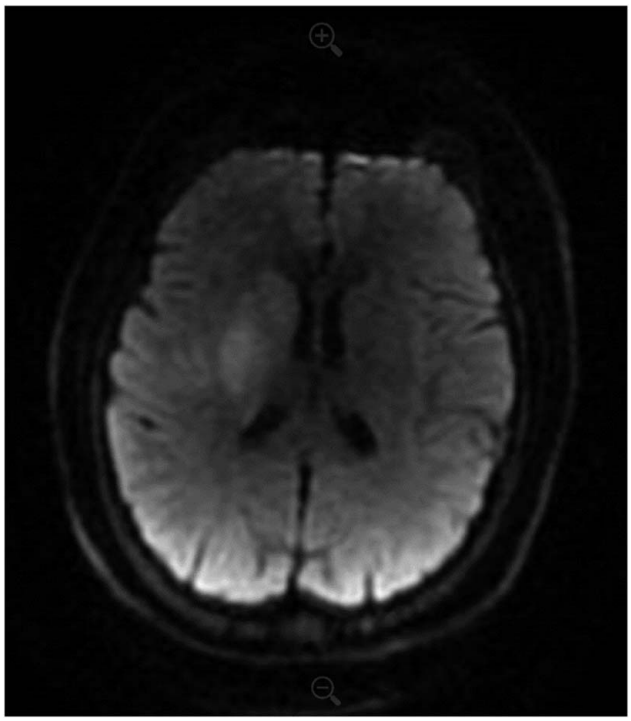

Figure 1. MRI of brain, reveals acute infarction in the right basal ganglia, confirmed by abnormal restricted diffusion and T2 FLAIR hyperintensity, suggestive of a significant ischaemic event.

worsening diffuse and hazy pulmonary opacities in the lungs bilaterally concerning pulmonary oedema. There was marked cardiomegaly and dilated hilar pulmonary vasculature.

Based on the patient's clinical course and serology findings of positive Coxsackie type B antibody and severely reduced left ventricular systolic function on echocardiography, a diagnosis of viral myocarditis or viral cardiomyopathy with subsequent embolic stroke was made. The patient's hospital course was

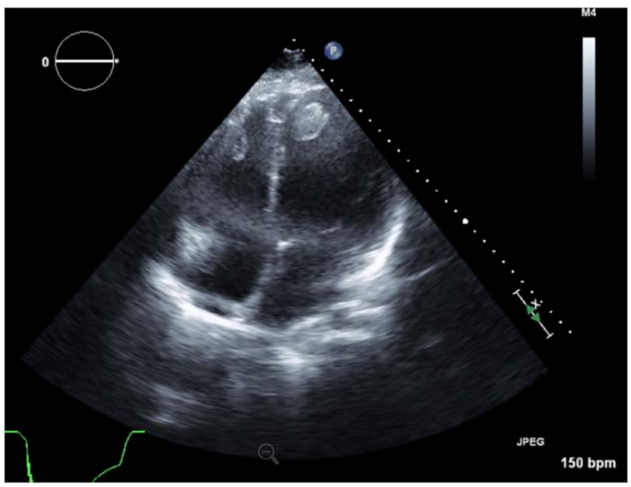

Figure 2. Transthoracic echocardiogram reveals severe left ventricular systolic dysfunction with global hypokinesia, an enlarged left ventricle, and a large mobile apical thrombus, indicative of dilated cardiomyopathy and associated complications.

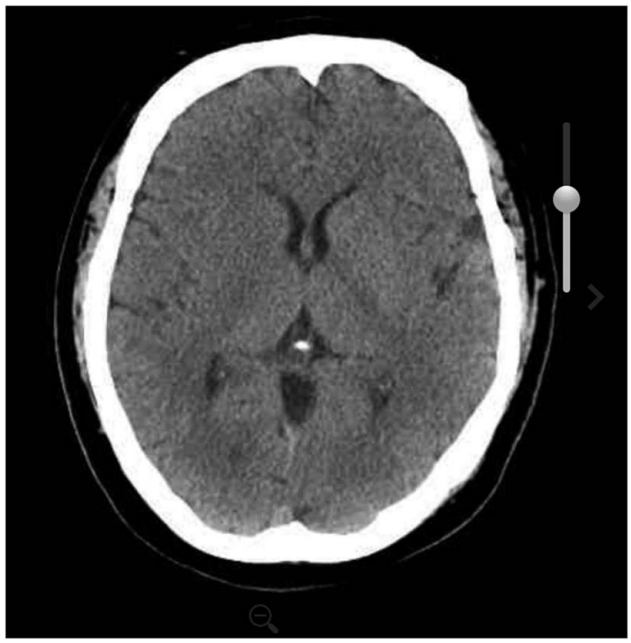

Figure 3. Computed tomography head (without contrast), maturation of acute infarction in the right basal ganglia.

complicated, with seizures likely secondary to evolving acute right hemispheric infarcts in the areas of the basal ganglia and temporal lobe, and he was started on Levetiracetam. He also needed intubation due to worsening respiratory failure and was subsequently extubated to bilevel-positive airway pressure (BiPAP). Guideline-directed medical therapy was started for heart failure with a reduced ejection fraction. Warfarin anticoagulation with a heparin bridge was started to reach a therapeutic goal of 2–3. Heparin was subsequently stopped, and the patient was discharged to rehab on warfarin in a clinically stable condition. The patient was asked for follow-up after a month to assess cardiac function, monitor anticoagulation therapy, and manage heart failure symptoms.

Discussion

Ischaemic stroke is a leading cause of death and disability globally. Understanding the aetiology is extremely important; however, it is not clear in around a third of the cases, despite standard investigations[1]. Ischaemia could be thrombotic or embolic in origin[4]. Among embolic strokes, cardioembolic strokes are the most significant and result from atrial fibrillation, ventricular dysfunction, or valvular dysfunction with subsequent thrombus formation in the heart[5]. The infectious aetiology of intracardiac thrombi with embolization to cause stroke is of interest to us in this study as it is the most likely aetiology behind stroke in our patient. There have been reported instances of intracardiac thrombi formation in cases of myocarditis, especially in young adults like our patient[3]. Cases have been described with COVID-19-induced myocarditis and myocarditis due to Mycoplasma pneumoniae, in which patients later developed systolic heart failure, a left ventricle thrombus, and subsequent embolic stroke[6,7].

Myocarditis is an inflammation of the heart muscle, with mostly viral or autoimmune triggers. Viruses like enteroviruses, adenoviruses, influenza, cytomegaloviruses, hepatitis B and C viruses, mumps, RSV, and herpes viruses have been implicated, among many others[8,9]. Among these, the CBV has been implicated most commonly in human heart infections, being associated with as many as 25–40% of acute myocarditis cases in kids and adolescents. Outbreaks of myocarditis are more common in kids, but sporadic cases are seen among adults as well[10]. Myocarditis can remain asymptomatic or present with mild symptoms of mild ventricular dysfunction. In such cases, it spontaneously resolves without any specific treatment. However, it can sometimes present with a fulminant hemodynamic collapse or progress to dilated cardiomyopathy (DCM) in which case the prognosis is poor[9]. The majority of the cases are, however, asymptomatic. Due to this, the actual incidence of CBV myocarditis is not well established. The incidence of DCM has been estimated to be between 2.0 and 8.3 per 100 000 cases of viral myocarditis worldwide[8].

CBV binds to the transmembrane receptor on cardiac myocytes via the coxsackievirus and adenovirus receptor (CAR). This leads to direct injury to the myocardium with disruption of cytoskeletal structure, triggering an uncontrolled immunological response that can keep on propagating even if the virus itself has been eradicated[11,12]. Chronic CBV infection of cardiac myocytes is associated with impairment of ventricular function. Severe impairment of LVEF and associated LV dilatation have a strong association with inflammatory cardiomyopathy[12]. Despite extensive research, inflammatory cardiomyopathy complicated by LV dysfunction, heart failure, or arrhythmias continues to have a poor prognosis. There are considerable gaps in our understanding of why some patients recover completely from such myocardial injuries while others end up with worsening cardiomyopathy[11].

Myocarditis has been found to be an uncommon cause of stroke that may be caused by heart failure with hypotension, hypercoagulability, arrhythmias, and following specific therapies[13]. The formation of intracardiac thrombi has been seen in cases of myocarditis, which in turn has the potential to embolize other organ systems. This thrombotic phenomenon can occur in people of all ages but is more often seen in young adults. Cases have been reported where large right ventricular thrombi have led to extensive pulmonary embolism in patients suffering from myocarditis[3]. Fulminant myocarditis can result in a new-onset heart failure of less than 2 weeks duration with associated hemodynamic compromise. Apart from this, it can also progress to an inflammatory cardiomyopathy[14]. These can lead to the formation of areas of akinesia and/or dyskinesia in the left ventricle, which would increase the risk of mural thrombi with subsequent thromboembolism[2]. The prevalence of left ventricle thrombus in patients with dilated cardiomyopathy with reduced ejection fraction is as high as 13%, with increasing left ventricle size being independently associated with left ventricle thrombus, all of which predispose a person to cardioembolic stroke[6]. This pathophysiologic mechanism behind a cardioembolic stroke has been reported in patients with COVID-19 myocarditis as well as Mycoplasma pneumoniae, and can logically be assigned to CBV myocarditis as well. However, further studies are necessary in order to make a confirmatory statement[6,7].

Further, viral myocarditis has been found to promote myocardial tissue factor activity and procoagulant activity, leading to hyperactivation of the coagulation system. Also, the inflammatory cytokines produced may play a role in activating the coagulation cascade. This necessitates close monitoring and follow-up of myocarditis patients due to the increased risk of extensive thrombosis and subsequent complications[3].

The current treatment of myocarditis is largely supportive, with appropriate management of complications like heart failure, arrhythmias, and thromboembolic phenomena in accordance with established standard clinical practice guidelines[12].

Conclusion

CBV myocarditis can be complicated with heart failure, cardiomyopathy, and thromboembolic phenomena like pulmonary embolism and embolic stroke. This necessitates close monitoring of these patients for complications, with an emphasis on the management of these complications as they develop while the treatment of primary disease remains largely supportive.

Ethical approval

None.

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.

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Author contribution

N.T., S.A. and A.K. wrote the original manuscript, reviewed, and edited the original manuscript. H.B.B., P.M., M.K. and I.M. reviewed and edited the original manuscript.

Conflicts of interest disclosure

The authors declare that they have no conflicts of interest.

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None.

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All the required information is in manuscript itself.

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