

# Coxsackie B Virus-Induced Cardiac Tamponade and Adrenal Insufficiency

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## Abstract

We report a case involving a young male patient without a significant medical history who exhibited symptoms of fatigue, shortness of breath, chest and back pain, and syncope with vomiting. He was found to have adrenal insufficiency and cardiac tamponade requiring pericardiocentesis. Further inpatient workup revealed the patient had positive IgM and IgG antibody titers for the coxsackie B virus, which we believe caused his presentation. The coxsackie B virus strain can cause mild gastrointestinal to more severe cardiac and neurological complications, including meningitis and myocarditis. On rare occasions, the virus can appear in an unexpected fashion, such as in cardiac tamponade or hormonal disruption. This case raises attention to the broad manifestations of the virus and recognizing its more uncommon presentations.

**Categories:** Cardiology, Internal Medicine, Infectious Disease

**Keywords:** pericardial effusion, adult internal medicine, adrenal insufficiency, cardiac tamponade, coxsackie b virus

## Introduction

The coxsackievirus is a form of *Enterovirus* in the Picornaviridae family that is typically spread through the fecal-oral route. Within the virus, there are 29 recognized serotypes belonging to either group A or group B [1]. With the number of serotypes that exist, it is unsurprising that the coxsackievirus manifests in many different fashions. The disease typically affects children, and both groups can cause fevers, rashes, upper respiratory symptoms, and aseptic meningitis. However, the illness is relatively benign, with 90% of infections being asymptomatic or causing a mild fever [2]. The coxsackie A virus group specifically is a common cause of hand, foot, and mouth syndrome. On the other hand, the coxsackie B virus can target the heart, causing symptoms of chest pain or palpitations. These symptoms are oftentimes managed supportively or with non-steroidal anti-inflammatory drugs but on occasion can progress to conditions including pericarditis, myocarditis, and heart failure. Less frequently, we see virus-induced cardiac presentations including cardiac tamponade. Pathophysiology for this presentation is poorly understood, and the virus is normally not on the differential.

Strains of the coxsackie B virus have been observed to target the pancreas, resulting in conditions such as acute pancreatitis or type 1 diabetes mellitus [3]. Other conditions involving the endocrine system are uncommon. Rarer still, few reports depict the virus simultaneously infecting the cardiac and endocrine systems.

Our patient showcases a unique scenario of the coxsackie B virus causing both cardiac tamponade and adrenal insufficiency. This case highlights the importance of awareness in identifying the virus and the need for further research regarding pathophysiology and treatment.

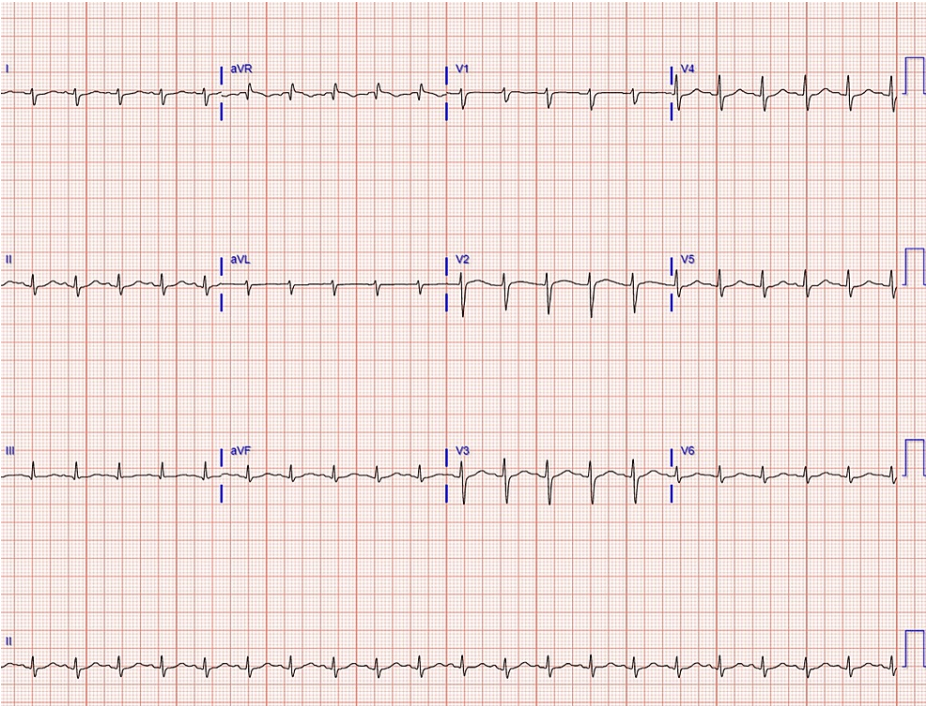
## Case Presentation

This 30-year-old male without significant medical history arrived with complaints of chest pain and shortness of breath for the past three days. He was sitting up as he could not tolerate being supine. Just prior to arrival, his spouse noted a syncopal episode with some non-bloody, non-bilious vomiting.

Vitals on admission include a heart rate of 122 beats per minute, respiratory rate of 27 beats per minute, blood pressure of 63/48 mmHg, SpO2 of 90% requiring 4 L of oxygen, and a temperature of 96.8°F. On physical examination, the patient was alert and oriented ×3 with no focal deficits but was noted to be very lethargic. His heart sounds displayed a regular rhythm but were tachycardic and diminished. The patient was tachypneic on lung auscultation but had normal breath sounds. His chest X-ray demonstrated no acute cardiopulmonary abnormalities, and his electrocardiogram (EKG) showed sinus tachycardia, left posterior fascicular block, borderline low voltage (Figure 1), and a QTc of 522. Initial laboratory results are listed in Table 1.

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**FIGURE 1: EKG on admission**

The patient's EKG showed sinus tachycardia, left posterior fascicular block, borderline low voltage, extremity leads, and prolonged QT interval.

EKG: electrocardiogram

	Day of admission	Day of discharge	Reference ranges
Sodium	139 mmol/L	139 mmol/L	135-145 mmol/L
Potassium	3.3 mmol/L	4.3 mmol/L	3.6-5.5 mmol/L
Chloride	102 mmol/L	110 mmol/L	96-112 mmol/L
CO2	14 mmol/L	19 mmol/L	20-33 mmol/L
Glucose	62 mg/dL	125 mg/dL	65-99 mg/dL
BUN	26 mg/dL	29 mg/dL	8-22 mg/dL
Creatinine	3.35 mg/dL	0.99 mg/dL	0.50-1.40 mg/dL
AM cortisol	<0.2 ug/dL	0.7 ug/dL	0-23 ug/dL
C-reactive protein	5.69 mg/dL	-	0-0.75 mg/dL
ACTH	1,461 pg/mL	-	7.2-63.3 pg/mL
Troponin T	71 ng/L	-	6-19 ng/L

**TABLE 1: Initial chemistry panel on admission highlighting hypoglycemia, acute kidney injury, and metabolic acidosis versus chemistry panel on discharge four days later**

BUN: blood urea nitrogen, ACTH: adrenocorticotrophic hormone

Bedside focused assessment with sonography for trauma (FAST) revealed a large pericardial effusion with tamponade. Given hypotension and hypoglycemia, he was provided dextrose with fluid boluses and started on a norepinephrine drip. Cardiology was consulted, and computed tomography (CT) angiogram ruled out

aortic dissection but again showed pericardial effusions and concerns for tamponade (Figure 2).



**FIGURE 2: CT angiogram showing pericardial effusion (arrows)**

CT: computed tomography

Once pressures improved, the patient went to the catheter laboratory for pericardiocentesis where 450 cc of fluid was removed (Table 2).

	Value
Body fluid color	Yellow
Total WBC	6,700 cells/uL
Total RBC	<2,000 cells/uL
Polys	93%
Lymphs	3%
Mononuclear cells	12%
FI mono-macrophages	4%
Total protein	5.1 g/dL
Albumin	3 g/dL
Culture	Negative

**TABLE 2: Pericardial fluid studies**

WBC: white blood cells, RBC: red blood cells

Post-procedure, vitals quickly stabilized. Blood work revealed the patient had 1:320 positive antibody titers for the coxsackie B virus and had adrenal insufficiency with low cortisol levels. Treatment with colchicine and steroids was initiated, and 48 hours later, transthoracic echocardiogram was negative for pericardial effusion. He was discharged the following day with recommendations for follow-up with endocrinology and his primary care physician.

Discussion

The coxsackie B virus traditionally affects adults with a benign and uneventful course. This case functions as a demonstration that the virus can sometimes present in a unique fashion. The coxsackie B virus knowingly causes pericarditis, but the pathophysiology for tamponade is unclear with only a handful of reported

cases. One case involving a 58-year-old male with hemorrhagic pericardial effusions and tamponade from the coxsackie B virus postulated that since the virus has been shown to cause chronic infection, the long-term damage to the myocardium could in theory result in fluid buildup [4]. There are multiple explanations that focus on the virus' ability to cause prolonged infection. Some research uncovered a process of antibody-dependent enhancement where antibodies paradoxically increase the ability for infection by failing to neutralize the virus while still bringing it closer to its target cell [5]. This in turn would assist the virus in invading cells, lengthen the duration of infectivity, and finally elicit a stronger inflammatory response. Another study detailing the chronicity of the coxsackie B virus found that the virus may have a latency state where it slowly replicates within quiescent G(0) cells [6]. When the same study observed these dormant cells progress through the cell cycle into the G1 and S phases, the cells began to rapidly increase viral load production. A third paper shed light on the presence of residual RNA long after acute symptom resolution that may be toxic to cells and contribute to a prolonged inflammatory response [7].

However, what sets this report apart is the additional component of virus-mediated adrenal insufficiency. There are examples of the coxsackie virus affecting different aspects of the endocrine system. Acute pancreatitis is a well-known complication seen from coxsackie virus infections [8]. Unfortunately, the literature is sparse when it comes to understanding the effects of the virus on the adrenal glands. What is known from previous studies is that the coxsackie B virus has been reported to accumulate in the adrenal cortices [9]. Given the virus' ability to persist in its host, it is reasonable to assume direct cellular injury through increased inflammatory factors in the same manner as with cardiac tissue. A few cases in children even observe adrenal necrosis as a result of direct cellular injury [10].

A second process by which the virus causes adrenal disruption is through transient suppression of the hypothalamic-pituitary system. There are instances of temporary hypogonadism seen in coxsackie virus-mediated encephalitis that resolves shortly after the resolution of infectious symptoms [11]. Although our patient had neither neurological symptoms nor sex hormone deficiencies, the intimate relationship between the hypothalamic-pituitary system and adrenal glands suggests a connection. We acknowledge that the evidence here is limited as these other cases showed a remarkably isolated disruption of gonadal hormones while maintaining adequate levels of thyroid or adrenal function. Further research would be needed to explore this relationship.

## Conclusions

The coxsackie virus clearly manifests in various and hard-to-predict ways. Most of the presentations are benign and ultimately harmless. However, we cannot be complacent when confronted with the disease. The virus on occasion can be challenging and sometimes fatal for the patient, such as in cardiac tamponade or adrenal insufficiency. The pathophysiology of these conditions and the coxsackie B virus is unclear and not extensively researched. This case brings awareness to better understand the virus when dealing with these uncommon findings.

## Additional Information

### Disclosures

**Human subjects:** Consent was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

## References

1. Pozzetto B, Gaudin OG: Cocksackieviruses (Picornaviridae). *Encyclopedia of Virology*. 1999, 305-11. [10.1006/rwvi.1999.0057](#)
2. Förster W, Bialasiewicz AA, Busse H: Cocksackievirus B3-associated panuveitis. *Br J Ophthalmol*. 1993, 77:182-3. [10.1136/bjo.77.3.182](#)
3. Horwitz MS, Bradley LM, Harbertson J, Krah T, Lee J, Sarvetnick N: Diabetes induced by Cocksackie virus: initiation by bystander damage and not molecular mimicry. *Nat Med*. 1998, 4:781-5. [10.1038/nm0798-781](#)
4. Kandah F, Dhruva P, Ruiz J, Martinez A, Kogler W: Cocksackievirus B infection presenting as a hemorrhagic pericardial effusion causing tamponade. *J Geriatr Cardiol*. 2020, 17:642-4. [10.11909/j.issn.1671-5411.2020.10.010](#)
5. Porterfield JS: Antibody-dependent enhancement of viral infectivity. *Adv Virus Res*. 1986, 31:335-55. [10.1016/s0065-3527\(08\)60268-7](#)
6. Feuer R, Mena I, Pagarigan R, Slifka MK, Whitton JL: Cell cycle status affects coxsackievirus replication, persistence, and reactivation in vitro. *J Virol*. 2002, 76:4430-40. [10.1128/jvi.76.9.4430-4440.2002](#)
7. Tam PE, Messner RP: Molecular mechanisms of coxsackievirus persistence in chronic inflammatory myopathy: viral RNA persists through formation of a double-stranded complex without associated genomic mutations or evolution. *J Virol*. 1999, 73:10113-21. [10.1128/JVI.73.12.10113-10121.1999](#)
8. Chrysos G, Kokkoris S, Protosaltis J, Korantzopoulos P, Giannoulis G: Cocksackievirus infection associated

- with acute pancreatitis. JOP. 2004, 5:384-7.
9. Iwasaki T, Monma N, Satodate R, Kawana R, Kurata T: An immunofluorescent study of generalized Coxsackie virus B3 infection in a newborn infant. Acta Pathol Jpn. 1985, 35:741-8. [10.1111/j.1440-1827.1985.tb00615.x](https://doi.org/10.1111/j.1440-1827.1985.tb00615.x)
  10. Fechner RE, Smith MG, Middelkamp JN: Coxsackie B. virus infection of the newborn . Am J Pathol. 1963, 42:493-505.
  11. Chen Z, Jiang C, Cheng X, Ma L, Xin Y, Liu T, Sun R: Secondary hypogonadism following hand, foot, and mouth disease in an adult: a case report and review of literature. BMC Infect Dis. 2022, 22:56. [10.1186/s12879-022-07030-0](https://doi.org/10.1186/s12879-022-07030-0)