A Case of Coxsackie B Causing Multiorgan Failure

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Abstract

Coxsackie B typically affects one organ system at a time – heart, liver or lungs. There is sparce literature on multiorgan failure induced by the Coxsackie B virus. Here we describe a case of Coxsackie B in a young female with type 1 diabetes mellitus. At admission to the hospital, the patient was presented with complaints of fatigue, lethargy, nausea, vomiting and hypoglycemia. Additionally, the patient was found to have myopericarditis, transaminitis, and acute renal failure requiring temporary hemodialysis. While myopericarditis is frequently associated with Coxsackie B, both hepatic and/or renal failure are uncommon presentations. Treatment is largely supportive with NSAIDs as the most effective treatment for myopericarditis.

Keywords: Coxsackie, Coxsackie A, Coxsackie B, myopericarditis, hepatitis, renal failure.

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Introduction

Coxsackieviruses, a type of RNA *Enterovirus*, are divided in two main groups – A and B. While Coxsackie A has most commonly been implicated in hand, foot and mouth disease in children, Coxsackie B tends to have multiorgan effect, typically in the heart, pancreas, and liver [1]. Coxsackie B is the most common cause of myocarditis and pericarditis in adults [1]. Despite its multiorgan effects, Coxsackie B typically affects a single organ system. In contrast, multiorgan failure, defined by the presence of three systems, has only previously been documented in a few case reports [2]. Here we present a case of Coxsackie B affecting renal, hepatic, and cardiac tissue in a young female.

Case Presentation

A 31-year-old woman with a medical history of type 1 diabetes mellitus complicated by gastroparesis presented to the hospital with complaints of fatigue, lethargy, nausea, and vomiting for a few days. On arrival, patient was hemodynamically stable with blood glucose level of 35 mg/dL. Liver enzymes were elevated with aspartate aminotransferase (AST) 191 U/L, alanine aminotransferase (ALT) 112 U/L, total bilirubin 2.4 mg/dL, direct bilirubin 1.0 mg/dL, and alkaline phosphatase 176 U/L. She had leukocytosis with white blood count (WBC) 16.9 $\times$ $10^3/\mu$L with neutrophilic predominance, elevated procalcitonin (33.68 ng/mL), and elevated lactate (3.6 mmol/L). HIV antigen/antibody and testing for viral hepatitis A, B, and C were negative. Urinalysis was positive for moderate blood without red blood cell (RBC) casts and large leukocyte esterase without nitrites. Her hemoglobin A1C was 11.9%, and she reported non-compliance with insulin for a few months prior. She reported smoking hookah and occasional alcohol use.

She was treated for hypoglycemia with resolution of most presenting symptoms, besides fatigue and low appetite. On the second day of admission, the patient was hypotensive requiring pressors and was transferred to the medical intensive care unit (MICU). Laboratory results at this time are outlined in Table 1. The patient became anuric and required emergent hemodialysis for fluid overload. She developed worsening anemia, with Hgb dropping 10.4 g/dL on admission to 6.0 g/dL, requiring two blood transfusions without evidence of bleeding. Physical examination was significant for jaundice, scleral icterus, lethargy, and neurologic ataxia with weakness of the

Table 1 Comparing labs on presentation to hospital and at day 2, indicating persistent transaminitis and acute kidney injury. Increased values are shown in bold. Shown are the patient's labs from presentation to hospital at day 2. The results indicate an increase in creatinine and persistent transaminitis, suggesting kidney and liver disease

Lab Tests	Admittance	Hospital – Day 2	Normal Range
WBC	**16.9 × $10^3/\mu$L**	**16.9 × $10^3/\mu$L**	4.0–11.0 × $10^3/\mu$L
Hgb	10.4 g/dL	10.4 g/dL	14.0–18.0 g/dL
Platelets	280 × $10^3/\mu$L	280 × $10^3/\mu$L	150–450 × $10^3/\mu$L
Glucose	32 mg/dL	161 mg/dL	70–109 mg/dL
BUN	18 mg/dL	28 mg/dL	6–20 mg/dL
Creatinine	1.1 mg/dL	**1.9 mg/dL**	0.7–1.2 mg/dL
Sodium	138 meq/L	131 meq/L	133–145 meq/L
Potassium	3.0 meq/L	3.0 meq/L	3.5–4.8 meq/L
Chloride	98 meq/L	95 meq/L	97–110 meq/L
Alkaline phosphatase	**176 u/L**	**173 u/L**	40–130 u/L
Total bilirubin	2.4 mg/dL	6.9 mg/dL	<1.0 mg/dL
Direct bilirubin	1.0 mg/dL		<0.3 mg/dL
AST	**191 U/L**	**122 U/L**	0–40 U/L
ALT	**112 U/L**	**102 U/L**	0–41 U/L

lower extremities. Additional labs are outlined in Table 1. Peripheral smear revealed mild to moderate schistocytes. Rheumatologic workup was non-revealing, with negative anti-nuclear antibody (ANA), double stranded DNA (dsDNA), and normal complement levels. The patient was initially managed with broad-spectrum antimicrobial coverage, which was discontinued once no bacterial agent was isolated. She completed a course of doxycycline due to seasonal concern for tick-borne illness.

The patient underwent a lumbar puncture and was found to have a high opening pressure of 26 mmHg. Cerebrospinal fluid studies (CSF) revealed glucose 160, protein 31, and 2 WBCs with 100% lymphocyte. CSF cultures were negative. The patient developed chest pain with an electrocardiogram revealing ST-segment elevations and PR-segment depression in leads V2–V6. The patient started to receive aspirin 650 mg every 8 hours for myopericarditis. Ibuprofen or colchicine were contraindicated due to multiorgan dysfunction, and glucocorticoids were not initiated due to the possibility of infection.

Once the patient was hemodynamically stable and making urine, hemodialysis was halted. She continued to improve and was discharged

after 12 days. Of all infectious work-up ordered, titers for Coxsackie B2-Ab returned positive at 1:32, Coxsackie B4-Ab at 1:16, Coxsackie B5 Ab at 1:64 (ref. <1:10). She was lost to follow up and paired serologic testing was unable to be obtained. Due to high titers of the virus, combined with compatible syndrome, the team diagnosed Coxsackie B myopericarditis with hepatitis and acute renal failure.

Discussion

Myopericarditis is pericardial inflammation to the myocardium, which can present with elevated troponin levels and ST-segment elevations on electrocardiogram [3]. Causes include autoimmune disorders, neoplastic diseases, viral infections, and more rarely, vaccinations including the smallpox vaccine and the COVID-19 vaccine [4]. Risk factors include young age, male sex, and recent febrile illness [3]. As diagnosed in our patient, acute pericarditis is diagnosed by chest pain that worsens positionally, with diffuse ST-segment elevations on EKG or with friction rub [5]. Coxsackievirus is typically spread through the fecal–oral route and enters the gastrointestinal tract, although the virus can spread to the myocardium. While most cases of Coxsackie B in adults are associated with a benign course, it is the most common cause of myocarditis and pericarditis in adults, causing up to 50% of viral causes of cardiac cases [5, 6]. Our patient had both presence of ST-segment elevations and troponinemia, which lead us to believe that she had myopericarditis. We did not obtain an MRI which would be best suited to visualize tissue changes including edema and capillary leakage [7]. Myocarditis occurs in animal models due to direct binding and internalization through the receptor, which then mediates transcription of the viral genome [8].

Specifically, Coxsackie B 1, 2, and 6 groups have been associated with both myopericarditis and acute liver failure from hepatitis [6]. Our patient tested positive for groups 2, 4, and 5, with highest titers to group 5, likely the etiologic agent of her syndrome. Hepatic damage is rare and has been associated in only a few cases of Coxsackie B [9]. Transaminitis was noted to be transient and self-limiting in nature, similarly to the case of our patient with peak levels between day 1 and 7 at levels >5000 units/L [10]. Similar reports have been described in other cases of Coxsackie with acute infectious hepatitis, suggesting a recovery mechanism [11].

Interestingly, few cases have been reported with acute renal failure due to Coxsackie viral infection with severe rhabdomyolysis [12]. Rhabdomyolysis has been associated with direct viral invasion [13]. There have been described

cases of acute glomerulonephritis caused by coxsackievirus [14]. Our patient required temporary intermittent hemodialysis with resolution and recovery of renal function within a few days, similar to previously described cases [15]. In this report, there was no associated rhabdomyolysis with the acute renal failure. We did not pursue renal biopsy, which would have been diagnostic for disease.

Treatment of Coxsackievirus is largely supportive and based on affected systems. The most effective treatment for myopericarditis is non-steroidal anti-inflammatory drugs (NSAIDs) [16]. Colchicine and low dose glucocorticoids can be used to reduce recurrence rates of symptoms [16]. In our patient's case, we were unable to use NSAIDs and colchicine treatment modalities due to acute renal failure requiring dialysis and use of glucocorticoids was limited due to concern for concomitant infection. In her case, the myopericarditis was a late manifesting symptom in the hospital course. However, in the presence of remitting chest pain and hepatitis, Coxsackie should remain a leading clinical diagnosis.

One additional limitation to our case is that we did not perform enterovirus polymerase chain reaction (PCR) on blood or cerebrospinal fluid (CSF). The clinical utility of enteroviral PCRs is questionable because there is no treatment for these infections, so we do not routinely send them in our practice. Unfortunately, the meningoencephalitis panel is not done in-house at our facility and, due to the long turnaround time of the send out, it was not sent on this patient. There was no pericardial effusion on echocardiogram, and we did not pursue a myocardial biopsy due to the high risk of the procedure. Liver biopsy was not pursued as the liver function improved after initial worsening. Unfortunately, the patient moved out of state after discharge and paired serological testing could not be obtained [12].

Conclusion

We describe a rare case of coxsackievirus B infection causing multiorgan effect, including pericarditis, hepatitis and acute renal failure requiring temporary intermittent dialysis in a young female with type 1 diabetes mellitus. Like most viral illnesses, it was self-resolving and self-limited in nature. Unlike previous cases, our patient did not present with acute renal failure secondary to rhabdomyolysis and while the mechanism is unknown, there have been previous cases of acute glomerulonephritis secondary to Coxsackievirus. Further research into early identification and treatment modalities is necessary to identify varied presentations of Coxsackievirus in adults.

Author Statement

All authors were involved in the care of the patient and writing and editing of the manuscript.

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