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# Coxsackie B Virus Infection as a Rare Cause of Acute Renal Failure and Hepatitis

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## ABSTRACT

We report a 37 year female patient, admitted with complains of fever, jaundice and myalgia of seven days. There was no history of trauma, drug abuse, seizure or vigorous exercise nor history of renal and musculoskeletal disease. Here we have discussed the clinical features, biochemical derangements, diagnosis of coxsackie B virus, multi organ involvement and need of urgent hemodialysis for appropriate management of the case.

## KEY WORDS

*Acute renal failure, Coxsackie B, Hemodialysis, Hepatitis*

## INTRODUCTION

The Coxsackie viruses are Ribonucleic acid viruses of the Picornaviridae family, Enterovirus genus which also includes echoviruses and polioviruses. Infections are mostly asymptomatic. They are divided into groups A and B. Coxsackie virus A virus usually affects skin and mucous membranes, presents with rashes, fever, an acute respiratory infection; only a few with central nervous system infection resulting in encephalitis. Coxsackie B virus usually affects the heart, lungs, pancreas and liver; causes Bornholm disease, hepatitis, myocarditis and pericarditis. Clinical and experimental evidence suggests that Coxsackie virus can induce kidney injury, but the susceptibility of human renal cells to these viruses is unknown. Pathogenic effects observed are proximal tubular epithelial cells, glomerular podocyte injury and impair the phagocytic and contractile activity of mesangial cells causing acute and progressive renal injury, mesangioproliferative glomerulonephritis and IgA-nephropathy in mice.[1,2] We report a case of Coxsackie virus B infection causing acute renal failure required hemodialysis with concomitant acute hepatitis from Bir Hospital, Kathmandu.

## CASE REPORT

A previously healthy 37-year-old female was admitted to our hospital with complains of fever of 7 days, jaundice of 4 days, severe muscle pain, especially the lower limbs, and discoloured urine. She also had history of malaise, headache, sore throat and fever recorded up to 103.2°F. There was no history of trauma, drug abuse, vigorous exercise or family history of renal or musculoskeletal disease. On physical examination she was icteric, pale, ill looking, had mild edema and tender calves with a blood pressure of 110/70 mmHg, pulse rate of 96 beats/min and a temperature of 100.6°F. Examination of lungs, heart and abdomen was unremarkable.

Relevant laboratory values included a hemoglobin of 8.6g/dl, maximum urea of 184mg/dl and creatinine 8.6mg/dl, uric acid 8.2 mg/dl, sodium 134meq/l, potassium 4.9meq/l, total bilirubin 39.1mg/dl, direct bilirubin 23.5mg/dl, aspartate transaminase 710U/L, Alanine transaminase 289U/L, alkaline phosphatase 238U/L, INR 1.8, PT 20sec, LDH 4435U,Creatine phosphokinase 8682U/L, calcium 8.3mg/dl, phosphorous 5.5mg/dl, albumin 2.6g/dl. The maximum white blood cell count was 24600/$mm^3$ with

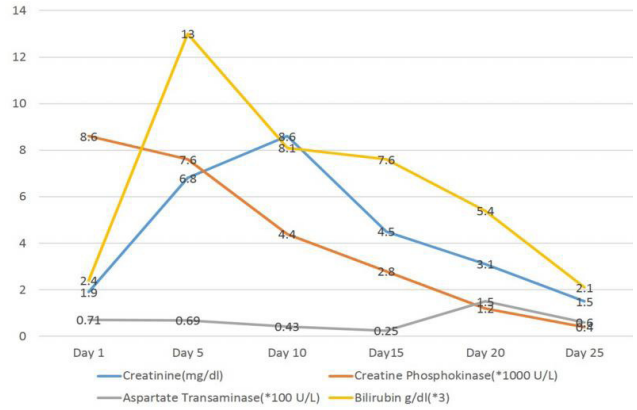


**Figure 1. Time course of serum creatine phosphokinase (CPK), creatinine and aspartate transaminase level and total bilirubin**

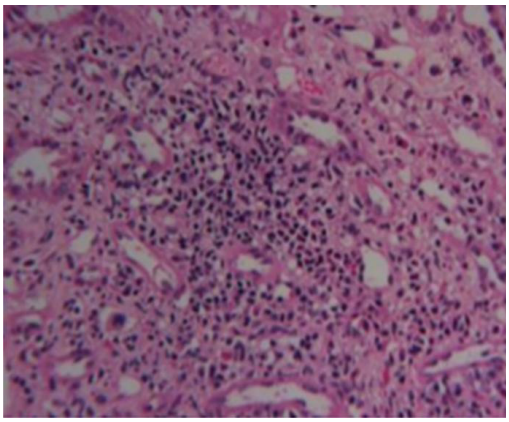

**Figure 2. Hematoxylin and eosin stain of renal parenchyma showing normal appearing glomeruli with focal dilatation and congestion of capillary lumen with pigment cast in tubular lumen**

neutrophils count of 58% in the differential count and a platelet count of 4190000/mm$^3$. Serum creatinine on day of admission amounted to 1.9mg/dl, urea 56mg/dl, which progressively increased to above mentioned maximum value (fig. 1). Percutaneous renal biopsy showed non proliferative glomerular morphology without immune deposits with features of acute tubular injury and presence of several granular/pigmented casts in tubular lumen (fig. 2).

Routine urine analysis revealed haematuria (plenty RBC per field) but no casts, and proteinuria (0.82g/day). Additional testing for ANA, ds DNA, complement factor C3 and C4 levels, anti GBM and ANCA-P/C were negative or within the normal range. Chest radiograph and electrocardiogram revealed no abnormality. Blood and urine cultures did not show any growth. Serology for dengue, chikungunya, influenza virus types A and B, respiratory syncytial virus, hepatitis A, B, C and E virus, toxoplasma gondii, leptospira and brucella was all negative. However, a Coxsackie B2 IgM antibody titre was 20U/ml (normal < 10U/ml) on enzyme immune assay on 4$^{th}$ day of admission suggesting a recent infection. Myoglobin level in blood and urine could not be determined due to unavailability of service.

Arterial blood gas analysis showed a pH of 7.25, pCO2 28.2mmHg, bicarbonate 10.1 mmol/l, $pO_2$ 94 mmHg and oxygen saturation of 96%. Despite immediate and vigorous hydration with normal saline and alkalisation with sodium bicarbonate to maintain a serum pH above >7.30 and bicarbonate level of 14 mmol/dl, she developed non oliguric renal failure requiring renal replacement therapy in the form of intermittent haemodialysis on fifth day after admission for a total of eight sessions, which continued for two weeks. Recovery was otherwise uneventful with gradual disappearance of calf swelling and muscle pain, progressive decline in the serum Creatine Phosphokinase (CK level) and complete recovery of renal function (creatinine 1.1mg/dl). She had no further symptoms, normal creatinine (0.8 mg/dl), normal liver function and negative Coxsackie B2 IgM titre at 5 month of discharge.

## DISCUSSION

We present here a rare case of Coxsackie B virus-induced rhabdomyolysis complicated by acute renal failure and hepatitis. No features of recurrent rhabdomyolysis was present, which suggest that an inherited disorder of muscle metabolism was highly unlikely. Other precipitating factors (alcohol, trauma, heavy exercise, seizure, drugs etc) were absent in our patient. However, the onset of the disease with prodromal features characterized by fever, headache, sore throat and myalgia suggest a viral infection, which we had confirmed by Coxsackie B2 IgM antibody titre. It is generally accepted that there should be a fourfold rise in antibody titre over a period of four to six weeks to make a definitive diagnosis of acute Coxsackie virus infection.[3]

Although considered rare, it is known that viral infections (mostly Influenza viruses) may induce a wide range of muscle disorders, ranging from acute nonspecific myalgia to myositis.[4] The precise mechanism of virus-induced rhabdomyolysis has still not been defined, it is assumed that initial acute tissue damage may be caused by the lytic effects of the virus on the muscle cell with subsequent release of myoglobin.[5,6] In few reported cases, the course of disease was complicated by acute renal failure (ARF) necessitating intermittent haemodialysis for two to three weeks; all of them subsequently showing a complete recovery of renal function.[7,8] Our patient also developed (nonoliguric) ARF despite vigorous hydration, alkalization therapy and supportive medications, temporary intermittent haemodialysis was needed for two weeks but subsequent recovery of renal function was complete. ARF development caused by myoglobin may occur as a result of tubular obstruction by myoglobin, direct toxicity by heme pigment, cortical ischaemia and decreased glomerular permeability resulting from fibrin strand deposition.[7,8] Dehydration, hypovolaemia and aciduria will accelerate this process of renal damage. ARF has also been shown to occur as a result of an immune complex mediated acute glomerulonephritis associated with recent Coxsackie virus B4 infection.[9] Hepatitis associated with myocarditis and

encephalitis are also other menifestations of Coxsackie Virus B infection to be more clinically vigilant.[10,11] Inability to test myoglobin level and serial measurement of Coxsackie B virus antibody titre is the limitation in our case.

We describe a case of a young woman who developed acute renal failure and acute hepatitis from recent Coxsackie B infection. This is only the case report to describe Coxsackie B infection leading to ARF needing hemodialysis with concomitant acute hepatitis to our knowledge in Nepal. Our case highlights the need for screening of systemic organ dysfunction due to potential multi organ involvement, particularly with Coxsackie B virus infection in all cases of unexplained febrile illness.

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