

# Streptococcal Pharyngitis: Delving Deeper than the Throat

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## ABSTRACT

Acute rhabdomyolysis and elevated transaminases during *streptococcal* pharyngitis are rare presentations. The proposed pathophysiological mechanisms include direct bacterial invasion and toxin generation. Physicians should be aware of the association between these infections and the above-mentioned complications to facilitate optimal treatment of these patients. We present the case of a 18-years-old gentleman with  $\beta$ -haemolytic *streptococcal* pharyngitis complicated by rhabdomyolysis and elevated liver function tests. Such high levels of creatine phosphokinase of 111856 IU/L and elevated liver function tests with aspartate aminotransferase (AST) of 1862 U/L and alanine aminotransferase (ALT) of 1003 U/L in *streptococcal* pharyngitis is rare to find in the literature. He was treated with aggressive intravenous hydration, antibiotics and hemodialysis.

**Key Words:** Rhabdomyolysis,  $\beta$ -haemolytic Streptococci, Creatine phosphokinase, Liver function tests.

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## INTRODUCTION

$\beta$ -haemolytic *streptococci* infections can manifest as pharyngitis, cellulitis, primary bacteremia, arthritis, endocarditis, meningitis, pneumonia, necrotizing fasciitis, myositis, and even fatal toxic shock-like syndrome.<sup>1</sup> Pathophysiological mechanism linking  $\beta$ -haemolytic *streptococci*-related pharyngitis and rhabdomyolysis yet remain unclear.<sup>2</sup> We, herein, present a case of an 18-year gentleman with rhabdomyolysis and raised transaminases. The clinical presentation showed unrelenting muscle pain, concentrated urine output and fever.  $\beta$ -haemolytic *streptococci*-related upper respiratory tract infection with raised anti-streptolysin (ASO) and creatine phosphokinase (CPK) is very suggestive of rhabdomyolysis as a complication of *streptococcal* pharyngitis. Deranged kidney function and raised urine myoglobin levels further supported the diagnosis for rhabdomyolysis. It is a significant piece of information to alert the emergency physician to the possibility of such significant muscle damage and raised liver function tests in a case of *streptococcal* pharyngitis.

## CASE REPORT

A previously healthy, 18-year gentleman with a history of fever and sore throat for 10 days, managed at a tertiary care hospital, was referred to our hospital due to worsening renal functions with the laboratory report showing serum creatinine of 8.1 mg/dL (normal: 0.7-1.2 mg/dL). According to the patient, he developed fever 10 days back, which was high grade, with chills, was continuous, and partially relieved with oral acetaminophen. Patient complained of severe body aches. There were no urinary symptoms, cough, abdominal pain or headache. The patient was initially managed as an upper respiratory tract infection and was started on amoxicillin. After 5 days course of antibiotics, fever remained unsettled and the patient developed nausea and vomiting with decreased appetite and proximal muscle pain. The patient was hospitalised and initial laboratory workup revealed elevated total leukocyte count (TLC) of  $25.2 \times 10^9/L$  (normal:  $4.3 - 10.8 \times 10^9/L$ ), elevated liver enzymes with aspartate aminotransferase (AST) of 1862 U/L, alanine aminotransferase (ALT) of 1003 U/L and serum creatinine of 7.2 mg/dL. Malarial parasite smear and ICT malaria antigen were negative. The patient was empirically started on intravenous ceftriaxone 2 grams once daily. The patient's renal functions worsened further and he was referred to our hospital. In addition to prior symptoms, patient now complained of worsening muscle pain and difficulty in getting up from sitting position. There was no history of trauma, no related prior family history, no involvement in contact sports or no prior medication history.

On examination, he was afebrile, with normal blood pressure, normal pulse rate and normal oxygen saturation on pulse

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oximeter with normal respiratory rate. General physical examination was unremarkable except for hyperemic throat. There was no jaundice, anemia, cyanosis, clubbing, palpable lymph nodes, edema, or enlarged thyroid. The chest was clear with normal vesicular breathing. Cardiovascular examination was unremarkable except for the tapping apex beat. There was no audible murmur and examination revealed normal first and second heart sounds. The abdominal and genitourinary examination was unremarkable. The patient was catheterised at the outside setting with the urine bag containing about 400 ml of urine with gross hematuria.

Initial workup repeated at our hospital revealed elevated TLC of  $28.3 \times 10^9/L$ , with neutrophilic shift of 87.9%, normal hemoglobin, normal platelet count, blood urea nitrogen of 84 mg/dl, creatinine of 9.3 mg/dl, serum potassium of 7.2 mmol/l, serum magnesium of 3.1 mg/dl, and serum calcium of 8.8 mg/dl. Liver function tests revealed AST of 994 U/L, ALT of 1529 U/L, normal total bilirubin, direct bilirubin, indirect bilirubin, gamma glutamyl transferase (GGT), normal alkaline phosphatase, and prothrombin time of 10.6 seconds. CPK was 111856 IU/L (normal: 46-171 IU/L). Urinalysis was positive for hemoglobin 5+, protein 2+, leukocyte esterase 3+, RBC >20/HPF, and leukocytes, 12/HPF. Coombs, HEV IgM, HAV IgM, HBsAg, anti-HCV antibody, malarial parasite smear and ICT malaria antigen were negative. Additional workup revealed elevated ASO titres of 400 IU/ml (normal <200 IU/ml), and erythrocyte sedimentation rate (ESR) of 49 mm/1st hr (normal: 0-15). Antinuclear antibody (ANA) was positive with the homogenous pattern and procalcitonin was 0.52 ng/ml (normal <0.5). Blood cultures grew no organisms.

Management was started on the lines of non-traumatic rhabdomyolysis with aggressive intravenous fluids resuscitation and sodium bicarbonate infusion. Potassium lowering therapy was given twice, with rectal polystyrene sodium to correct hyperkalemia. Potassium repeated after 4 hours was 6.3 mmol/l. The patient was planned for hemodialysis due to low urinary out and refractory hyperkalemia. Two sessions of hemodialysis were performed. Due to the history of prior hospitalisation, intravenous piperacillin / tazobactam was started empirically at renal adjusted dose due to presumed sepsis. Later intravenous vancomycin was also added. The patient's laboratory work-up on the fourth day of admission showed marked improvement in CPK level, i.e., 7904 IU/L. TLC improved to  $19.7 \times 10^9/L$ , blood urea nitrogen improved to 43 mg/dl and serum creatinine to 4.9 mg/dl. The patient also improved symptomatically. Fever, nausea and vomiting were improved. The patient's family was counselled for the continuous need of inpatient care with the possible need of dialysis during hospital stay and additional need for intravenous hydration; but due to extreme financial constraints, the patient refused further workup and left against medical advice on 4th day of admission.

## DISCUSSION

Group A  $\beta$ -hemolytic *streptococci* are the most frequently isolated pathogens in acute pharyngitis.<sup>1</sup> *Streptococcal* infec-

tion causing acute rhabdomyolysis is a rare entity with few case reports published in the literature. Pathophysiology inquiring causal relationship is yet not well known and revolves around direct invasion or toxin damage with sepsis as a trigger in this case. However, no exact toxin has been isolated.<sup>2</sup> Other triggers could be alcohol ingestion, smoking, compression injury and generalised seizures. Whatever the mechanism of rhabdomyolysis in such invasive infections, released myoglobin itself is a direct renal toxin causing cortical ischemia and results in the rise of CPK from 261 IU/L to >50,000 IU/L.<sup>3</sup>

Our case manifested relatively mild pharyngitis with *streptococcal* infection which got resolved in a week with unsettling myalgias. There was no history of any muscle injury. We found very high levels of CPK, which have not been reported in the literature. We feel it is important to alert other physicians to the possibility that  $\beta$ -haemolytic *streptococcal* infections can be associated with significant muscle destruction and liver damage. Our patient underwent hemodialysis twice to help normalise the creatinine and help the patient to make adequate urine output.

Elevated transaminases is a rare complication of  $\beta$ -haemolytic *streptococci*-related pharyngitis. Although the exact prevalence and pathophysiological mechanisms are undetermined; direct bacterial injury, toxicity and immunologic mediation have been proposed.<sup>4</sup> Liver biopsies have shown granulocytic infiltration of the portal areas and hepatocytic degeneration. In most patients, the prognosis is excellent.<sup>5</sup>

As a food for thought and to avoid morbidity and mortality from  $\beta$ -haemolytic *streptococcal* infections, physicians should be aware of rhabdomyolysis in patients presenting with pharyngitis, skin infections or pneumonia with myalgia and consider checking CPK at admission, which could help managing the critically ill patients.

### PATIENT'S CONSENT:

Verbal consent was obtained from the patient to publish the data concerning this case.

### CONFLICT OF INTEREST:

None to declare.

### AUTHORS' CONTRIBUTION:

SS, UJ, MAB: Significantly contributed in drafting and editing the work.

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