

Compartment Syndrome and Fatal Rhabdomyolysis in Sickle Cell Trait

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ABSTRACT

Sickle cell trait is a relatively common condition in the African-American population. Individuals with this condition may have any of several complications under rare circumstances. We report a patient who presented with extensive compartment syndrome leading to death. A 31-year-old African-American male with known history of sickle cell trait developed extensive compartment syndrome followed by rhabdomyolysis, severe acidosis, acute renal failure, and coagulopathy. Although the patient underwent multiple fasciotomies for extensive compartment syndrome and received aggressive resuscitation with massive transfusions of blood, blood products and intravenous fluids, he died. Multiple compartment syndromes in patients with sickle cell trait represent a very unusual complication and can cause significant morbidity and mortality. Avoidance of strenuous exercise, especially in hot climates, early diagnosis, and aggressive therapy are very important to prevent this catastrophic complication.

INTRODUCTION

Sickle cell trait is a prevalent condition and is present in 8% of African-Americans.¹ Sickle cell trait is recognized incidentally in most cases due to absence of symptoms. Although it is a benign condition and individuals who have the condition are not labeled as sick, these individuals are prone to have rare complications that may predispose them to sudden death under certain circumstances. A mild degree of rhabdomyolysis and compartment syndrome can be seen in “healthy individuals” after vigorous exercise. Sickle cell trait is believed to increase the risk of severe rhabdomyolysis,

compartment syndrome, and subsequent death. Here we describe a 31-year-old patient with sickle cell trait and no other hemoglobinopathy detectable by electrophoretic examination who experienced extensive compartment syndrome after routine physical training. To the best of our knowledge, this is the first patient with sickle cell trait who developed multiple compartment syndrome, severe rhabdomyolysis, and disseminated intravascular coagulation after “routine” physical exercise that led to death despite aggressive therapy.

CASE REPORT

A 31-year-old African-American man transferred to our hospital for management of rhabdomyolysis and acute renal failure. He had served in the Army for 23 months and was used to heavy exertion and training involving runs of up to 8 miles. One day prior to admission, the patient collapsed and became unconscious following a routine physical training in a cool weather condition (ambient temperature of 70°F). The training included only a 5-mile run. It was reported that he did not have any problems during prior similar exercises. His peers observed no seizure activities. He was brought to the nearest hospital for observation where he remained unconscious for an hour. He complained of muscle aches once he was awake. Initial vital signs revealed temperature of 98°F, heart rate of 85, blood pressure of 125/78 mmHg with a SpO₂ of 98% on 2L oxygen per nasal cannula. His drug screen, including cocaine and amphetamines, was negative. Diagnoses of compartment syndrome of both lower extremities, rhabdomyolysis, and acute renal failure were made based upon clinical examination and laboratory data, and the patient underwent fasciotomy of anterior compartments of both legs. Initial laboratory results are shown in Table 1. The patient was intubated during the surgery and remained intubated for airway protection. On arrival to our institution, he was sedated, intubated, and was able to follow commands. Physical examination revealed a muscular man who was complaining of generalized muscle pain. He was afebrile, blood pressure was 85/45 mmHg, and

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Table 1. Laboratory Data

	Prior to Admission	Time of Admission (Values Prior to Transfusions)	3 Hours After Admission (Post-op)	8 Hours After Admission
CBC				
WBC	15,200	16,700	13,700	—
Hemoglobin	11.3	12.3	11.6	4.9
Hematocrit	35	36	34	12
Platelet	135,000	121,000	128,000	66,000
Hb Electrophoresis				
% A1	—	69	—	—
% S	—	29.6	—	—
% A2	—	1.6	—	—
Coagulation and DIC				
Prottime	—	29.6	26.3	34.2
INR	—	3.44	2.95	9.5
PTT	39.1	38	85.2	—
Fibrinogen	—	107	—	68
D-dimer	—	>4	—	>4
FDP	—	>40	—	<10
Metabolic Panel				
Na	131	—	136	137/137
K	7.0	7.4	5.6	8.4
Cl	107	104	103	104
HCO ₃	7.4	13	17	11
BUN	18	29	25	20
Creatinine	4.0	3.8	2.6	1.7
Glucose	128	220	175	198
Ca	—	5.5	6.7	15.3
PO ₄	—	14.7	—	11.4
CK-total	—	266,460	—	26,650
Urine myoglobin	—	+	+	+
Lactic acid	—	5.4	—	13.1
Arterial Blood Gases				
FiO ₂ (%)	—	60	60	80
pH	7.25	7.3	7.51	7.02
PCO ₂	35	31	24	59
PO ₂	125	179	197	230
HCO ₃	14.5	15	19	12
SaO ₂ (%)	99	99	100	100

WBC=white blood cells; INR=International Normalized Ratio; PTT=partial thromboplastin time; FDP= fibrin degradation products

pulse rate was 115. His neck, chest, and heart examinations were normal. His abdomen was tender to palpation, and mildly distended with no organomegaly. He had elastic pressure bandages on his lower extremities. His peripheral pulses were diminished in both lower extremities, but he had good pulses in upper extremities. He had decreased sensation in his upper right and both lower extremities. There was no motor deficit in any of the limbs. Stryker pressures are shown in Table 2.

After hemodynamic stabilization with IV fluids, blood transfusions, and low dose of dopamine (3µ/kg/

min), he was started on bicarbonate infusion and hemodialyzed for 2 hours to reduce high potassium level. The patient underwent releases of bilateral upper extremity deep and superficial flexor and extensor, carpal tunnel, thenar, hypothenar, volar dorsal interossei, and all 4 compartments in the both lower extremities. Upper extremity muscles were contractile with Bovie cautery, however no contractility was noted in the muscles of the lower extremity. The patient became hypotensive during the surgery and received 10 units of packed red blood cells and 3 units of fresh frozen plasma. On ar-

rival to the medical intensive care unit, his blood pressure was 75/45 mmHg and heart rate was 125/min. His repeat laboratory data are shown in Table 1. He was noted to have significant oozing from fasciotomy sites. He was continued on intravascular volume resuscitation with blood and blood products. He was also given repeated doses of bicarbonates and calcium gluconate for severe acidosis and hyperkalemia. Hemodialysis could not be performed because of persistent hypotension. He received a total of 56 units of packed red blood cells, 27 units of fresh frozen plasma, 3 units of cryoprecipitate, and 3 units of platelets through 2 different fast infusion pumps. Cardiopulmonary resuscitation was initiated due to pulseless electrical activity and ventricular fibrillation. The patient died in spite of aggressive resuscitation.

DISCUSSION

Sickle cell trait, the heterogeneous condition characterized by the presence of HbAS, occurs in approximately 8% of American Americans, and as many as 30% of some African populations, whereas its incidence is less than 1% in those of nonAfrican descent.^{1,2} Sickle cell trait is rarely associated with clinical or hematological manifestations of significance, so most of the individuals affected are unaware of their status. Studies have indicated that affected individuals have no deficiencies in growth or development, no risk for cerebrovascular accident, no evidence of low physical performance or higher risk for perioperative complications, and have normal life expectancy.³⁻⁶

Complications of sickle cell trait are rare but well documented, including hematuria, isosthenuria, urinary tract infections, compartment syndrome, splenic infarction, and even sudden death. The concern about sickle cell trait and sudden death emanated from over 40 case reports of military recruits.⁷⁻⁹ A comprehensive analysis of unexplained sudden deaths demonstrated a small but convincing increase of such deaths in patients with sickle cell trait.¹⁰

The pathophysiologic sequence that may potentially trigger sickling or rhabdomyolysis in individuals with sickle cell trait is described in Figure 1. Because these individuals are unable to concentrate urine and conserve water in the presence of excessive heat and strenuous exercise, they are prone to develop muscle injury (rhabdomyolysis) as a result of hemoconcentration. Several predisposing factors have been thought to cause muscle injury in these individuals after strenuous exercise. These include high temperature, humidity (by causing dehydration), altitude (higher chance of sickling of

Table 2. Tissue Pressures in Patient's Muscle Groups (mmHg)

Right Upper Extremity	
Dorsal	78
Volar	52
Left Upper Extremity	
Dorsal	41
Volar	38
Right Lower Extremity	
Dorsal	38
Volar	32
Left Lower Extremity	
Dorsal	78
Volar	52
Normal interstitial tissue pressures range from 0 to 15 mmHg	

erythrocytes), aging, deconditioning, presence of higher percentage of HbS, and recent viral infections.^{4,7-9,11} But it is still not clear why some individuals with sickle cell trait with the same degree of exercise and similar acclimatization conditions develop muscle injury or die and others do not. This raises the suggestion that some individuals with sickle cell trait develop excessive sickling of erythrocytes in the face of strenuous exercise with or without the above-mentioned predisposing factors. Our patient's muscle biopsy revealed extensive muscle necrosis and sickling of erythrocytes in the vessels (Figure 2). Excessive sickling of erythrocytes is probably the initiating factor in muscle injury and its consequences. However, it is difficult to say how much sickling of erythrocytes contributed to our patient's outcome, as sickled erythrocytes can be found routinely in autopsies of individuals who have died from a variety of causes and were known to have sickle cell trait. However, the muscle biopsy was performed during the surgery while his oxygenation was well controlled with mechanical ventilation as opposed to post-mortem studies where hypoxemia and anoxia would cause sickling.

Compartment syndrome, one of the orthopedic emergencies, is a condition of increased pressure within a limited space that results in compromised tissue perfusion and, ultimately, necrosis.¹² It can develop anywhere skeletal muscle is surrounded by substantial fascia and is classified as acute or chronic depending on the cause of the increased pressure and the duration of the symptoms. The most common causes of acute compartment syndrome are fractures, soft tissue trauma, arterial injury, and burns. Exercise can increase muscle volume by as much as 20%, causing an increase in pressure in a noncompliant compartment. Strenuous exercise may



Figure 1. Muscle injury in sickle cell trait.

cause compartment syndrome in limited muscle groups. Sickle cell trait may also predispose to compartment syndrome.¹³

The most important symptom is pain that is out of proportion to what can be expected with the injury. Others are paresthesia, pallor, paresis, and lack of pulse (4 Ps). The diagnosis may be delayed in some patients with altered consciousness. If compartment syndrome is suspected and adequate examination cannot be performed, compartment pressure levels of muscles should be measured. The pressure can be measured by using one of the commercially available tonometers (ie Stryker, ACE). With the patient under local anesthesia, the catheter of tonometer is inserted into the appropriate compartment and the pressure is measured. If compartmental pressures are greater than 30mmHg in the presence

of the appropriate clinical setting, or when compartment pressure is 40 mmHg below the mean arterial pressure¹⁵ immediate fasciotomy is indicated. Normal interstitial tissue pressures range from 0 to 15 mmHg.

Severe exertion can lead to rhabdomyolysis, limited compartment syndrome, and renal failure in healthy individuals without sickle cell trait.^{16,17} However, multiple compartment syndromes are extremely rare in normal individuals or those with sickle cell trait with exercise.¹³

Multiple compartment syndromes may occur in conjunction with underlying problems including multiple fractures, or as a final stage of chronic intermittent compartment insufficiency.

Our case is an example of a fatal complication of sickle cell trait. We believe that his death was secondary to hyperkalemia, DIC, and massive bleeding from fas-

ciotomy sites. Sick cell trait may be considered a potentially fatal condition in proper settings. We propose that all individuals, especially the African American population, should be screened for sick cell trait before they participate in any competitive sports or military training. Those who have sick cell trait should be aware about the activities that may predispose them to excessive erythrocyte sickling and be alert about the early warning symptoms and signs of complications such as hematuria, splenic infarct, and compartment syndrome. Adequate hydration before and during the strenuous activities and avoidance of excessive heat would be some basic measures. Increased awareness in predisposed populations and physicians working in emergency rooms and intensive care units may prevent significant morbidity and mortality associated with this condition. Once developed, prompt early recognition, aggressive therapy, and multidisciplinary approach involving intensive care physicians, trauma or orthopedic surgeons, hematologists, and nephrologists may prove to be lifesaving. Individuals who experience any of the complications of sick cell trait should probably discontinue similar activities in the future.

SUMMARY

Multiple compartment syndrome is a rare complication of sick cell trait. The most likely explanation of this complication is excessive sickling leading to tissue edema and necrosis. Physicians' awareness, early diagnosis, and timely aggressive management with release of compartments will prevent morbidity and mortality.

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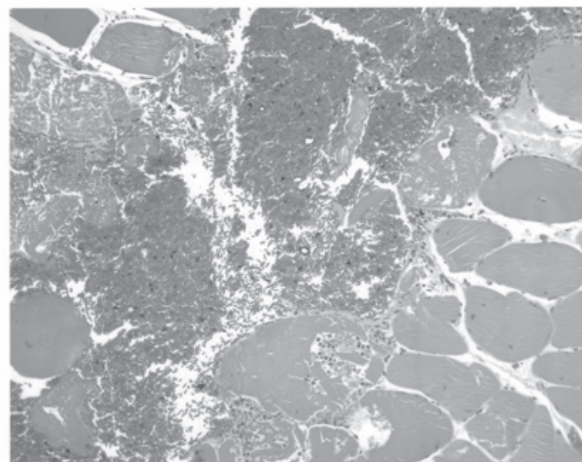


Figure 2. Muscle (thigh) biopsy showing extensive muscle necrosis and intravascular erythrocytes sickling.

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