

## CASE REPORT

# A rare case of compartment syndrome and myonecrosis in a patient with hemoglobin SC disease

Muntadhar Al Moosawi<sup>1</sup>  | Hatoon Ezzat<sup>2</sup>

<sup>1</sup>Department of Pathology and Laboratory Medicine, University of British Columbia, Vancouver, BC, Canada

<sup>2</sup>Division of Hematology, St. Paul's Hospital, UBC, Vancouver, BC, Canada

**Correspondence**

Muntadhar Al Moosawi, Department of Pathology and Laboratory Medicine, University of British Columbia, Vancouver, BC, Canada.

Email: muntadhar.almoosawi@vch.ca

**Abstract**

Myonecrosis and compartment syndrome are rarely seen in sickle cell disease (SCD), and they have not been previously reported in HbSC disease. This case can potentially be recognized as the first case of a patient with HbSC presenting with spontaneous myonecrosis and compartment syndrome.

**KEYWORDS**

compartment syndrome, HbSC, hemoglobin SC, myonecrosis, sickle cell disease

## 1 | INTRODUCTION

Sickle cell anemia (SCA) is an inherited blood disorder caused by a single nucleotide substitution (A to T) in the codon of the sixth amino acid at the  $\beta$ -globin gene (*HBB*) in chromosome 11, resulting in a conversion of glutamic acid residue to a valine residue (Glu6Val). Consequently, the mutation leads to the synthesis of the well-known abnormal and unstable hemoglobin S (HbS). The substitution of a glutamic acid with lysine at the same position of the  $\beta$ -globin gene results in the formation of hemoglobin C (HbC), which is a milder variant of sickle cell disease. Hemoglobin SC disease occurs as a result of the coinheritance of one HbS allele and another HbC allele.<sup>1</sup> In the US, HbSC accounts for nearly 30% of patients with SCD with an incidence of 1 in every 6,173 newborns.<sup>2</sup> However, the disease is more prevalent in parts of West Africa, where HbSC accounts for more than 50% of SCD.<sup>3</sup>

HbSC disease has unique pathophysiological characteristics. The proportions of HbS and HbC in the red blood cells (RBCs) of patients with HbSC is roughly equal.<sup>4</sup> Due to alterations of RBC membrane, HbC has a particular tendency to crystallization and loss of  $K^+$  and water, causing intracellular dehydration, which leads to an increase in HbS polymerization in the cytoplasm of HbSC cells. This biochemical

process is the main reason for the clinical manifestation of HbSC patients.<sup>5</sup>

Hemolysis is less intense in HbSC disease as compared with homozygous HbSS, but the presence of mild hemolysis results in mild chronic anemia. Nevertheless, the mean hemoglobin concentration in patients with HbSC tends to be higher than that of HbSS, and the erythrocyte lifespan is twice that of HbSS (29 vs 15 days) with the RBC indices indicating low mean cell volume (MCV) in most cases.<sup>6</sup> The blood film shows characteristic findings including boat-shaped cells, and sometimes, cells with straight-edged, six-sided hemoglobin C crystals can be seen. Characteristic HbSC poikilocytes can also present in the blood film along with numerous target cells, but irreversibly sickled cells are rare.

The clinical phenotype of patients with HbSC is unique, with painful vaso-occlusive crises being less frequent compared with SCA. However, proliferative retinopathy is seen more commonly.<sup>7</sup>

Myonecrosis has not been previously described in patient with HbSC, and in the field of hemoglobinopathy; only 15 cases of myonecrosis are reported in the literature, all of which occurred in patients with HbSS. In SCD, this phenomenon is believed to be caused by muscle hypoxia due to vaso-occlusion by irreversibly sickled RBCs. On the other hand, muscle hypoxia leading to exertional rhabdomyolysis

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has been well described in patients with sickle cell trait (SCT). In a retrospective cohort study of approximately 48 thousand soldiers in the U.S army, individuals with SCT had 54% higher risk of developing rhabdomyolysis compared to individuals with normal genotype.<sup>8</sup> This potentially lethal complication is caused by severe breakdown of skeletal muscle tissue that is precipitated by strenuous physical exertion, leading to systemic manifestations.<sup>9</sup> Furthermore, analysis of post activity changes in SCT individuals showed marginally diminished RBC deformability, hyperviscosity, and increased concentration of circulating adhesion molecules.<sup>10</sup> The alteration in vascular cell adhesion mechanisms and the vascular endothelium damage in SCT carriers, if extensive, can affect muscle microcirculation, causing ischemia and rhabdomyolysis. Hyperkalemia as a result of the release of intracellular potassium is suspected to cause cardiac arrhythmias and death.<sup>11-13</sup>

We report a case of a 20-year-old man who is known to have HbSC disease with mild clinical phenotype presenting to the emergency department (ED) with bilateral leg swelling and pain that was more pronounced in the left leg, and was associated with numbness and weakness of mainly the distal part of the left foot. The patient was eventually diagnosed with nontraumatic compartment syndrome and myonecrosis.

Using EMBASE and MEDLINE databases, we found no previous reports of compartment syndrome and myonecrosis in patients with HbSC disease. Hence, this is probably the first report of this condition in this patient population.

## 2 | CASE REPORT

### 2.1 | History and physical examination

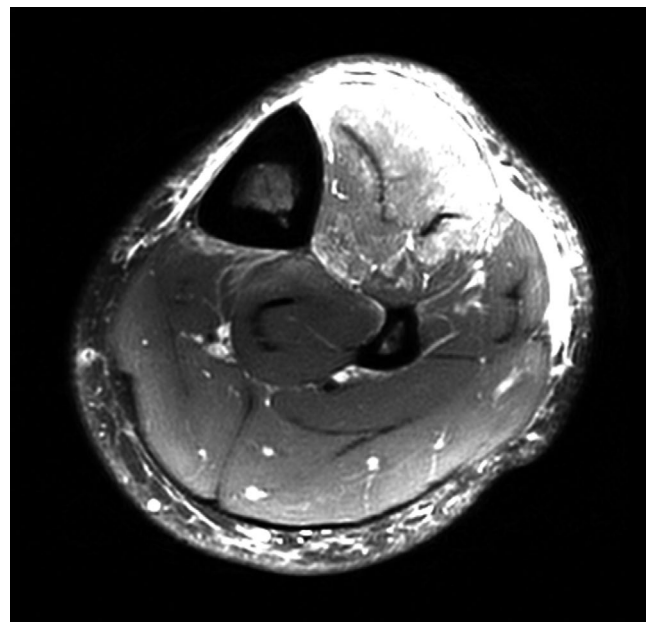
This is a 20-year-old man with a known history of hemoglobin SC disease and a previous nontraumatic compartment syndrome involving the anterior compartment of the right leg, which resolved spontaneously without medical or surgical intervention. This incident resulted in mild sensory loss of the first webspace of the right foot. Approximately 2 years after the first episode, the patient presented at the ED after a sudden onset of bilateral shin pain that was more pronounced at the mediolateral aspect of the left shin and was accompanied by weakness and decreased sensation in the distal part of the left foot. The pain in the right leg subsided before the patient's arrival at ED.

The patient had a mild clinical phenotype with fewer than five episodes of painful vaso-occlusive crises during his lifetime and no other sickle cell complications. The left leg was swollen, tense, and tender with power of 1 to 2 of 5 in dorsiflexion, 2 of 5 plantar flexion, 2 of 5 inversion, and 2 of 5 eversion. A decreased light touch, pinprick, and temperature sensation were noted in the first webspace of the left foot.

The pressure measurement in the anterior compartment of the left foot was over 125 mm Hg (normal is < 10 mm Hg).

### 2.2 | Investigations and clinical management

Microcytic anemia was noted in the complete blood count (CBC) with hemoglobin just below the patient's baseline (Hb 103 g/L, MCV 66 fL) and signs of hemolysis explained by the patient's baseline of mild chronic hemolysis (reticulocyte count  $170 \times 10^9/L$ , haptoglobin <0.07 g/L [normal is 0.3-2.0], lactate dehydrogenase 373 U/L [normal is 115-230]). High-performance liquid chromatography (HPLC) was done 3 weeks before the incident and demonstrated the presence of HbS at 47%, HbC at 45%, and a small proportion of HbF

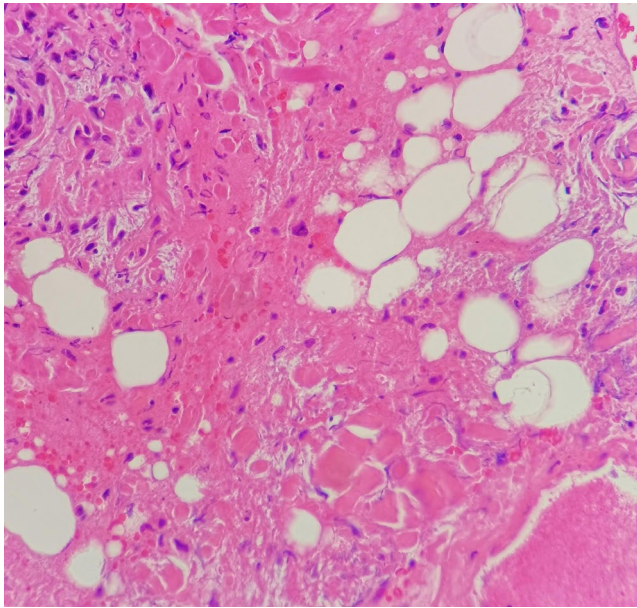


**FIGURE 1** Magnetic resonance imaging; fluid sensitive sequence showing pathological high signal consistent with tissue edema. Low signal on T1 and mild hyperintensity on T2 weighed images were also observed



**FIGURE 2** Fasciotomy wound was allowed to heal with support of vacuum dressing

accounting for only 1.5%. Creatine kinase (CK) was elevated at 4,955 U/L at presentation (normal is < 165 U/L), suggesting underlying rhabdomyolysis. An urgent magnetic resonance imaging (MRI) of the left leg demonstrated findings in



**FIGURE 3** Anterior tibialis muscle biopsy demonstrating muscle necrosis and inflammation; H&E stain; original magnification  $\times 40$

favor of rhabdomyolysis and myonecrosis with signs of compartment syndrome (Figure 1) warranting urgent surgical intervention. Successful and uncomplicated left anterior and lateral compartment fasciotomies were performed (Figure 2), and a tissue from the left anterior tibialis muscle confirmed the diagnosis of myonecrosis (Figure 3). The wound was allowed to heal for 16 days after which a fasciotomy closure using a split-thickness skin graft was performed.

Over the course of 3 weeks of hospital admission, creatine kinase significantly increased, reaching a peak of 22 000 U/L on the third day of admission and then decreased steadily and normalized over a week. The kidney functions were overall preserved, except for a transient mild acute kidney injury that lasted approximately 5 days. Only, one unit of packed red cells was transfused over the course of hospitalization as a preoperative preparation when the hemoglobin was 73 g/L. Aggressive hydration and pain management were the mainstay of treatment and were maintained until patient's full recovery.

### 3 | DISCUSSION

Myonecrosis and compartment syndrome are known but rare complications of SCA. To date, there have been 16 reported

**TABLE 1** Reported cases of myonecrosis in patients with sickle cell disease

Age (years)	Sex	Disease genotype	Bilateral or unilateral involvement	Muscles involved	Reference
28	F	Homozygous SS	Bilateral	Deltoids and triceps	14
24	F	Homozygous SS	Bilateral	Thighs	15
30	M	Homozygous SS	Bilateral	Deltoids and quadriceps	16
22	M	Homozygous SS	Bilateral	Deltoids and thighs	16
26	F	Homozygous SS	Bilateral	Thighs and knees	17
4	M	Homozygous SS	Unilateral	Right thigh and knee	17
44	F	Homozygous SS	Bilateral	Deltoids	18
36	M	Homozygous SS	Bilateral	Quadriceps	18
26	M	Homozygous SS	Bilateral	Quadriceps	18
30	M	Homozygous SS	Bilateral	Thighs	19
42	F	Homozygous SS	Unilateral	Left elbow	20
24	M	Homozygous SS	Unilateral	Left leg	21
28	M	Homozygous SS	Unilateral	Left thigh	22
30	M	Homozygous SS	Unilateral	Plantar muscles	23
27	M	Homozygous SS	Unilateral	Left plantar muscles	24
20	M	Compound heterozygous S/C	Unilateral	Left leg	Our case

cases of sickle cell myonecrosis, including this case. All of the previously reported cases occurred in patients with HbSS genotype. Details of the previously reported cases and this case are shown in Table 1.

The clinical presentation of this case is consistent with that of HbSS cases in many ways. The pain and neurologic symptoms are characteristic of muscle and nerve injury seen in HbSS cases with similar complication. Although presented with bilateral symptoms, the condition involved the patient's left lower limb, particularly the anterior and lateral compartments of the left lower leg. However, this problem has occurred in the deltoid and quadriceps muscle groups in some of the reported cases.<sup>14</sup> Creatine kinase was significantly elevated, a finding that is not usually observed in myonecrosis and usually indicates an underlying rhabdomyolysis, which was the case in our patient. Tajeja et al reported only three patients with elevated CK levels.<sup>14</sup> MRI is a key diagnostic tool in cases of myonecrosis with characteristic findings observed in the form of enhancement of T1 images, and an increased signal intensity of T2-weighted images is observed.<sup>15</sup> A muscle biopsy is the confirmatory diagnostic procedure and because the muscle necrosis can be focal and involve a small area, a large biopsy is necessary to make the diagnosis.

No standards are available for the management of myonecrosis in this group of patients, given the rarity of this condition. However, compartment syndrome generally requires urgent surgical intervention. Four weeks after the patient's presentation, an electromyogram revealed a significant injury to the left deep peroneal nerve, although the superficial peroneal nerve was spared for the most part. The condition was debilitating, but with the support of physiotherapy, the patient slowly regained mobility and was able to walk independently.

## 4 | CONCLUSION

Myonecrosis has been previously reported in patients with HbSS. This can potentially be recognized as the first report of this condition in HbSC disease. The mechanism and pathophysiology of this condition are not very well understood in this group of patients. Prompt diagnosis and management are warranted to prevent long-term debilitation. More research is required in this area to help further understand the pathophysiology of myonecrosis in patients with SCD.

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## CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

## AUTHOR CONTRIBUTIONS

Muntadhar Al Moosawi: conceptualized the data and performed writing of the original draft. Hatoon Ezzat: reviewed and edited the data.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

## ORCID

Muntadhar Al Moosawi  <https://orcid.org/0000-0002-4350-6218>

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