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Myonecrosis in Sickle Cell Anemia: Case Study

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Data Collection B
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Data Interpretation D
Manuscript Preparation E
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Conflict of interest: None declared

Patient: **Male, 27**
Final Diagnosis: **Myonecrosis of sickle cell anaemia**
Symptoms: **Pain • redness to feet • swelling foot**
Medication: **—**
Clinical Procedure: **MRI**
Specialty: **Podiatry**

Objective: **Rare disease**





Background: Myonecrosis is one of the more poorly studied, painful manifestations of sickle cell crisis. Medical literature is sparse detailing the manifestations and management of such symptoms. In myonecrosis, red cells containing sickle hemoglobin become rigid, resulting in reduced blood flow and myonecrosis.

Case Report: We present a case study of a patient in sickle cell crisis with an episode of acute pain and swelling to the intrinsic muscles of the foot as a prominent feature of the crises. Although muscle biopsy is considered the gold standard for the diagnosis of myositis or myonecrosis, a low intensity signal on T1 and high intensity signal on T2 at the affected muscle belly can be as conclusive as imaging studies. In an actively sickling patient any invasive intervention should be avoided as it can result in ischemic necrosis of the tissues, due to interruption of capillary flow in end-arteries.

Conclusions: Early recognition is critical in sickle cell disease management, allowing for prompt and aggressive fluid resuscitation which remains a cornerstone in the management of most sickle cell vaso-occlusive crises. In this instance, off loading the extremity and early fluid resuscitation resolved the pain and swelling and prevented myonecrosis.

MeSH Keywords: **Anemia, Sickle Cell • Foot • Myositis**

Full-text PDF: <http://www.amjcaserep.com/abstract/index/idArt/900538>

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Background

Sickle hemoglobin is a mutant hemoglobin in which valine has been substituted for the glutamic acid normally at the sixth amino acid of the β -globin chain. This hemoglobin polymerizes and becomes poorly soluble when the oxygen tension is lowered, and red cells that contain this hemoglobin become distorted and rigid [1]. These rigid SS-RBCs bind to post capillary venules, which leads to vascular trapping and reduced blood flow, precipitating vaso-occlusive crisis which can result in myonecrosis [2]. Timely identification and treatment remains critical in preventing debilitating short- and long-term sequelae. Literature on sickle cell myonecrosis remains sparse and is confined to scattered case reports and series. In a review of the literature, only 13 publications were found on the topic. This may be secondary to the fact that sickle cell myonecrosis is a poorly recognized complication amongst diagnosing physicians, and signs and symptoms may not always be corroborated by positive muscle injury biomarkers [3].

Case Report

In our case, a 27-year-old African American male presented with sickle cell anemia myonecrosis involving the plantar musculature. He presented to the emergency department (ED) complaining of pain and swelling involving the plantar aspect of his left foot. The foot pain had started three weeks prior, and was not alleviated with over-the-counter pain medications. At that time he had presented to an outside hospital, where an aspiration of the swollen area was performed and infection work-up yielded negative results. At that time, no purulence or other signs of infection were noted in the aspirate, but he was placed on empiric antibiotic therapy. The patient's pain got noticeably worse over the next few days and was again exacerbated by ambulation. Worsening pain and a new nodular mass on the underside of his left foot prompted him to present to our institution's ED. On examination, vitals were found to be stable and examination was remarkable for a nodular ill-defined mass on the plantar aspect of his left foot. The lesion was tender to palpation but was not warm to touch and there was no evident overlying erythema or surrounding edema. In addition, there were no signs of compartment syndrome. Labs were remarkable for Hb: 6.7 g/dL, LDH 689 IU/L. The peripheral smear showed extensive anisocytosis and poikilocytosis without any schistocytosis. The following labs were within normal limits: WBC, platelets, cell differential CRP, CK, UA, and iron saturations. Hemoglobin electrophoresis pattern revealed hemoglobin (Hb)A₂ 3.2%, HbF 6.6%, and HbS 90.2%. The nodule was not drained in this case and it was decided to be treated the patient conservatively. An MRI of the left lower extremity was ordered and the finding noted a prominent flexor digitorum brevis muscle bellies with surrounding edema and particularly discrete enhancement at

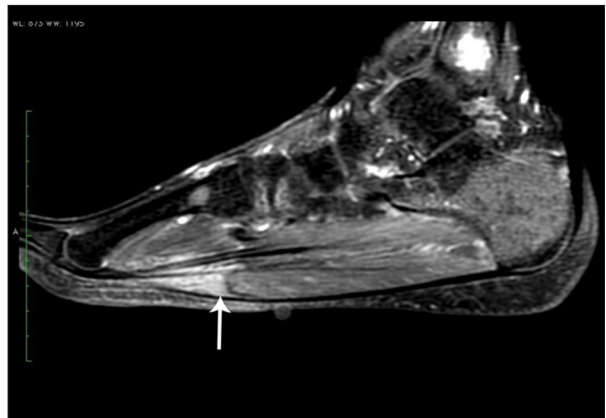


Figure 1. Sagittal post contrast T1 fat saturation image. Sagittal post contrast T1 fat saturation images demonstrated focal enhancement within the plantar muscles of the forefoot, specifically within flexor digitorum and the lumbricales. In addition, there was a focal patchy abnormal increased signal within the calcaneus and distal fibula.

levels of flexor tendons (Figure 1). No focal fluid collection or soft tissue defect was identified. Distinct enhancement at the level of the lumbricales and flexor tendons were best seen on post-contrast axial short axis and long axis images (Figure 2). Sagittal T1 image demonstrated subtle expansion of the plantar forefoot musculature deep to the skin marker (Figure 3). In addition, this image also demonstrated patchy low T1 signal within the calcaneal body and the distal fibula corresponding to marrow changes from long standing sickle cell infarcts (Figure 4).

The primary consideration at this juncture was sickle cell myonecrosis in the clinical setting of vaso-occlusion crisis secondary to active sickling. MRI findings corroborated with clinical suspicion and the authors did not feel this required further biopsy confirmation. Surgical intervention was not warranted as the patient had no evidence of compartment syndrome. Hence the nodule was not drained. Treatment was initiated with intravenous hydration and analgesics for pain control. His symptoms improved over the next three days of admission after which he was discharged and asked to follow-up as an outpatient. The patient was followed every three weeks for a total of nine weeks post hospital visit.

Discussion

The clinical presentation of this case is consistent with one of the known, but rare manifestations of sickle cell crisis. Soft tissue, in particular muscle vaso-occlusive disease, is often overlooked in patients with sickle cell anemia. This is probably more common than recognized [4]. The MRI results and the clinical presentation of muscle inflammation especially after exertion,

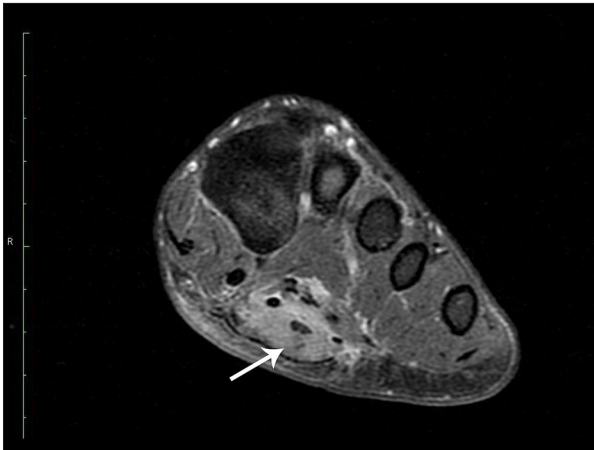


Figure 2. Short axis post contrast t1 fat sat image. Short axis post contrast T1 fat saturated image showed focal enhancement within the plantar musculature, specifically the flexor digitorum and the lumbricales. The quadratus plantae muscle appears spared.

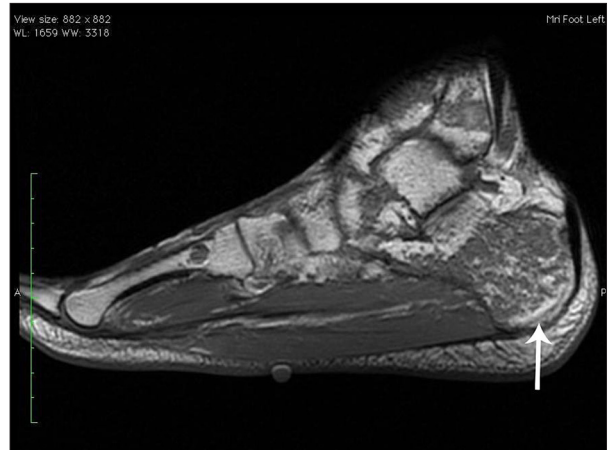


Figure 4. Sagittal T1. Patchy low T1 signal within the calcaneal body and the distal fibula corresponding to marrow changes from long standing sickle cell infarcts.

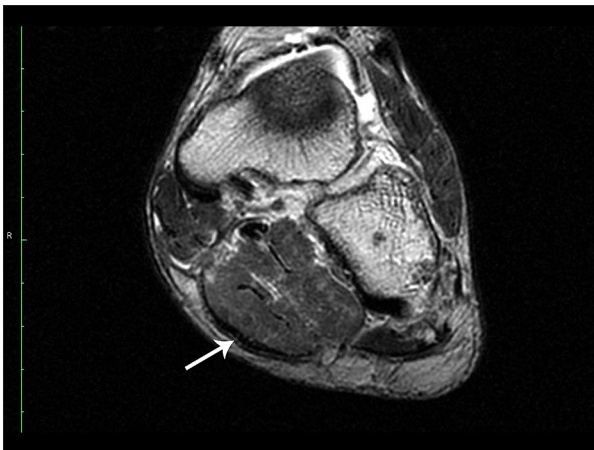


Figure 3. Short axis T1 image. The short axis T1 image demonstrated an expansile appearance of the flexor digitorum and lumbrical muscles.

and pain on range of motion is characteristic of myositis with possible myonecrosis. If sickle cell crisis is associated with vascular insufficiency to the muscles, one would expect to find diminished warmth to the area which was consistent with the presentation of this patient [5]. Our patient did not have elevated CK levels, a finding which goes in favor of myonecrosis, which was also described by Tageja et al. where only three patients had elevated CK/LDH levels and the remaining three did not [3]. A similar case was described by Rubio et al. where the patient was a heterozygous carrier of sickle cell anemia, who presented with normal CK levels and due to non-conclusive etiologic study, an MRI was performed with a diagnosis of fasciitis [4].

Sickling occurs as a result of polymerization of hemoglobin S when erythrocytes are exposed to acidic environments increased

osmolality, dehydration, and hyperthermia [6,7]. This patient most likely had homozygous sickle disease based on the electrophoresis pattern revealing HbA₂ of 3.2%. Although electrophoretic patterns in homozygous sickle cell disease ($\beta^s\beta^s$) are similar to sickle cell-beta⁰ Thalassemia ($\beta^s\beta^0$) with no HbA and up to 90% HbS, HbA₂ levels are typically <3.5% in homozygous sickle cell disease and this helps differentiate sickle cell disease from sickle cell variant [8]. Also, sickle cell disease with hemoglobinopathy variant syndromes tend to present with microcytosis compared to the normocytic picture expected in pure sickle cell disease [9]. The relative macrocytosis of our patient's peripheral smear sample is explained by the massive reactive reticulocytosis [10]. Of note, greater sickling is known to occur in individuals when HbS levels exceed 40% [11].

A proposed model adapted from Kerle [12] states conditions which shift the hemoglobin oxygenation curve to the right, i.e., when erythrocytes are exposed to acidic environments, increased osmolality, dehydration and hyperthermia result in polymerization of HbS [6,7]. These events can initiate a cascade of events which can lead to tissue necrosis or even death.

To date, there have been 13 cases of myonecrosis reported [3]. Almost all reported cases involved sickle cell myonecrosis affecting the large proximal and distal musculature. To our knowledge, the case presented here is only the second case of sickle cell myonecrosis involving the plantar muscles [13]. Pain out of proportion and pain on movement of associated muscles is characteristic of myonecrosis. If myonecrosis is left untreated, progressive necrosis of myocytes can lead to muscle atrophy, fibrosis, contractures, and finally liquefactive necrosis can occur resulting in the formation of a sterile abscess. The latter was seen on initial presentation to the outside hospital in this case. These abscesses are typically non purulent on aspiration or drainage [14]. It is debatable if these abscesses

require drainage given the risk of furthering ischemic necrosis from surgical intervention during an active phase of vaso-occlusive sickling. Other atypical features may include compartment syndrome from myoedema which is one of the few indications necessitating surgical intervention [13]. Another differential of this presentation could include fasciitis which has been described by Rubio et al. where the patient with sickle cell trait presented with acute pain in her lower extremities and due to non-conclusive etiology, an MRI was performed which revealed perifascial hyperintensity with no significant signal changes or focal muscular hypertrophy [4]. In our case, prominent flexor digitorum brevis was noted on MRI, a phenomenon which could be related to restricted blood flow, as cited by Yasuda et al. [15]. Although poorly understood it was reported Fry et al. that “blood flow restriction stimulates the anabolic cell signaling mammalian target of mTOR pathway, resulting in increased muscle protein synthesis” [16]. Non-specific pathological findings of myonecrosis correspond to MRI findings of mild to moderate low intensity on T1 and hyperintensity on T2 [17,18]. Since the MRI was conclusive of myonecrosis in our case, and no symptoms of compartment syndrome were present, a muscle biopsy was not performed. The optimal management of this syndrome has not yet been determined, but an early diagnosis and involvement of physical therapy seems crucial in preventing disabling sequelae [3].

Conclusions

Myonecrosis in foot muscles secondary to sickle cell crisis is a rare presentation and could lead to muscle atrophy if left untreated. Proper hydration and strict non-weight bearing of the

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Conflicts of interest

I have no conflicts of interest to declare.