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T2-blackout effect on DWI as a sign of early bone infarct and sequestration in a patient with sickle cell disease☆

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ABSTRACT

Differentiation of bone infarct from osteomyelitis is one of the most challenging issues in the evaluation of acute bone pain in sickle cell patients. The imaging modalities that are currently being used for assessment of bone marrow in this population have several limitations. We present a case of an 18-year-old male with a history of sickle cell disease, who was transferred to our emergency department with progressively severe headache and jaw pain for one-week. Initial evaluation was concerning for osteomyelitis and epidural abscess formation. Due to the lack of response to the current antibiotic treatment, he was transferred to our institution. On further review of the images, atypical DWI findings that were identified in the early phase of presentation helped to differentiate bone infarct from osteomyelitis. Radiologists should be aware of this phenomenon, as it can help in the differentiation between these two pathologies and can affect the patient's management overall.

1. Introduction

Sickle cell disease (SCD) is an inherited hematological disorder by which deformed red blood cells circulate throughout the body with the potential of adversely affecting any organ system. It can present with vaso-occlusion, chronic hemolytic anemia, and even infections as a result of functional asplenia, though the clinical manifestation can vary greatly [1]. Acute bone pain is a common complication of SCD caused by vaso-occlusive crisis or acute infarction (AI), but it can also be due to acute osteomyelitis (AO). Both conditions have an almost identical presentation. Image-based diagnosis of acute bone pain in these children to differentiate AI from AO is still a challenge for radiologists [2,3]. However, early diagnosis and specific therapy is crucial in preventing unnecessary empirical antibiotic therapy and provides advantages such as fewer investigations, shorter hospital stays, lower community microbial resistance to antibiotics, and significant cost savings [2]. The purpose of this paper is to contribute to the discussion of a possible mechanism of bone infarcts in SCD and to help differentiate AI from AO with imaging.

2. Case report

An 18-year-old male was initially admitted to the emergency department complaining of a severe headache, jaw pain, and fever. The symptoms appeared one week previously but had progressively worsened with time. The headache was located on the right parieto-temporal side of the head and characterized as pulsating with an intermittent stabbing pain. The patient also reported a loose tooth on the right side and mild facial swelling that occurred during the same time. No other signs were observed.

The initial CT scan of the brain taken 2 h after ED presentation revealed right frontal extra-axial collection with subtle enhancement, which was interpreted as secondary to an epidural empyema, along with thickening of the calvarium (Fig. 1). He was started on Vancomycin and Zosyn as a result. Blood cultures were taken and were negative for growth of aerobic and anaerobic organisms. Lumbar puncture showed cerebrospinal fluid (CSF) that was clear and colorless in appearance, contained 9 RBC/μL, 1 WBC/μL, glucose 80 mg/dL, protein 20.6 mg/dL, had no growth of organisms, and was negative for both HSV and Enterovirus.

Follow-up MRI conducted 6 h after presentation demonstrated a

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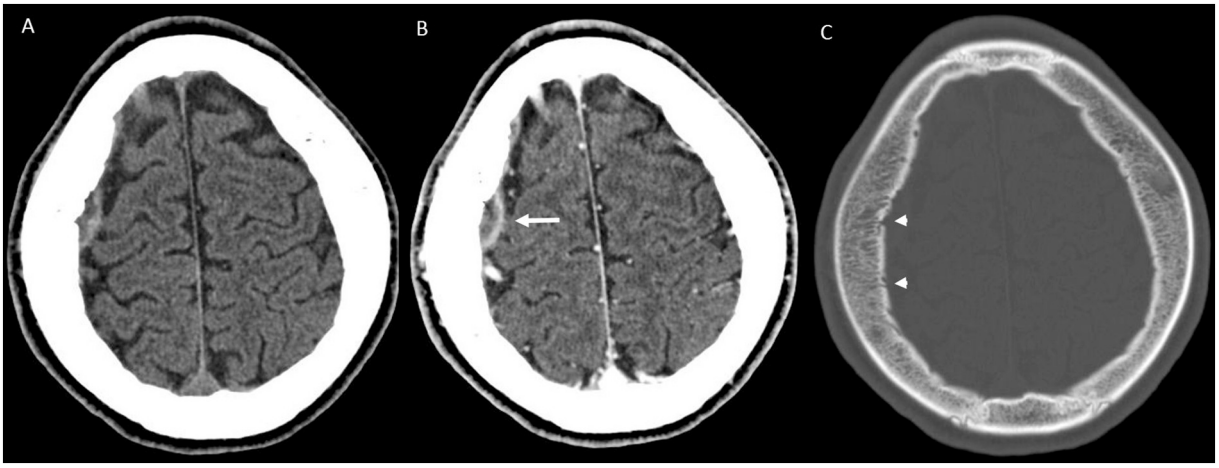

Fig. 1. Axial head CT images from the initial ED presentation with pre-contrast brain window (A), post-contrast brain window (B) and bone window (C) demonstrate small iso/hypodense epidural collection with peripheral enhancement (white arrow). There is diffuse thickening of the calvarium with areas of focal bony dehiscence along the inner table (arrowheads).

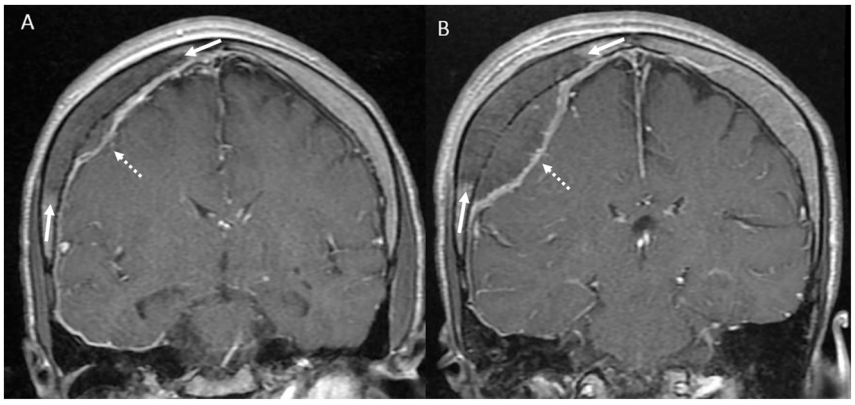

Fig. 2. Coronal T1 weighted contrast enhanced follow-up MRI at 6 h after ED presentation (A) demonstrates a 1.8 cm right parietal non-enhancing epidural collection with dural thickening and enhancement (dashed arrow), causing mild mass affect upon the adjacent brain. Subsequent coronal post-contrast T1 weighted MRI 3 days later (B) demonstrates significant increase in size of the lesion, causing further mass effect upon the adjacent brain parenchyma. There is diffuse calvarial thickening with focal non-enhancing bone marrow in the adjacent right frontoparietal bone (arrows).

1.8 cm right parietal non-enhancing extra axial collection with dural enhancement that was causing mild mass affect upon the adjacent brain without significant midline shift (Fig. 2). However, subsequent brain MRI 3 days later demonstrated significant increase in size of the lesion, causing further mass effect upon the adjacent brain parenchyma (Fig. 2). For this reason, the patient was transferred to our institution.

On admission, he had normal vital signs except for a low-grade fever. Physical and neurological examinations were unremarkable. Blood tests, including a complete blood count, showed WBC 20.8 with 17% neutrophils, H/H 11.5/35.5, and platelets 238. His acute drop in hemoglobin was indicative of a sickle cell crisis, a complication that led to increased reticulocyte production and marrow expansion.

Further review of the early MRI obtained within 6 h from initial presentation demonstrated decreased DWI as well as ADC signal in the right parietal bone with sharp margins. There was a thin hemorrhagic collection with dura enhancement seen after administration of contrast. Although there was increased homogeneous enhancement of the remaining thickened calvarium, there was lack of enhancement in the abnormal right parietal bone marrow (Fig. 3). Follow-up MRI 3 days later demonstrated a significant increase in the hemorrhagic epidural collection with peripheral enhancement, causing an increased mass effect upon the adjacent fronto-parietal lobe. However, there was restricted diffusion within the bone marrow as well as in the adjacent collection, which demonstrated heterogeneous increased DWI signal and decreased ADC signal. There was persistent lack of enhancement in the affected calvarium (Fig. 4). Follow-up MRI 1 week later demonstrated evolution of subacute epidural hematoma and persistent restricted diffusion in the affected calvarium (Fig. 5). However, there was no further growth of the epidural collection. As the size of the hematoma decreased, the headache gradually disappeared. Subsequent physical and neurological examinations were unremarkable and blood investigations were normal. Follow up MRI 4 months later demonstrated complete resolution of the epidural hematoma and collection, as well as normalization of restricted diffusion in the parietal calvarium with mild edema (Fig. 6).

3. Discussion

Bone infarct is the most common cause of hospitalization in children with sickle cell disease [4]. Fifty percent of children homozygous for hemoglobin S experience a vaso-occlusive crisis by 4.9 years old [4]. Bone marrow infarcts frequently affect the extremities, vertebrae, and sternum; however, bone infarcts can occur anywhere within the skeleton with hematopoietically active marrow, including the craniofacial bones [5]. Although infarction is nearly 50 times more common than infection in patients with sickle cell disease, differentiation between acute bone infarct and osteomyelitis based on initial clinical presentation is often challenging as the patient's history, physical examination,

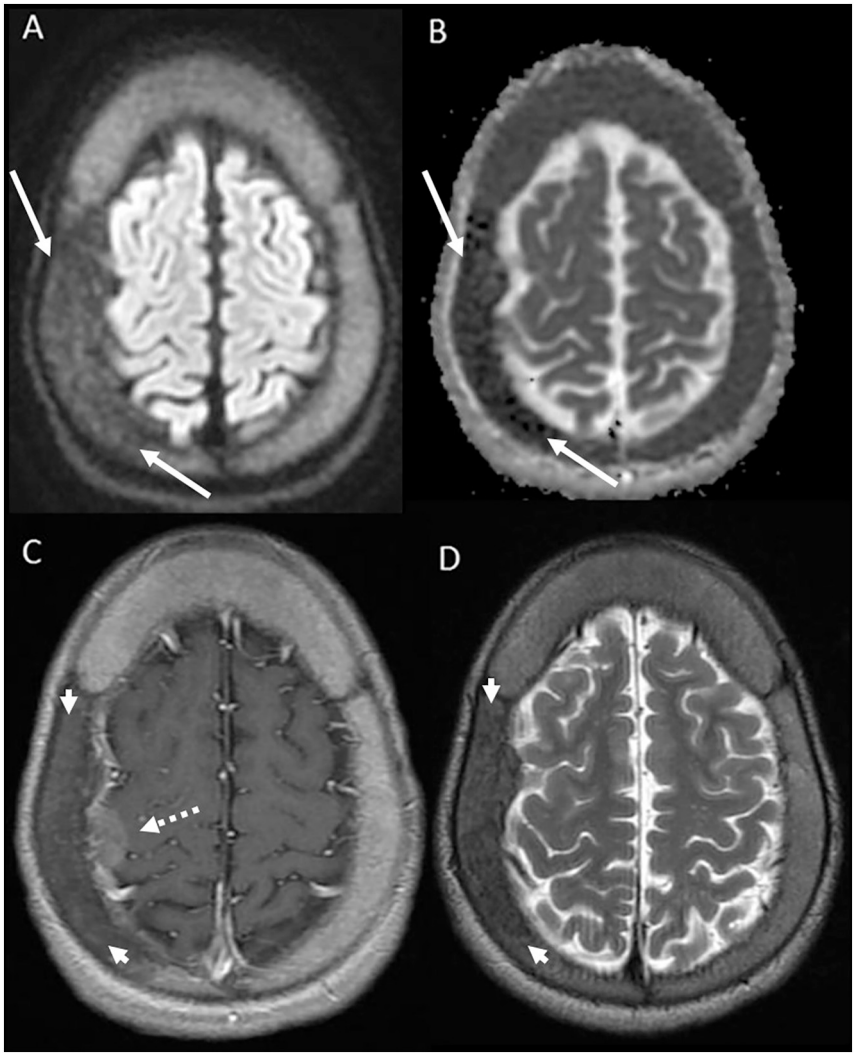

Fig. 3. Axial images from initial MRI within 6 h of presentation demonstrates decreased DWI (A) as well as ADC (B) signal (arrows) in the right parietal bone. There is thin soft tissue prominence underlying the skull abnormality, which demonstrates enhancement after administration of contrast on T1 weighted image (C) (dashed arrow). Although there is homogeneous enhancement of the remaining calvarium, there is lack of enhancement (arrowheads at C) and decreased signal on T2 weighted image (D) in the affected bone marrow (arrowheads).

and laboratory tests cannot reliably differentiate between these two entities. Peripheral blood cultures have limited sensitivities, and bone biopsy is often not performed due to its invasiveness and because it has to be done before administration of antibiotics for highest diagnostic yield of identifying the offending organism.

Unfortunately, the most current imaging techniques are unreliable in the distinction between bone infarct and osteomyelitis in children with SCD [6]. However, early diagnosis is very important, as it allows for early specific therapy, prevents empirical intravenous broad-spectrum antibiotic therapy, reduces the number of diagnostic investigations, morbidity, and duration of hospital stay with significant reduction in costs [2]. Factors predisposing children to bone infarcts are not completely understood, although trauma, systemic infection, fever, stress, dehydration, viral infections, cold weather, and psychological stress are potential triggers for bone infarction [7].

The pathophysiology of vaso-occlusive crises is complex and begins with polymerization of hemoglobin S and sickling of the non-deformable, dense red blood cells which results in endothelial adherence, and microvascular occlusion [8]. This leads to sequestration in the bone marrow spaces in the early phase, which later causes microvascular occlusion. This then promotes local hypoxia and results in increased erythrocyte sickling and sequestration, with the end result of marrow infarction. The similar pathology extends to the overlying cortex, with extravasation of sequestered erythrocytes and/or serum into the subperiosteal space, extra-osseous soft-tissues and inter-muscular fascial planes [3].

Sequestration and bone infarct later activates the inflammatory pathways leading to white blood cell activation and: 1.) an increase of acute phase reactants such as tumor necrosis factor-alpha, interleukin-1, tissue factor and thrombin, 2.) endothelial modulation with expression of P-selectin and subsequent increase in adhesion, and 3.) activation of platelets. There is a parallel inflammatory pathway in AO, which can also result in vascular obstruction and tissue hypoxia. The similar pathophysiology of both entities leads to overlapping clinical symptoms, laboratory abnormalities and imaging findings in later phases [9].

The MRI findings of acute bone infarcts include abnormal bone

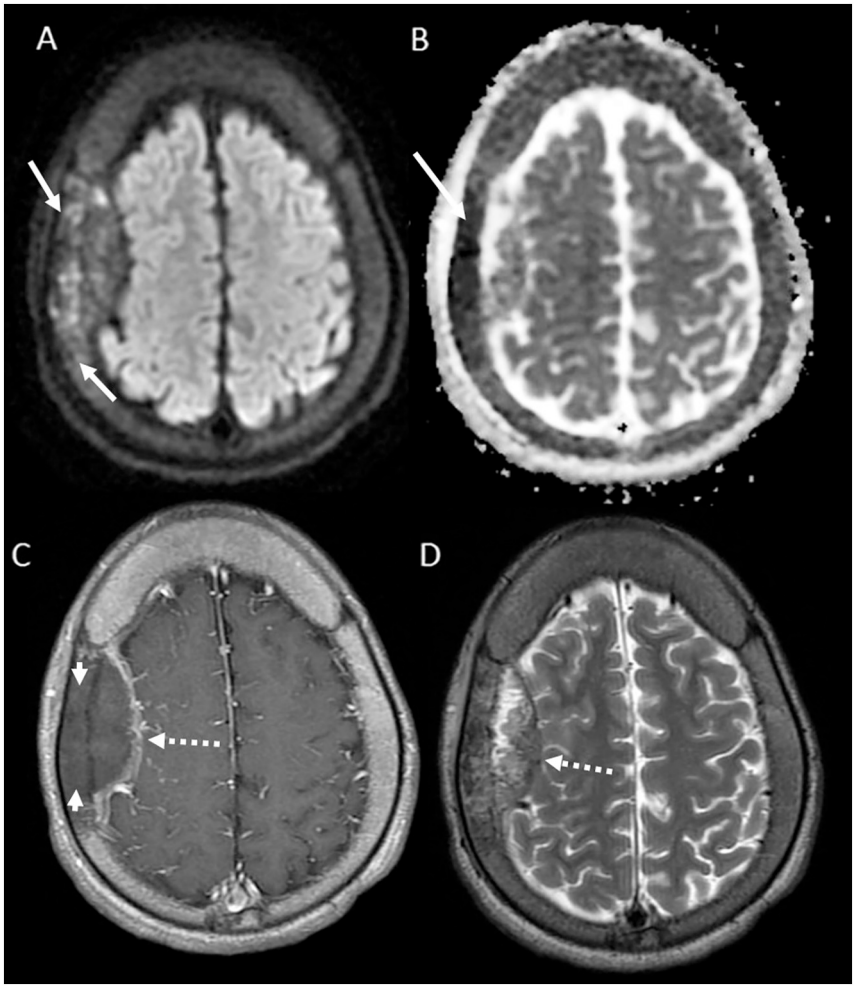

Fig. 4. Follow up contrast enhanced MRI 3 days later including axial DWI (A), ADC (B), postcontrast T1 weighted (C) and T2 weighted (D) sequences were obtained. There is heterogeneous restricted diffusion within the bone marrow with increasing heterogeneous DWI trace (A) signal (arrows) and decreased ADC (B) signal (arrow). There is subjacent epidural hemorrhagic collection with peripheral enhancement (dashed arrows) with persistent lack of enhancement in the affected calvarium (arrowheads).

marrow signal, subperiosteal fluid collections, and heterogeneous enhancement mixed with areas of non-enhancement within the bone marrow [1]. The initial atypical DWI and ADC findings seen within 6 h of first presentation involving the right parietal bone on the presented case that were compatible with T2 blackout effect was likely due to the increased erythrocyte sickling and sequestration within the affected bone marrow, which can be associated with vaso-occlusive crisis. Later, this phenomenon resulted in bone marrow infarction, which then demonstrated as restricted diffusion with DWI hyperintensity and ADC dark signal. Infarcted bone can cause breakage of adjacent inner table, which is the etiology of the increasing epidural hematoma in the presented case. Spontaneous extradural hematoma is a rare complication of sickle cell disease, which should be suspected when patients present with a sudden headache or other signs of intracranial hypertension [10].

Diffusion weighted imaging (DWI) is a method of MRI that exploits the phenomenon of Brownian motion and can provide information about the functional environment of water in tissues [11]. Because diffusion-weighted images are inherently T2 weighted, tissue T2 properties can affect the appearance of diffusion-weighted images independent of tissue diffusivity, potentially resulting in T2 shine-through and T2 blackout effects [12]. Application of DWI in osseous abnormalities has been growing. Both bone infarct and osteomyelitis can cause restricted diffusion with bright DWI signal and dark on ADC signal. However, in the early phases of vaso-occlusive crisis, we believe in 24 h, there is restricted diffusion with dark DWI and T2 signal, which we think is valuable in differentiating bone infarct from an infectious process. Additionally, the poor enhancement of the infarcted bone, geographical pattern of the lesion, paucity of edema on T2, and lack of permeative or erosive changes all support the diagnosis of bone infarction instead of infection.

To the best of our knowledge and literature investigation, early atypical findings of DWI/ADC in the calvarial bone marrow has not been described in vaso-occlusive crisis. DWI T2-blackout is the opposite of the T2-shine-through phenomenon, where lesions with very short T2 (or T2*) values reduce signal intensity in the DW image, potentially masking or destroying its diffusion sensitivity. In extreme cases, even the ADC map calculation will be affected and unreliable. The T2 and The T2*-weighted b0 image has extremely low signal due to the paramagnetic effects of intracellular deoxyhemoglobin. As in our case, due to sickling and sequestration, there is increased number of erythrocytes with intracellular deoxyhemoglobin, causing T2-blackout on DWI.

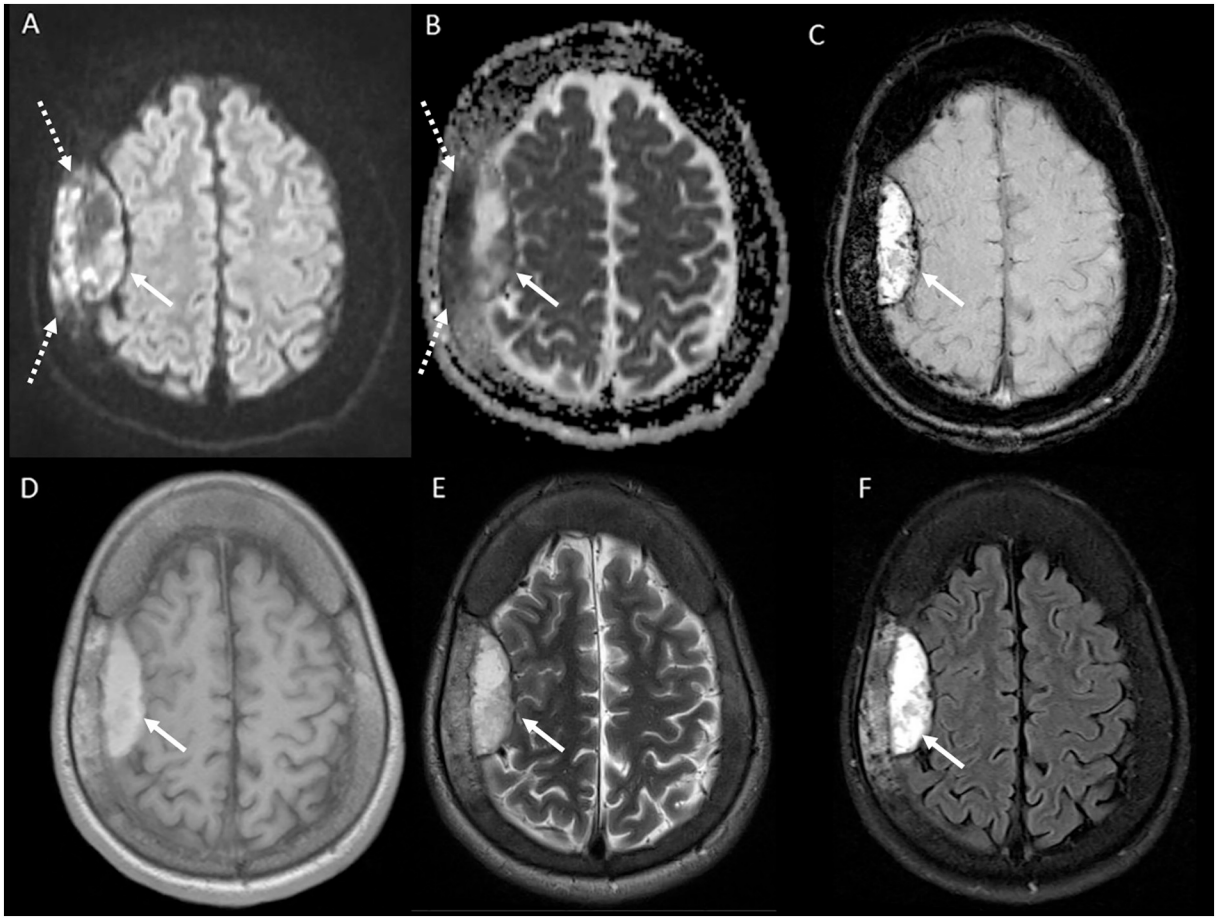

Fig. 5. Follow up MRI one week later including axial DWI (A), ADC (B), SWI (C), T1 weighted (D), T2 weighted (E), and fat saturated T2 FLAIR (F) sequences demonstrate evolution of subacute epidural hematoma (arrows) and persistent heterogeneous restricted diffusion in the affected calvarium (dashed arrows).

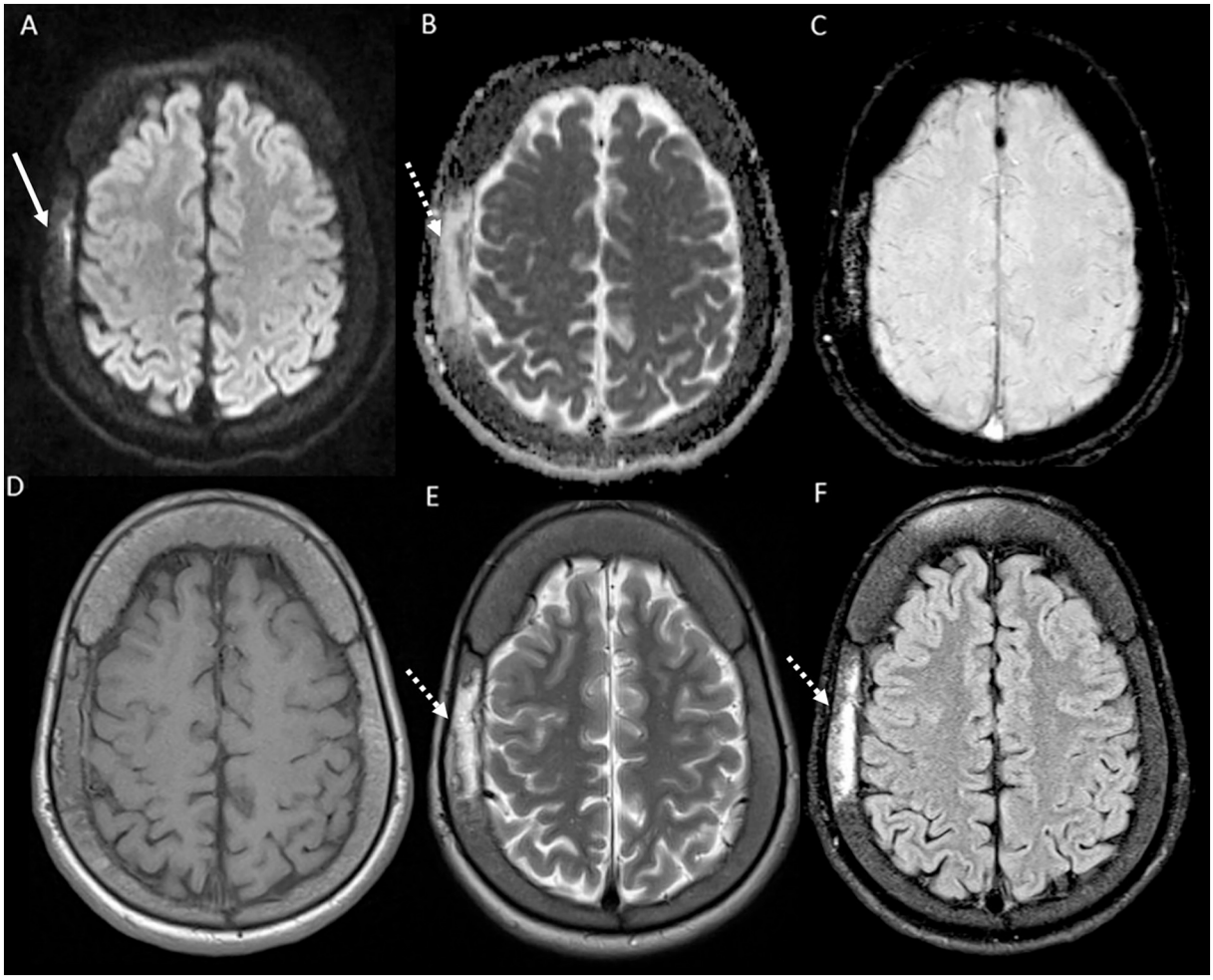

Fig. 6. Follow up MRI 4 months later including axial DWI (A), ADC (B), SWI (C), T1 weighted (D), T2 weighted (E), and fat saturated T2 FLAIR (D) sequences demonstrate complete resolution of epidural hematoma and collection. There is near complete normalization of restricted diffusion (arrow) in the parietal calvarium with mild residual edema (dashed arrows).

4. Conclusion

Although the differentiation of bone infarct from osteomyelitis is one of the most challenging issues clinically and radiologically in the evaluation of acute bone pain in sickle cell patients, the described case and the novel early DWI findings seen in 24 h could potentially help in management of this patient population. Further research and evaluations would better support our findings.

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Conflict of interest

The authors declare that they have no conflict of interest.

References

[1] Saito N, Nadgir RN, Flower EN, Sakai O. Clinical and radiologic manifestations of sickle cell disease in the head and neck. Radiographics 2010;30(4):1021–34.
[2] Jain R, Sawhney S, Rizvi SG. Acute bone crises in sickle cell disease: the T1 fat-saturated sequence in differentiation of acute bone infarcts from acute osteomyelitis. Clin Radiol 2008;63(1):59–70.
[3] Wong AL, Sakamoto KM, Johnson EE. Differentiating osteomyelitis from bone infarction in sickle cell disease. Pediatr Emerg Care 2001;17(1):60–3. [quiz 4].
[4] Gill FM, Sleeper LA, Weiner SJ, Brown AK, Bellevue R, Grover R, et al. Clinical events in the first decade in a cohort of infants with sickle cell disease. Cooperative Study of Sickle Cell Disease. Blood 1995;86(2):776–83.
[5] Watanabe M, Saito N, Nadgir RN, Liao JH, Flower EN, Steinberg MH, et al. Craniofacial bone infarcts in sickle cell disease: clinical and radiological manifestations. J Comput Assist Tomogr 2013;37(1):91–7.
[6] Delgado J, Bedoya MA, Green AM, Jaramillo D, Ho-Fung V. Utility of unenhanced fat-suppressed T1-weighted MRI in children with sickle cell disease — can it differentiate bone infarcts from acute osteomyelitis? Pediatr Radiol 2015;45(13):1981–7.
[7] Wright J, Ahmedzai SH. The management of painful crisis in sickle cell disease. Curr Opin Support Palliat Care 2010;4(2):97–106.
[8] Embury SH. The not-so-simple process of sickle cell vasoocclusion. Microcirculation 2004;11(2):101–13.
[9] Wun T. The role of inflammation and leukocytes in the pathogenesis of sickle cell disease; haemoglobinopathy. Hematology 2001;5(5):403–12.
[10] Babatola BO, Salman YA, Abiola AM, Okezie KO, Oladele AS. Spontaneous epidural haematoma in sickle cell anaemia: case report and literature review. J Surg Tech Case Rep 2012;4(2):135–7.
[11] Malayeri AA, El Khouli RH, Zaheer A, Jacobs MA, Corona-Villalobos CP, Kamel IR, et al. Principles and applications of diffusion-weighted imaging in cancer detection, staging, and treatment follow-up. Radiographics 2011;31(6):1773–91.
[12] Hiwatashi A, Kinoshita T, Moritani T, Wang HZ, Shrier DA, Numaguchi Y, et al. Hypointensity on diffusion-weighted MRI of the brain related to T2 shortening and susceptibility effects. AJR Am J Roentgenol 2003;181(6):1705–9.