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Painless recurrent orbital wall infarction secondary to sickle cell disease: A case report

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ABSTRACT

Purpose: Describe the various presentations of the rare entity of orbital wall infarction secondary to sickle cell disease and highlight the importance of magnetic resonance imaging in differentiating the entity from other similar diagnoses.

Observation: A 4-year-old child presented to the hospital with bilateral recurrent painless orbital wall infarction secondary to sickle cell disease. Orbital wall infarctions have been described before in the literature; However, the painless and recurrent nature is intriguing.

Conclusion: Orbital wall infarctions secondary to sickle cell disease represent an unusual presentation of the disease and often pose a diagnostic dilemma. When considering differentiating orbital wall infarctions from other resembling entities, magnetic resonance imaging is considered superior to computed tomography due to its ability to delineate the ischemic changes in the bone marrow, which further aids in the diagnosis. In situations where the orbital wall infarction does not lead to orbital compression syndrome, a conservative approach should suffice.

1. Introduction

Sickle cell disease (SCD) is a monogenic hemoglobinopathy that manifests secondary to the production of defective hemoglobin. The disorder is a consequence of a single-point mutation resulting in the substitution of Valine for Glutamic acid on the beta globin chain.[1,2] The hallmark of the condition is the hemoglobin polymerization during periods of oxidative stress, which in turn may lead to vaso-occlusion across various systems, typically occurring in long bones due to the abundance of active bone marrow present. Orbital wall infarctions are however less often encountered due to the limited bone marrow space in the facial bones.[3] These orbital infarctions may entice an inflammatory response which in turn may lead to compression of the optic nerve, an entity known as orbital compression syndrome.[4] Various sickle cell disease-related ocular findings exist, of which the predominant features include conjunctival signs, iris atrophy, angioid streaks, non-proliferative and proliferative sickle cell retinopathy.[5,6] However, a limited number of case reports present in the literature describe isolated periorbital edema as a presenting feature of orbital wall infarction consequence of sickle cell disease, with no association with pain or visual compromise.

In this report, we present a case of a sickle cell patient with two episodes of isolated painless bilateral periorbital edema as the only clinical manifestation of orbital wall infarction, with the aim of highlighting the various presentations of the entity and the diagnostic role of various modes of imaging in order to further aid in the diagnostic predicament this entity poses.

2. Case report

A 4-year-old child, diagnosed with homozygous genotype sickle cell disease (HBSS), presented to the emergency department with a complaint of sudden onset bilateral periorbital swelling for one day (Fig. 1). Upon review of the patient's medical records, he had multiple preceding visits to the emergency department due to vaso-occlusive crises (VOC) that necessitated hospitalization and the appropriate care for his condition. His medications included hydroxyurea, prophylactic penicillin, and folic acid supplementation. During his emergency visit, prior to the ophthalmology referral and assessment, and given his history of multiple food allergies, the emergency care team assumed an

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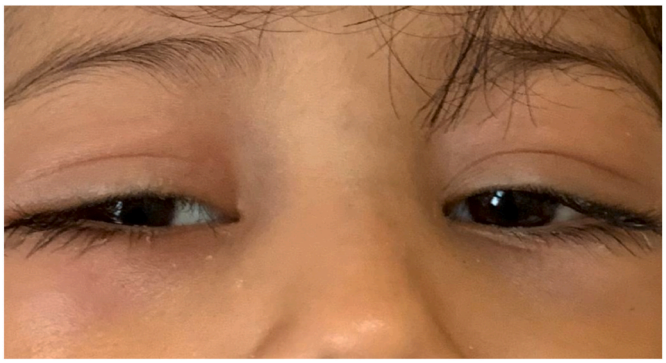

Fig. 1. External photograph showing bilateral periorbital swelling associated with mild erythema noted mostly on the right upper and lower eyelid.

allergic component to his current condition, and intravenous diphenhydramine was administered, yet no improvement was observed. Upon ophthalmological referral and assessment, the patient denied any pain, nor was any discharge noted. There was a mild non-tender erythematous right upper and lower eyelid swelling, which later on became more diffuse and took a bilateral course. On examination, the uncorrected Snellen visual acuity was 20/25 in both eyes, pupils were noted to be of equal size, reactive to light, and showed no relative afferent pupillary defect. The intraocular pressure was within the normal range and a bilateral limitation of supraduction was noted while the rest of the extraocular muscles were functioning accordingly. Hertel exophthalmometer revealed no proptosis with a measurement of 15 mm in both eyes. Anterior segment examination was unremarkable, and there was no congestion or chemosis of the conjunctival vessels. A dilated fundus examination revealed a healthy optic nerve in both eyes, and the remaining fundus examination was unremarkable.

During the patient's current episode, laboratory investigations revealed low levels of hemoglobin and red blood cells, high C-reactive protein levels, and a high erythrocyte sedimentation rate. Blood cultures were drawn and yielded negative results. The patient had multiple spikes of a high-grade fever of 38.6 °C, to which antipyretic therapy was initiated and a broad-spectrum third-generation cephalosporin (Cefotaxime) was given.

A computed tomography (CT) scan of the orbits with contrast was performed and revealed suspected areas of fluid collection in the inferolateral aspect of extraconal space with a thin rim of enhancement bilaterally and inhomogeneous soft tissue swelling bilaterally (Fig. 2). Conservative medical therapy consisting of hydration, oxygen, and pain management was advised. He also received an urgent blood exchange transfusion, which successfully lowered sickle hemoglobin (HBS) levels from 83 % to 30 %. Moreover, a triple antibiotic regimen (vancomycin, ceftriaxone, and metronidazole) was initiated. Two days after the beginning of the antibiotic regimen, clinical improvement was noted in the patient's condition subjectively and objectively, and a decline in the inflammatory markers was observed. The patient's swelling gradually started to regress and was fully resolved within a week. A repeat CT displayed no changes in the patient's condition. Following the resolution of the periorbital swelling and further stabilization of the patient's condition, brain and orbital magnetic resonance imaging (MRI) with contrast was performed and revealed signal alterations and intense enhancement involving temporal and zygomatic bones, however, the previously peripherally enhancing fluid had now resolved. Two months after the presentation, a subsequent MRI confirmed the resolution of the fluid collections that were previously noted. However, abnormal heterogenous enhancement of the zygomatic bone marrow was noted bilaterally, which represents avascular necrotic bone marrow changes consistent with presumed infarction secondary to the vaso-occlusive crisis. (Fig. 3).

Upon reviewing the patient's medical records, on one particular episode in which he was admitted for a VOC one year prior to this visit, very mild bilateral eyelid swelling was noted. It should be noted that during the previous visit, MRI findings detected bilateral intra-orbital inferotemporal fluid collections with abnormal signal enhancement in the bone marrow of bilateral zygomatic bones, which resolved with the resolution of his episode, conservatively (Fig. 4). This is presumed to be a previous episode in which an orbital wall infarction occurred secondary to his condition, and conservative management was sufficient for his condition to subside.

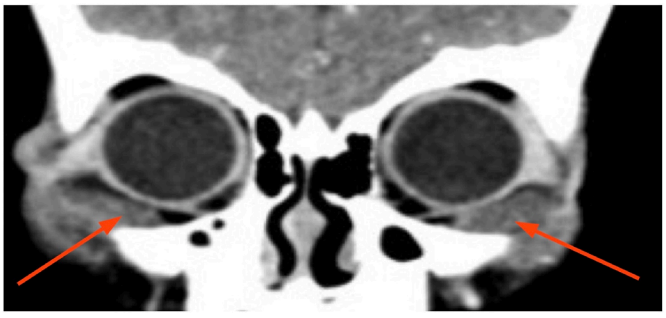

Fig. 2. Computed tomography (CT) scan with contrast, coronal cut, revealing suspected areas of fluid collection (red arrows) in the inferolateral aspect of extraconal space with thin rim of enhancement bilaterally and inhomogeneous soft tissue swelling bilaterally. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

3. Discussion

Sickle cell disease is an inherited hemoglobinopathy that poses a significant disease burden worldwide and specifically in Saudi Arabia, due to its prevailing nature in the region and more precisely in the southern and eastern regions of the country.[7] After first being reported in Saudi Arabia in the 1960s, the increasing numbers of SCD cases led to the establishment of a pre-marital screening program, in which it has been estimated that of the Saudi adult population, 4.2 % and 0.26 % are sickle cell trait carriers or are sickle cell diseased individuals, respectively.[8] The most prevalent area was found to be the eastern region of the country, with a striking 17 % sickle cell trait and 1.2 % sickle cell diseased individuals, thus posing a significant disease burden on healthcare.[8]

Patients affected by SCD may suffer from frequent episodes of VOC owing to obstruction of the blood supply secondary to the sickled hemoglobin, necessitating hospitalization and may even result in organ

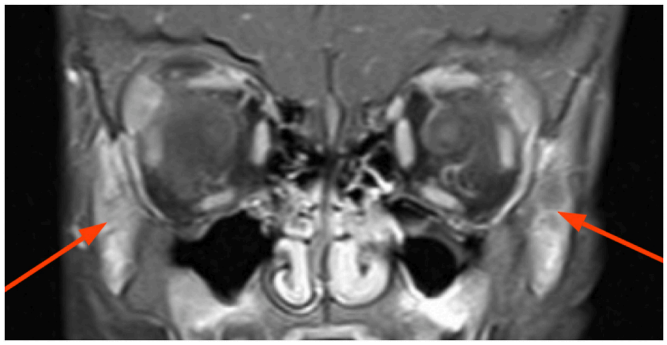

Fig. 3. Magnetic resonance imaging (MRI), coronal cut, T1 fat suppression images with contrast taken two months after the presentation, confirming the resolution of the fluid collections noted previously and showing abnormal heterogenous enhancement (red arrows) of the zygomatic bone marrow bilaterally attributed to avascular necrotic changes. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

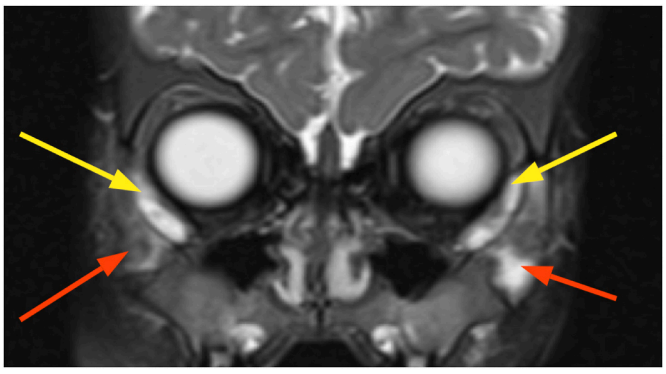

Fig. 4. Magnetic resonance imaging (MRI), coronal cut T2 with fat suppression, taken during previous episode 1 year ago, indicating bilateral orbital inferolateral fluid collections (yellow arrows) with abnormal signal changes in bilateral zygomatic bone marrow (red arrows). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

dysfunction.[9] Vaso-occlusive crises are rendered as the most common cause of hospital admissions among SCD-affected children.[9] Ocular complications related to the disease include but are not limited to anterior segment ischemia, secondary glaucoma, angioid streaks, retinopathy, and retinal artery occlusions.[10] In contrast to the prevalent nature of bony infarction and VOC of long bones in SCD patients, the incidence of orbital wall infarction is rather uncommon, with a sparse number of cases reported.[10] The rare prevalence of orbital wall infarction secondary to VOC is attributed to the scant bone marrow space in the facial bones and more specifically the orbit walls; this, however, is an exception in younger patients due to the greater marrow space, which further highlights the population at risk.[11]

When considering other differential diagnoses, including but not limited to periorbital cellulitis, osteomyelitis, and subperiosteal abscess formation, imaging is considered pivotal in differentiating between these entities, albeit might still pose a diagnostic dilemma.[12] Owing to their low immunity status, SCD patients are more prone to infections, thus a low threshold for antibiotic use is usually suggested in cases where differentiating between orbital wall infarction and osteomyelitis is challenging.[12] Furthermore, the absence of growth in blood cultures and the specific radiographical features aid in ruling out infection rather than infarction.[13] Distinguishing between bone infarction and other entities radiologically also poses another challenge. Contrast-enhanced MRI has been shown to aid in differentiating between infarction and infection.[14] Computed tomography is helpful in diagnosing pre-septal and orbital cellulitis; however, it does not delineate the changes in osteomyelitis and bone infarcts, except for the associated soft tissue swelling.[15] Magnetic resonance imaging is considered more advantageous than CT due to its ability to outline the ischemic alterations present in the bone marrow space.[15] Nuclear scintigraphy via technetium-99 m (Tc-99 m)-labeled sulfur colloid can demonstrate marrow infarction by showing a reduction in tracer uptake.[16] Sequential Tc-99 m bone marrow and Ga-67 imaging have been proven to be effective methods of differentiating between bone infarction and infection in SCD patients.[17] The timing of the imaging has been found to affect the bone scintigraphy outcomes. During the first 48 hours, there is a decreased tracer uptake, which suggests marrow loss and decreased vascularity. Subsequently, bone scans may reveal a higher uptake indicating the enhanced vascularity of the healing phase.[11] Ultrasonography is another proposed imaging technique that can be utilized to distinguish between infarction and infection in SCD patients. However, in regard to orbital wall involvement in SCD patients, its effectiveness has not been studied.[18]

While the majority of prior studies have characterized orbital wall infarction as a painful condition, two studies have observed it as a painless occurrence in their patient.[11,19,20] In addition, two previous studies have also described recurring episodes of orbital wall infarction, as in our case.[19,21] Symptoms such as proptosis, limitation of extraocular muscle motility, corneal hypoesthesia, and diminished optic nerve functions are attributed to the inflammatory response in the limited orbital space, an entity known as orbital compression syndrome (OCS).[22] In addition, orbital infarction may also be associated with a superimposed infection.[19] Conservative treatment for a typical sickle cell crisis episode—hydration, oxygen, and appropriate pain management—alongside or without antibiotics is sufficient for the majority of patients to recover.[11] Since infections occur frequently in sickle cell patients, and it can be challenging to definitively rule out infection due to the resemblance between changes seen in infection and infarction, intravenous antibiotics are recommended to be used in all SCD patients presenting with acute orbital or periorbital swelling, in concordance with the medical management of VOC, to aid in reducing the inflammatory response due to the wall infarction.[13] In patients with frequent recurrences of VOC, or in specific circumstances in which the VOC does not respond to the conservative treatment previously mentioned, blood transfusions or exchange transfusions can be performed. Their goal is to lower the amount of sickle cells in the blood and help resolve the present crisis.[23] An exchange transfusion was indeed performed in our patient and helped decrease the HBS levels from 83 % to 30 %. Steroids should be considered if conservative measures do not alleviate the condition or if there is a risk of optic nerve damage due to OCS; and if the aforementioned management is provided in cases of OCS and fails to improve, surgical intervention should be considered.[13,24] However, in our case, the patient had isolated periorbital edema with no clinical signs of orbital compression syndrome; hence, a conservative approach along with an exchange transfusion was more appropriate.

As sickle cell disease is considered endemic in Saudi Arabia, constructed knowledge of the management of ocular involvement as a consequence of the hemoglobinopathy is crucial. This case report emphasizes that in uncomplicated presentations of periorbital swelling secondary to orbital wall infarctions, conservative therapy is most appropriate, given that there are no alarming signs of orbital compartment syndrome as previously described. Surgical management is typically unwarranted, especially when radiological findings are reassuring and if the vision is unaffected.

In conclusion, our study highlights that orbital wall infarction, albeit rare as it is, should be considered in the differential diagnosis of SCD patients presenting with acute onset periorbital swelling, whether painful or painless. In addition, it calls attention to the fact that recurrences may occur and should be taken into consideration in affected patients, especially in young age groups. We also would like to emphasize on the pivotal role that MRI plays in which it is considered an advantageous modality due to its ability to delineate ischemic changes in the bone marrow that further aid in reaching the diagnosis. Additional diagnostic imaging techniques, such as nuclear scintigraphy, can also demonstrate the presence of orbital wall infarction, especially in the acute phase of the disease.

4. Consent form

Consent was obtained from the patient's father for publishing this case and for the photographs taken.

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none

CRediT authorship contribution statement

Lujain Alqurashi: Writing – review & editing, Writing – original draft, Methodology, Investigation. **Omar Rozy:** Writing – original draft,

Visualization, Supervision, Data curation, Conceptualization. **Somaya Hanafi:** Writing – review & editing, Supervision, Project administration, Conceptualization. **Randa Khafaji:** Writing – original draft, Investigation, Data curation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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