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Acute Orbitopathy Manifesting as Periorbital Cellulitis in Sickle Cell Disease

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Abstract

Sickle cell disease is a hemoglobinopathy that results in paroxysmal vascular occlusion and tissue infarction that can manifest in a plurality of tissues. Vasoocclusive crises in sickle cell disease commonly involve bone marrow of the long bones and vertebrae. Involvement of bones with less marrow space, including the bones of the orbit, is reported rarely in the literature and can closely mimic orbital cellulitis, both clinically and radiologically. The present case is a 3 years old boy, a known case of sickle cell disease, who presented with what was thought to be orbital cellulitis and was treated accordingly. Subtle radiologic features of sickle cell orbitopathy were initially overlooked, resulting in an incorrect diagnosis and a treatment delay for the patient. Correctly treated most cases resolve with no adverse effects. This case highlights the importance of maintaining a high index of suspicion in patients with known sickle cell disease, even when the presentation is not classic.

Keywords

Sickle Cell Disease, Orbital Cellulitis, Orbital Infarction, Sickle Cell Orbitopathy

1. Introduction

Sickle cell disease (SCD) is a hemoglobinopathy characterized by chronic hemolytic anemia and vaso-occlusive crises. It is due to a single amino acid mutation on the β chain of hemoglobin. The disorder is inherited in autosomal fashion, and the patients that typically experience clinical manifestations are homozygous for the sickle cell β globin mutation (HbSS) or compound heterozygotes with 1 sickle cell allele and an abnormality in the other allele that disallows adequate transcription of normal β chain. In either case, the relative amount of hemoglobin with sickle mutation (HbS) is enough to allow red blood cells to assume a

sickled shape when the plasma oxygen content or pH decreases. The sickled red blood cells can occlude microcirculation and cause infarction to tissues downstream or vaso-occlusive crisis [1]. The most frequent complications requiring hospital admissions for patients with sickle cell disease are painful vaso-occlusive crises (**Table 1**) [2].

Vaso-occlusive crises affect virtually all patients with sickle cell disease, often beginning in late infancy and recurring throughout life. The pathogenesis of the microvascular occlusion, the hallmark of the painful sickle cell crisis, is complex involving activation and adhesion of leucocytes, platelets and endothelial cells as well as hemoglobin S-containing erythrocytes. While this process can occur in virtually any organ, it is particularly common in the bone marrow, resulting in bone marrow infarction typically in the medullary cavity or epiphyses. The reasons for the vulnerability of the bone marrow to microvascular occlusion are unclear but may be partly because of marrow hypercellularity leading to impaired blood flow and regional hypoxia. Clinically, patients complain of intense pain localized to one or more areas of their skeleton. This may be accompanied by localized tenderness, swelling and erythema over the site of infarction; fever and leukocytosis are also common. Most patients recover from vaso-occlusive crises with no further complications. However, when marrow infarction involves the epiphyses, this may give rise to joint effusions that are clinically similar to septic arthritis [2]. Involvement of the orbital bones in an acute vaso-occlusive crisis is an uncommon manifestation but has been reported in various case reports [3] (**Figure 1**).

There can often be great difficulty in differentiating orbital bone infarction from osteomyelitis/orbital cellulitis clinically as well as radiologically, which was the case with our patient. Orbital infarction usually presents with acute onset of periorbital tenderness, swelling, erythema, and pain to the orbit. Soft tissue swelling of the orbit can result in proptosis and attenuation of extraocular movements [4] [5].

Expedient diagnosis of sickle cell orbital infarction is crucial to avoid potentially irreversible visual loss through an orbital compartment syndrome. Although CT is readily accessible in an acute setting, the changes shown may be subtle and misinterpreted leading to an incorrect diagnosis and treatment plan. Magnetic resonance imaging is thought to be superior to CT (often not available acutely, however) as it can show bone marrow infarction, which helps confirm the diagnosis of sickle cell orbitopathy [2] [3] (**Figure 2**).

Table1. Acute bone problems in sickle cell disease.

- Painful (vaso-occlusive) crisis
- Osteomyelitis
- Stress fracture
- Orbital compression
- Dental complications
- Vertebral collapse
- Bone marrow necrosis

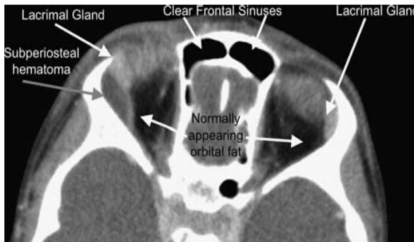

Figure 1. Axial computed tomographic soft tissue windows showing the subperiosteal hematoma, located on the lateral wall. This is an unusual location for a subperiosteal abscess. The adjacent orbital fat is not inflamed, and the frontal sinuses are clear. The right lacrimal gland has been displaced anteriorly.

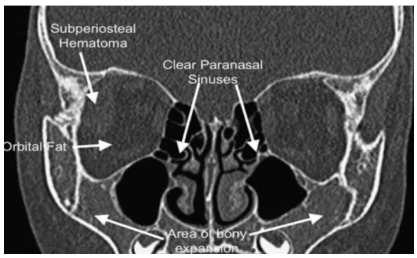

Figure 2. Coronal computed tomographic bony windows showing clear paranasal sinuses. The abnormal bony expansion of the maxillary bones is clearly seen. The marrow cavities are a similar density to orbital fat, indicating abnormally active bone marrow. These bony findings are typically seen in children with sickle cell. The subperiosteal hematoma is difficult to appreciate when the bony windows are examined.

Authors are herewith presenting such a case of orbital bone infarction and osteomyelitis in a 3-year-old boy with sickle cell disease, managed successfully with blood transfusion and intravenous antibiotics only, without steroid or surgical intervention.

2. Case Presentation

In October 2019, a 4-year and 7-months old Saudi boy known with homozygous sickle cell disease, presented at King Fahd Armed Forces Hospital after 2 days of progressive swelling of his upper and lower eyelids. He had no pain or mucopurulent discharge. Vision remained unchanged. He had no systemic symptoms, such as fever, rash, fatigue, or weight loss. Parents denied recent history of infection, chalazion, bug bite, or ocular or head trauma. Parents acknowledged a similar presentation in his left eye in July 2018, and he was diagnosed with bilateral preseptal collections by Computed Tomography (CT). He was treated with a blood transfusion, and eye symptoms resolved after 2 weeks. He had a history of multiple food allergies to (Wheat, Soya, and Eggs), that was confirmed using a radioallergosorbent (RAST) test, in-addition to Cow-milk-protein allergy. He had laparoscopic cholecystectomy (in 2017) and multiple times of hospitalization for vaso-occlusive pain crises in the head, chest, abdomen, and hip. Multiple

emergency room visits for left supracondylar fracture and right proximal humerus fracture. He was taking folate daily to maximize hematopoiesis and penicillin to prevent encapsulated bacteria.

On examination, his visual acuity was 20/30 OD and 20/25 OS. His external exam revealed mild proptosis OD and prominent right upper and lower eyelid swelling without erythema extending to the right cheek. He could not open his right eye without manual manipulation. He had no pulsation, tenderness, nodularity, or induration upon palpation. His left eye was normal. His pupils measured 4 mm in the dark and 2 mm in the light OU with no relative afferent papillary defect. His motility exam was full, and he was orthophoric. His intraocular pressures were normal. Anterior segment exam was normal. Ophthalmoscopy revealed normal discs, macula, and vessels OU. Cup-to-disc ratio was within normal. The patient was admitted given his complicated sickle cell history, high risk for infection, and concerning his previous similar orbital manifestations.

His complete blood count showed elevated white blood cells (17.3), reticulocytosis (17%), neutrophilia (88%), and thrombocytosis (388). His hemoglobin and hematocrit were low (8.4 and 28 respectively). Abnormal red blood cell morphology was noted on the peripheral smear, including sickled red blood cells. Computed tomography scan of the orbits and sinuses were performed two days following his admission and revealed a 1.5 cm × 0.5 cm × 1.6 cm thin rim-enhancing fluid collection in the inferiolateral aspect of the extraconal space (right orbit), without evidence of periosteal reaction. Also, about 1.7 cm × 0.6 cm × 1.7 cm thin rim-enhancing fluid collection in the inferiolateral aspect of the extraconal space (left orbit). No evidence of thrombosis in the vessels, sinuses, or lacrimal gland in both sides. No evidence of intracranial extension. Preserved and symmetrical appearance of the recti muscles. Unremarkable appearance of both globes (**Figure 3**).

Based on the fluid collection with rim enhancement on computed tomography (CT), he was diagnosed with orbital cellulitis with subperiosteal effusion, which can occur secondary to an orbital wall infarction in SCD. Despite being treated with broad spectrum intravenous antibiotics (ceftriaxone and vancomycin) for 72 hours, the periorbital edema was progressing, the patient continued to have intermittent spikes of fever, and his inflammatory markers were rising. On-top of his orbital presentation, the patient developed Acute Chest Syndrome by his fourth day of admission, which was complicated with left-side pleural effusion. Considering the clinical status of the patient, he was shifted to the Pediatric intensive care unit for close monitoring, and an urgent Manual Exchange Transfusion was performed. Two days after starting him on triple-antibiotics-regimen (Vancomycin, Metronidazole, and Ceftriaxone), the patient showed clinical improvement and decline in his inflammatory markers. An MRI of the orbits revealed bilateral orbital bone osteolytic changes with soft tissue accommodation of fluid, suggestive of orbital wall osteomyelitis (**Figure 4**). However, the child showed significant improvement in upcoming days with decrease in swelling

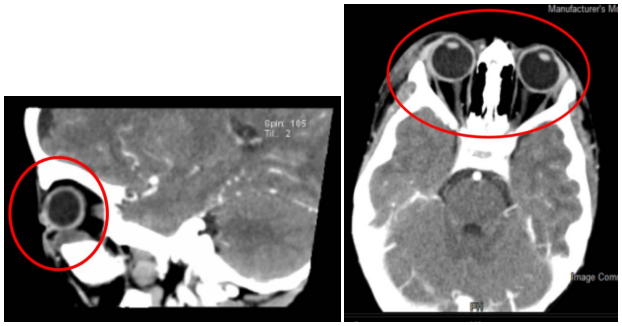

Figure 3. Computed tomography scan of the orbits and sinuses. The red circle points to a 1.5 cm × 0.5 cm × 1.6 cm thin rim-enhancing fluid collection in the inferiolateral aspect of the extraconal space (right orbit), and about 1.7 cm × 0.6 cm × 1.7 cm thin rim-enhancing fluid collection in the inferiolateral aspect of the extraconal space (left orbit).

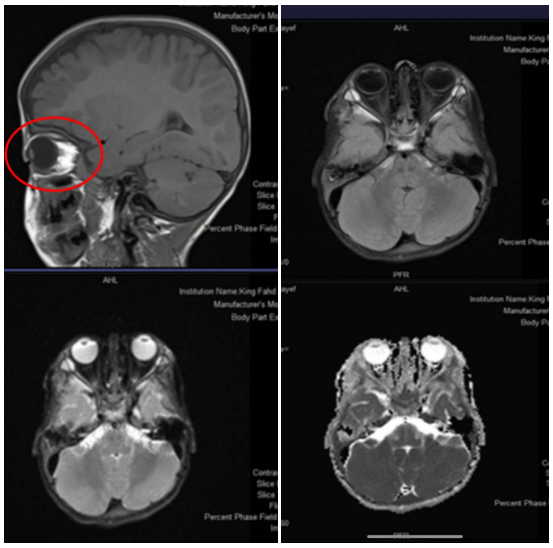

Figure 4. An MRI of the orbits revealed bilateral orbital bone osteolytic changes with soft tissue accommodation of fluid (red circle), suggestive of orbital wall osteomyelitis.

and erythema of eyelids, and improvement in eye opening. So, further imaging, surgical intervention or steroid was deferred. He was discharged after completing 21 days course of IV antibiotics with normal vision and no residual eyelid swelling. He was advised to continue on oral antibiotics for another three weeks, while being seen at the outpatient clinics weekly.

3. Discussion

Facial bone involvement is rare in SCD patients, and mainly seen in pediatric patients, who have a greater marrow space compared to older individuals. Bilateral orbital involvement is reported in 42% of cases of SCD with orbital infarction [6]. Patients with SCD are relatively immunocompromised and therefore more susceptible to infections. Orbital imaging and correct interpretation in SCD patients presenting with orbital swelling is paramount for differentiation

between hematoma and infection. Most of these cases, if timely diagnosed, can be managed successfully with exchange transfusion. A subperiosteal orbital hematoma (SOH) can be managed with supportive corticosteroid therapy, which is contraindicated with infection. Surgical decompression is indicated when SOH is associated by impaired ocular movement and deteriorating vision, termed orbital compression syndrome. Infection needs to be tackled with aggressive antibiotic treatment, and abscess may require drainage. Among the causes in the differential diagnosis of periorbital edema, the etiological factors that can be taken into consideration as causes of periorbital swelling in patients with sickle cell anemia are cavernous sinus thrombosis and periorbital bone infarctions. Normal results of fundus examination with no signs of papilledema may exclude the diagnosis of cavernous sinus thrombosis. The diagnosis of bone infarction is made by demonstration of activity-deficient area appearing in the infarcted regions by technetium Tc 99m medronate bone scintigraphy. Diagnosis of osteomyelitis is made by demonstration of hyperactive areas on technetium Tc 99m medronate and gallium citrate Ga 67 bone scans. Orbital cellulitis will show diffuse infiltration of orbital and/or periorbital tissue with enhancement. Periosteal abscesses will present as a hypodense biconcave mass with peripheral enhancement, in which gas inclusions can be present. Periosteal abscesses are often associated with sinusitis. Differentiation between facial bone infarction and osteomyelitis is a diagnostic challenge. Both can present with bone oedema, soft tissue enhancement, and collections. When cortical defects are present diagnosis of osteomyelitis is more likely.

4. Conclusion

This case report highlights the importance of maintaining a high index of suspicion in patients with known sickle cell disease presenting with pain, orbital swelling and restriction of ocular movement. Red blood cell transfusion immediately on clinical suspicion only may be sufficient for uneventful recovery, without steroids or surgical intervention. Expedient diagnosis of orbital bone infarction and orbital compression syndrome in children with sickle cell disease is crucial because this is a potentially sight-threatening entity.

Consent

An informed consent was obtained from patient's family to report the case.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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