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Case Report

Orbital compression syndrome in sickle cell disease

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الملخص

تعتبر مضاعفات حجاج العين لدى مرضى فقر الدم المنجلي غير شائعة، ولكن يمكن أن تكون شديدة بما فيه الكفاية لتؤدي إلى اعتلال بليغ. نعرض لحالة طفل عمره ١٠ سنوات، يعاني من مرض فقر الدم المنجلي راجع المستشفى يشتكي من حمى، ووذمة في الجفنين، وجحوظ في العينين، وضعف الإبصار في العين اليسرى بدرجة أكثر من العين اليمنى. أظهرت الفحوصات فقر الدم، ونقص الصفائح الدموية، واختلال في بيانات تخثر الدم متناسق مع مرض التخثر المنتشر داخل الأوعية، وعثر على جرثومة "السالمونيلا" بمزرعة الدم. أفاد تقرير أشعة الرنين المغناطيسي لحجاج العين وجود تجمع دموي تحت السمحاق على الجانبين. تضمن العلاج اعطاء المضادات الحيوية عن طريق الوريد، بالإضافة إلى "ميثايل بريدنسولون" وبضع اللحاظ الثنائي مع التصريف الجراحي للتجمع الدموي. وبتقييم النظر بعد العملية تبين وجود فقد كامل للبصر في العين اليسرى وسلامة البصر في العين اليمنى. تُبرز هذه الحالة أهمية التقييم المبكر ومراعاة التدخل الجراحي لحالات مرضى فقر الدم المنجلي مع وجود هذه المضاعفات النادرة.

الكلمات المفتاحية: ضغط؛ العين؛ احتشاء؛ فقر الدم المنجلي

Abstract

Orbital complications in sickle cell disease are uncommon, but can be severe enough to result in significant morbidity. We report a 10-year-old boy with sickle cell disease who presented with fever, bilateral eyelid edema, proptosis, and diminished vision with left eye involvement more than the right eye. Investigations revealed anemia, thrombocytopenia, and derangement of coagulation profile consistent with disseminated intravascular coagulopathy, and salmonella species was recovered from blood culture. MRI of the orbits showed bilateral large subperiosteal hematomas. The treatment included intravenous antibiotics, pulse methylprednisolone and bilateral canthotomy with surgical drainage of the hematomas. Postoperative visual assessment revealed complete loss of vision in the left eye with normal vision in right eye. This case highlights the importance of the early evaluation and consideration of surgical intervention in sickle cell disease with this rare complication.

Keywords: Compression; Eye; Infarction; Sickle cell

Introduction

Sickle cell disease (SCD) is an autosomal recessive disorder characterized by production of abnormal hemoglobin S and is associated with high morbidity and mortality. Studies have reported that SCD is a relatively common genetic disorder in this part of the world. The prevalence of SCD in Kingdom of Saudi Arabia varies significantly in different parts of the country, with the highest prevalence is in the eastern and the southwestern provinces respectively.[1] Ocular manifestations of sickle cell disease may include anterior segment ischemia, secondary glaucoma, angoid streaks, retinopathy and retinal artery occlusions.[2] Autoinfarction of the orbital bones has rarely been reported and

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can lead to acute proptosis, periorbital pain, limited motility, and potentially, compressive optic neuropathy, constituting orbital compression syndrome (OCS).

Case report

A 10-year-old Saudi boy known to have sickle beta-thalassemia referred from a peripheral hospital on 12th January 2013 after hospitalization there due to fever and left upper and lower limb pain for three days. Six hours prior admission to our hospital, he developed bilateral eyelids edema, proptosis and diminished vision in the left more than the right eye. He was managed in the referring hospital with intravenous fluids, antibiotics, analgesia and blood transfusions. There was no history of trauma or insect bite. He had history of repeated admissions due to vaso-occlusive crisis. He is on regular folic acid and prophylactic oral penicillin.

On examination, he looked sick, drowsy, pale and mildly icteric. His temperature was 38.7 °C; heart rate 120 /min; respiratory rate 22/min; blood pressure 105/66 mm Hg and O_2 saturation (room air) was 98%. His weight was 22 kg; height, 126 cm; head circumference 53 cm and all were within normal centiles. He had bilateral extensive periorbital edema and proptosis in left eye more than the right. There was bilateral conjunctival chemosis, subconjunctival hemorrhage and corneal haziness. Ocular motility was restricted in all directions and Pupils were not reacting to light bilaterally. Abdomen was soft with mildly enlarged liver and spleen. There was tenderness and restriction of the range of motion of the left shoulder and left hip joints with no other focal signs of inflammation.

Laboratory results showed a hemoglobin of 8.8 g/dL; mean cell volume 60.8 fl; white cell count 6.8 $\times$ 10^9/L, with neutrophils 66.9%; platelets 24 $\times$ 10^9/L. Serum bilirubin was 104 μmol/L, albumin was 25 g/L, ALT 108 U/L, AST 433 U/L. Blood urea was 3.5 mmol/L, and serum creatinine was 43 μmol/L. Coagulation parameters revealed a prothrombin time (PT) of 18 s (normal 10−13); International Normalization Ratio INR) 1.45 (normal 0.85−1.12) and activated partial prothrombin time (aPTT) 55 s (normal 26.4−36). D-Dimer was elevated 7.97 μg/mL. **Serum fibrinogen level was not available**. Erythrocyte sedimentation rate was 134 mm/h (normal <11 mm/h), and C-reactive protein was 12.8 mg/dL (normal <0.5 mg/dL). Hemoglobin electrophoresis showed HbS 58%, HbA 36%, HbF 2%, and HbA_2 4% (consistent with sickle β^+ thalassemia). Urine examination was normal and culture reported negative. Salmonella species was grown from blood culture. The organism was sensitive to third generation cephalosporins and ciprofloxacin. Magnetic resonance imaging (MRI) of the orbit showed bilateral orbital masses with heterogenous intensity suggestive of hematomas. The lesion size was 2 $\times$ 3 cm on left and 2 $\times$ 1.6 cm on right side (Figure 1A,B). Sagital and coronal, fat suppression T2-weighed images showed similar lesions arising from roof and lateral wall of each orbit. The eye globes were displaced anteriorly with more affection on left side. The optic nerve on left side small and is displaced with partial loss of its surrounding cerebrospinal fluid (Figure 2A,B). However, evidence of bone infarction could not be demonstrated.

He was managed in pediatric intensive care unit with hydration, analgesia, intravenous (IV) vancomycin and cefotaxime and IV pulse methylprednisolone. Ophthalmology service was consulted and to save potential vision in

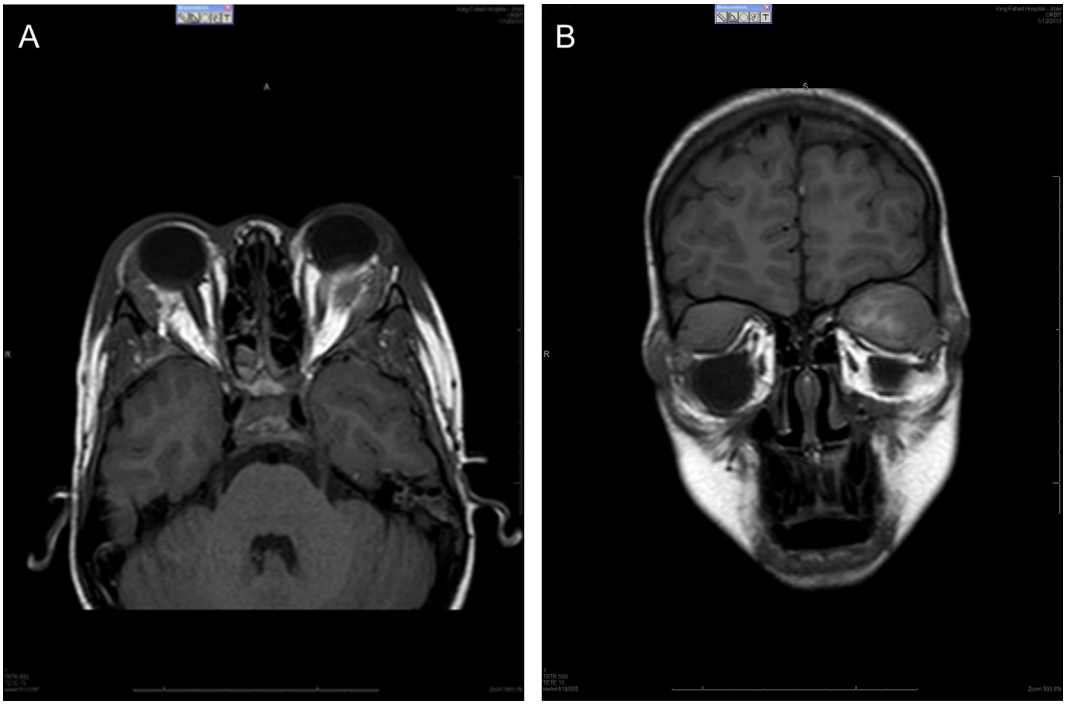

Figure 1: A, axial T1 weighted. B, coronal T1 weighted image show well defined mass lesions with heterogenous signal intensity, mostly iso-intense and includes hyper intense areas. Masses are seen to arise from roof and lateral walls of each orbit. On left side mass measures 3 $\times$ 2 cm while on right is 2 $\times$ 1.6 cm. On left, mass pushes and distorts eye globe, compressing and displacing left optic nerve.

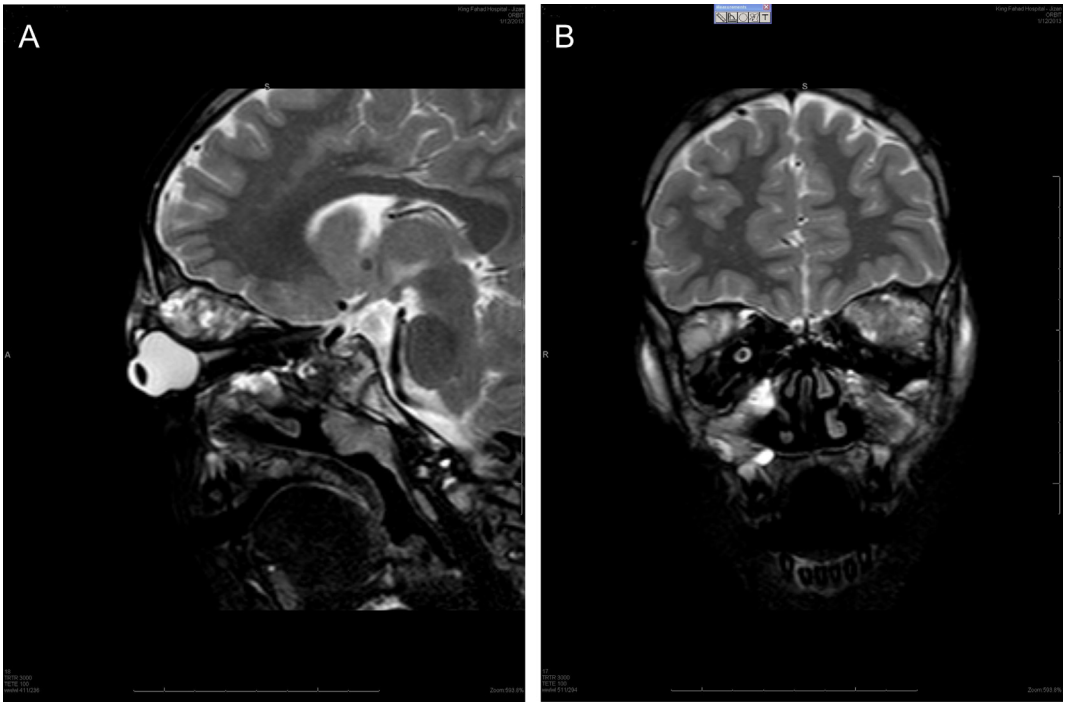

Figure 2: A, sagital T2 weighted fat suppression. B, coronal T2 weighted fat suppression. They show lobulated masses of heterogenous signal intensity in both orbits. On left the larger mass (2 × 3 cm)is noted to push eye globe anteriorly, compressing and displacing the optic nerve which appears small with partial loss of its surrounding cerebrospinal fluid.

right eye, decision for urgent drainage of subperiosteal hematomas was made. The patient was operated on the same day of admission after he received supportive management for coagulation derangement. Surgical approach was under upper orbital rim, about 10 ml of blood was drained from each orbit and drains were kept in place. Postoperatively he was kept on IV antibiotics and topical eye medications as well as regular assessment by ophthalmology and pediatric teams. After the result of blood culture, vancomycin was discontinued. The left eye had drained about 180 ml of blood in the first day, volume of drainage then reduced to minimal oozing over the next 5 days. He continued to receive blood and blood products and one dose of recombinant factor Vlla. He showed gradual improvement with reduction in swelling and ocular movement with mild restriction of upward gaze of left eye. Three weeks postoperatively, his visual acuity was 20⁄20 in the right and minimal perception of light in left eye. Fundoscopic examination was normal in right eye and documented optic atrophy in left eye. On fifth day of admission a swelling and tenderness were noted on proximal part of left humerus close to shoulder joint. Ultrasonographic examination of left shoulder revealed soft tissue swelling around the joint and small non-drainable collection at the subacromial region. X-ray of left shoulder including upper half of humerus were normal. This x-ray was repeated two weeks later and revealed cortical irregularity, periosteal new bone information of proximal one-third of left humerus and normal epiphysis. These findings were consistent with osteomyelitis of this bone. Antibiotics were continued for six weeks.

Discussion

Sickle cell disease (SCD) is an inherited hemoglobinopathy which results from a point mutation (GAG → GTG) in exon 1 of the β globin gene resulting in the substitution of glutamic acid by valine at position 6 of the β globin polypeptide chain.[3] An abnormal hemoglobin S molecule is formed, and tends to polymerize under conditions of hypoxia and acidosis. This will cause the red blood cell to become sickle in shape and rigid. These cells have short life span (chronic hemolysis) and tend to block capillaries (vaso-oclusion) which explain almost all clinical manifestations of sickle cell disease.[4] Ophthalmologic complications can result from vaso-occlusion in any vascular bed in the eye, including the conjunctiva, anterior segment, retina, choroid, or optic nerve with potentially vision-threatening consequences,[2] however, orbital involvement is a rare finding.[5] Orbital compression syndrome (OCS) is an acute condition characterized by eyelid edema, proptosis, periorbital pain, restriction of extra-ocular motility, with or without decreased visual acuity.[6,7] The main mechanism for development of OCS is orbital bone infarction with subsequent inflammatory response that can rapidly spread to the orbit resulting in orbital pain and proptosis and other features of OSC.[8] A unique feature of orbital wall infarction in sickle cell disease is the formation of hematomas, which may be orbital (subperiosteal) or intracranial (epidural).[8–10] Several mechanisms have been suggested for development of subperiosteal hemorrhage, such as extravasation of blood from necrosed vessel walls,

underlying bleeding diathesis, and minor trauma.[8,10] The presumed cause of orbital hematoma in our case is coagulopathy as a complication of salmonella septicemia in the setting of orbital infarction, but such infarction was not apparent on MRI of the orbital bones. In the initial reports, OCS has been thought to result from the occlusion of the ophthalmic vessels at the apex of the orbit by sickled cells.[11] To best of our knowledge, 36 cases of OCS have been reported.[7,12–17] Most of the cases, 83% (30/36), occur in homozygous hemoglobin S. However, OCS has been reported in other sickle cell disease variants, five cases in sickle β-thalassemia, and one case in hemoglobin SC disease.[7,17] Orbital wall infarction typically occurs in youths because there is more marrow space in the orbital bone in children than there is in adults.[8] The mean age of presentation in 36 reported cases was 13 years, with the youngest reported age at 2 years.[15] It affects almost twice as many male as females. The OCS has wide spectrum of manifestations ranging from its mild form which constitutes of pain and eyelid edema, the presentations that occur in all cases, to the most severe of bilateral proptosis, chemosis, limited ocular motility, and vision loss, like the presentation in our case.[6] Fever at presentation occur in almost all cases, and associated pain crises elsewhere was seen in more than two third of cases.[7] Bilateral orbital involvement is reported in one third of cases.[7] The differential diagnosis of acute periorbital pain and swelling with or without other manifestations of OCS in patient with sickle cell disease includes orbital cellulitis, orbital abscess, periorbital cellulitis, osteomyelitis of orbital bone, orbital tumor, and orbital bone infarction.[6,7,14,18] To differentiate between bone infarct and the infective process involving the orbit is crucial and can be challenging in case of orbital osteomyelitis. The presence of Leukocytosis and elevated erythrocyte sedimentation rate and C-reactive protein can occur in both bone infection and infarction.[14] Bone marrow abnormalities are well depicted at MR imaging, and orbital soft-tissue swelling, subperiosteal hemorrhage, and fluid collections often are seen in association with such abnormalities.[10] Bone marrow scan can confirm marrow infarction in 95% of cases by demonstrating decreased tracer uptake, in infection the uptake is normal.[6] MRI is the imaging modality of choice for evaluation of OCS in most of the reported cases. Our case is unique because the condition is associated with salmonella sepsis and disseminated intravascular coagulopathy which we think played a role in formation of the hematomas, and caused osteomyelitis of the left humerus. MRI shows bilateral large subperiosteal hematomas compressing the eye globes and optic nerves with more mass effect on the left side which contributed to loss of vision. However, infarction of orbital bones was not evident. Most cases of OCS resolve with conservative treatment.[6,7,19] Administration of intravenous corticosteroids may relieve orbital pressure caused by inflammatory component of orbital bone infarction. Concomitant antibiotic coverage is advisable as it is often difficult to clinically differentiate osteomyelitis from bone infarction.[6–8] Surgical exploration and evacuation of hematoma is warranted to prevent vision loss and to speed recovery if there are signs of optic nerve dysfunction or large hematomas are demonstrated by MRI.[8,19] 29 of 36 (80.5%) patients reported in the literature recovered with medical therapy, and seven (19.4%) required surgical interventions. Among the reported cases, only one case ends with permanent visual loss in the patient left eye. This patient had severe bilateral disease and was managed conservatively.[7] Our patient is the second case in which OCS is complicated by unilateral blindness. Clinical visual assessment; significant eye globe displacement, thinning and touristy of optic nerve on MRI were predictive of this poor outcome in left eye. The rational for surgical intervention and draining of hematomas despite laboratory evidence of DIC is to save whatever vision left in right eye and minimize morbidity of bilateral visual loss. Three months after discharge, postoperative and outpatient follow up assessment confirmed visual acuity of 20/20 in the right eye, permanent visual loss in the left eye and cure of osteomyelitis of left humerus.

Conclusion

The diagnosis of OCS should be considered when patients with SCD present with proptosis, decreased extra ocular motility, eyelid edema, and optic neuropathy. Children with SCD are susceptible to infections, and empirical use of broad spectrum antibiotics should be considered if infectious process is suspected. An ophthalmologist should always be consulted, as early evaluation and surgical intervention if evidence of optic nerve dysfunction or large hematoma is present can be vision saving.

Authors' contributions

Dr. Mada Yateem prepared the first draft including case history and physical examination. Dr. Mustafa Wasli provided information on surgery, follow up information on vision and reviewed the article. Dr. Thikra Sallam provided radiological information and reviewed article. Dr. Ibrahim Haqawi reviewed the article. Dr. Haider Arishi reviewed all article drafts including the final one and submission of the manuscript.

Conflict of interest

The authors have no conflict of interest to declare.

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