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Diplopia in A Post-splenectomy Thalassemic Patient

Abstract— We report a case of cavernous sinus thrombosis in a post-splenectomy male with underlying Haemoglobin E Thalassemia major. A 35-year-old man presented with a first episode of sudden onset of diplopia on lateral gaze for 1 week. He had no other ocular and systemic symptoms. There was no history of trauma or recent infection. However, he admitted that he was not compliant to his oral penicillin V and aspirin, which was prescribed to all post splenectomy patients. Unaided visual acuity in both eyes was 6/6. On examination, there was limited abduction over the left eye, suggestive of left lateral rectus palsy. Full blood count revealed leucocytosis with thrombocytosis. Magnetic resonance imaging, magnetic resonance angiography and magnetic resonance venography of the brain showed bulging of the left cavernous sinus, with a persistent focal filling defect, in keeping with left cavernous sinus thrombosis (CST). He was diagnosed with left isolated sixth nerve palsy secondary to aseptic cavernous sinus thrombosis with pro-thrombotic state post-splenectomy. He was started on subcutaneous fondaparinux and oral warfarin. His diplopia fully resolved after 1 month of treatment with complete resolution of CST on computed tomography venogram.

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1 INTRODUCTION

CST is a variant of cerebral venous thrombosis (CVT). It refers to thrombosis of the cortical veins, deep cerebral veins and dural sinuses, and was initially described by Bright in 1831 as a complication of epidural and subdural infections [1,2]. It is commonly associated with intracranial infection or infection from any of the tissues that drain into the cavernous sinus such as the mid-face, orbit and sinonasal cavity [3]. Other possible etiologies include a pro-thrombotic state in hypercoagulability syndrome, trauma, pregnancy and drugs [3]. Patients with thalassemia, especially those with a history of splenectomy, are at higher risk of developing venous thromboembolic events such as CST [4-7].

We reported an unusual presentation of unilateral isolated lateral gaze palsy in a post splenectomy adult thalassemia patient with non-septic cavernous sinus thrombosis (CST).

2 CASE REPORT

A Haemoglobin (Hb) E thalassemia major man in his mid-thirties complained of sudden onset of binocular diplopia on lateral gaze. His symptoms started a week prior to presentation. He denied any headache, vomiting, blurring of vision or other neurological symptoms. There was no history of trauma, fever or recent infection. He was diagnosed with thalassemia major 30 years ago, with multiple admissions for regular blood transfusion and administration of iron-chelating agents. Splenectomy was performed 14 years ago. He was poorly compliant to his post splenectomy medications which included oral penicillin V and aspirin.

On examination, there was limited abduction of the left eye, suggestive of left lateral rectus palsy (**Figure 1**). However, there was no proptosis. He had an unaided visual acuity of 6/6 bilaterally, with a normal ocular slit lamp examination. Neurological examination, including other cranial nerves examination was normal. Systemic examination was unremarkable except for a well healed old splenectomy scar during abdominal examination. He had no thalassemia facies such as frontal bossing, maxillary hypertrophy or malocclusion of the teeth.

Full blood count revealed leucocytosis with thrombocytosis. Infective, connective tissue and thrombophilia screening were negative. Computed Tomography (CT) imaging of the brain and orbit was normal and inconclusive for

diagnosis. Hence, he was proceeded for magnetic resonance imaging (MRI) after discussion with radiologist. MRI, magnetic resonance angiography and magnetic resonance venography (MRV) in brain showed bulging of the left cavernous sinus with a persistent focal filling defect suggestive of left CST (**Figure 2a**). He was diagnosed with left isolated sixth nerve palsy secondary to aseptic CST with underlying pro-thrombotic state post-splenectomy.

He was started on anti-coagulant therapy which was subcutaneous fondaparinux 7.5 mg once a day for 2 weeks then followed by oral warfarin 5mg once a day. His diplopia fully resolved with no more ophthalmoplegia after 1 month of treatment. There was also complete resolution of CST on computed tomography venogram (CTV) (**Figure 2b**).

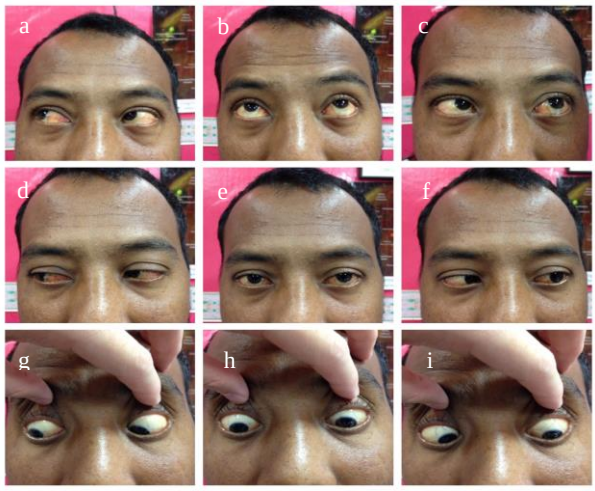

Figure 1: Nine-gaze view demonstrating extra-ocular muscle movement. Note the limited abduction of the left eye seen in panel f, suggestive of left lateral rectus palsy.
a. dextroelevation; b. supraversion; c. levoelevation;
d. Dextroversion; e. Primary gaze; f. Levoversion;
g. dextrodepression; h. infraversion; i. levodepression

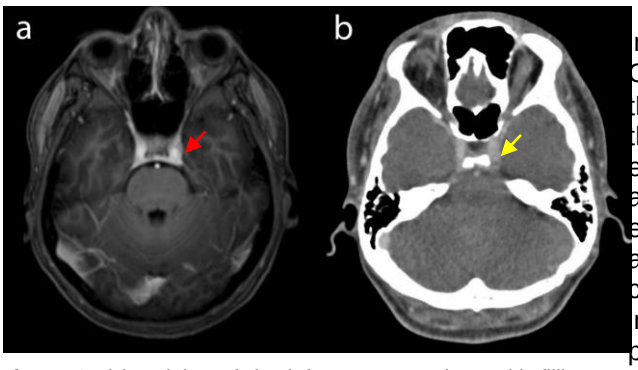

Figure 2: (a) Bulging of the left carvenous sinus with filling defect (red arrow) suggestive of left CST in MRV, (b) Resolution of left CST demostrated by absence of filling defect in CTV (yellow arrow) .

3 DISCUSSION

CST is relatively rare, accounting for only 1% of acute strokes. It usually presents with nonspecific symptoms and signs that may lead to a delay in diagnosis [2]. Up to 50% of cases of CVT progress to venous infarction [1]. Venous infarctions are frequently bilateral, hemorrhagic, and involve the para-sagittal area. Early diagnosis of CST is essential to prevent a further devastating cerebral vascular event [1].

The first ocular manifestations of CST are usually caused by venous congestion, and include conjunctival chemosis, periorbital edema and proptosis. Ptosis and painful ophthalmoplegia may follow as the disease progress. A lateral gaze palsy may develop before full-blown ophthalmoplegia, due to the anatomic position of the sixth cranial nerve (CNVI). CN VI has an intra-luminal course, which makes it more susceptible to damage compared to cranial nerves III and IV, which are protected by a fibrous sheath in the lateral wall of the cavernous sinus [8].

CT scan and MRI of the head are the primary radiological modalities used to confirm the diagnosis and are also used to assess causal and concurrent pathology [9]. MRI and specifically MRV can detect all stages of thrombus formation [9]. CT scan is considered superior to MRI for the detection of early clot formation in the cavernous sinuses [10]. Meanwhile MRI is superior for the rest of the dural venous sinuses. But, in cases with non-diagnostic CT scans, MRI is helpful [10]. Hence, our patient was offered CT scan at first then proceeded for MRI in view of inconclusive findings in CT.

In general, CVT is more frequently reported in young women and aging adults [11]. However, CVT in children is commonly associated with beta thalassemia major [11]. Hemostatic changes in thalassemia including platelet activation, endothelial, monocyte and granulocyte activation, alteration of coagulation factors and inhibitors, elevated plasma markers of hypercoagulability and abnormal thalassemic red blood cells are the contributing factors of the hypercoagulable state in thalassemia patients. Evidence supports the presence of a hypercoagulable state greatly exacerbated by splenectomy, due to a combination of platelet activation, enhanced red

blood cell adherence to the endothelium, reduced levels of the natural anticoagulants protein C and protein S, and increased thrombin generation [4,5,6]. In this case, we report this condition in a middle-aged man with Hb E thalassemia. His post-splenectomy status, with poor compliance to anti-platelets, could have contributed to development of the thrombosis. Clinically, there were no signs of infection suggestive of the more common septic CST. Anticoagulants have been shown to be beneficial in patients with aseptic CST, with low risk of haemorrhagic complications [12,13].

4 CONCLUSIONS

Isolated 6th nerve palsy in thalassemic patient warrants immediate attention and work up to rule out CST. A high index of suspicion is required in patients with atypical presentation of CST. Careful assessment of risk factors is vital in making a prompt diagnosis, to prevent fatal consequences. A multi-disciplinary approach is required for management and prevention of potential complications.

CONFLICTS OF INTEREST

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this paper.

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