



Case Report

Intracranial extramedullary hematopoiesis in a patient with beta-thalassemia presenting with head trauma

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ABSTRACT

Background: Beta-thalassemia is an inherited hemoglobinopathy, whereby reduced or absent expression of beta-globin genes causes impaired erythropoiesis. Extramedullary hematopoiesis (EMH) occurs in 1% of all patients with beta-thalassemia major receiving regular transfusions and is exceedingly rare intracranially.

Case Description: We report a case of a male in his 20s with beta thalassemia who presented with head trauma found to have intracranial EMH mimicking multiple extra-axial hematomas. Making the correct diagnosis was critical in avoiding prolonged neuromonitoring and unnecessary interventions.

Conclusion: Intracranial extramedullary hematopoietic pseudotumor is an exceedingly rare entity and seldom appears in a neurosurgeon's differential diagnosis. This case illustrates how this condition can easily mimic an acute intracranial hemorrhage in a patient with beta-thalassemia who presents with head trauma. We review the topic to further inform clinicians who may encounter this condition in their practice.

Keywords: Case report, Epidural hematoma, Extramedullary hematopoiesis, Thalassemia, Traumatic brain injury

INTRODUCTION

Beta-thalassemia is an inherited hemoglobinopathy characterized by reduced expression of beta-globin genes causing impaired erythropoiesis, peripheral hemolysis, and chronic anemia. Hematopoiesis normally occurs in the marrow of the medullary bones; however, extramedullary hematopoiesis (EMH) is a compensatory response observed in patients with chronic anemia. EMH occurs in 1% of all patients with beta-thalassemia major receiving regular transfusions.^[10] Liver, spleen, costal bones, and spine are common sites of EMH. Intracranial EMH is a rare phenotype. We report a case of intracranial EMH mimicking extra-axial hematomas in a patient with beta-thalassemia who presented with head trauma.

CLINICAL PRESENTATION

A male in his early 20s with a history of beta-thalassemia major requiring routine blood transfusions presented to a community hospital following an unhelmeted electric scooter

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accident with a head strike, without loss of consciousness. The patient had stable vital signs with a Glasgow Coma Score of 15 and no focal deficits on neurologic exam. Laboratory studies were notable for serum sodium 132 mmol/L, hemoglobin 7.5 g/dL, and INR 1.3. Computed tomography (CT) of the head demonstrated bifrontal extra-axial lentiform hyperdense mass lesions and an interhemispheric hyperdense lesion. Our differential diagnoses included convexity epidural hematomas and a falcine subdural hematoma [Figure 1]. The patient was transferred to our Level 1 trauma center and admitted to the surgical-trauma intensive care unit for close observation.

A repeat head CT scan was obtained 4 h after his initial scan which was interpreted by radiology as a mild interval

increase in the size of both convexity extra-axial hyperdense lesions. The right convexity lesion was interpreted to have expanded from 1.5×0.7 cm to 1.9×0.9 cm in the axial plane, while the left convexity lesion increased from 3.7×1.5 cm to 3.9×1.8 cm in the axial plane. Given this possible increase in size, a third head CT was obtained approximately 4 h later, which demonstrated stability of the extra-axial collections [Figure 1].

Given the patient's good neurological examination compared to the size and extent of the extra-axial lesions, and lack of associated skull fractures and other stigmata of head trauma on radiographic imaging, alternative diagnoses were considered after discussion with a senior neuroradiologist. On MRI, the brain parenchyma was without signs of

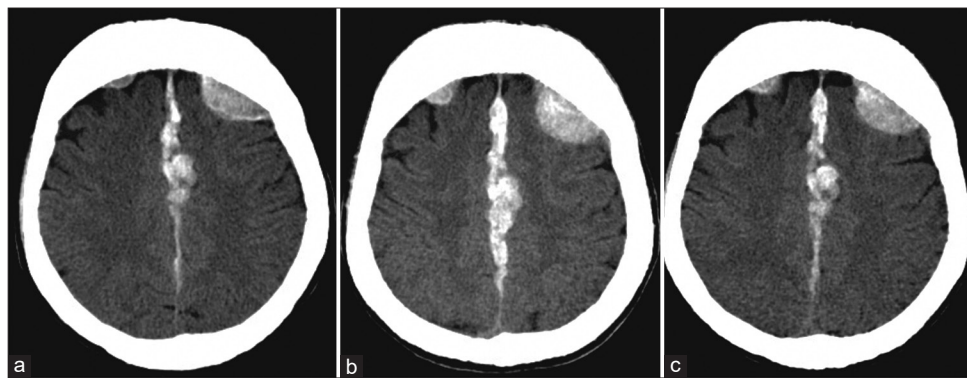


Figure 1: Axial slices of serial head computed tomography's without contrast obtained on admission (a) and then subsequently at 4 h intervals (b and c).

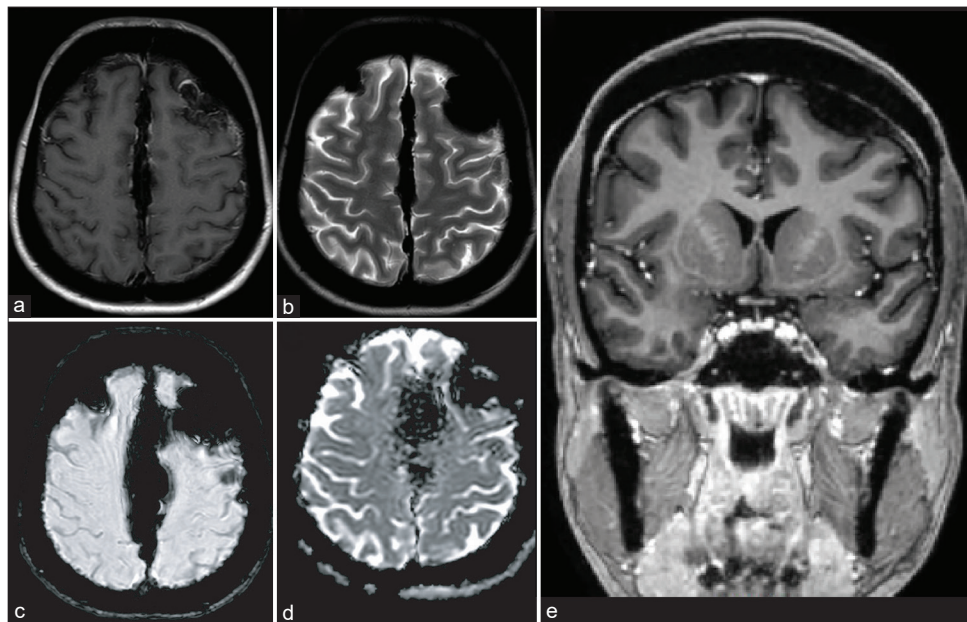


Figure 2: Selected MRI sequences of a beta-thalassemia patient with extramedullary hematopoiesis. (a) Axial T1-weighted image with contrast. (b) Axial T2-weighted image. (c) Axial susceptibility weighted imaging. (d) Axial apparent diffusion coefficient maps. (e) Coronal T1-weighted image with contrast.

Table 1: Reported cases of intracranial and spinal EMH in patients with beta-thalassemia.

Year	First Author	Age	Sex	Location	Time Course	Description	Treatment	Outcome
2016	Bukhari ^[1]	18	M	Thoracic, T9-10	3 Months	Eighteen-year-old male with a history of EMH causing cord compression underwent surgery for decompression and had complete resolution of symptoms. Onset of 3 months of progression myelopathy occurred 5 days after surgery.	Surgery for cord decompression and adjuvant radiotherapy.	At 2-year follow-up: Complete resolution of symptoms, no radiographic evidence of recurrence.
2012	Eskazan ^[2]	30	M	Falcine, interhemispheric	Not Stated	Thirty-year-old male presented with chronic, progressive headaches, found to have a large interhemispheric mass.	Hypertransfusion and hydroxyurea 1000 mg daily	At 6 months follow-up: Gradual symptom resolution and radiographic regression of mass.
1985	Fucharoen ^[3]	23	M	Right frontoparietal	1 Year	Twenty-three-year-old male experienced sudden generalized convulsions found to have a right frontoparietal lesion on CT and angiography.	Surgery and adjuvant radiotherapy	At 5 months follow-up: No convulsions and no longer taking anti-epileptic drugs.
1980	Fucharoen ^[4]	27	F	Interhemispheric lesion, spinal epidural lesion	15 Months	Twenty-seven-year-old female presented with episodic paraparesis, found to have multifocal intracranial and spinal epidural EMH.	Radiotherapy	Deceased
2017	Hisamud-Din ^[5]	26	M	Thoracic 5-8	14 Years, 4 days	Twenty-six-year-old male presented with 4 days of progressive lower extremity weakness after 14 years of lower extremity paresthesia.	Surgery, transfusions, hydroxyurea, and steroids	Walking without assistance a few months after surgery.
2012	Karki ^[6]	13	M	R temporoparietal	1 Year	Thirteen-year-old male presented with the left-sided weakness and gait disturbance found to have large right temporoparietal, extra-axial mass.	Surgery	Not Stated
2015	Mehta ^[9]	67	F	L frontoparietal	4 Days	Sixty-seven-year-old female presented 4 days after a mechanical fall with confusion and lethargy found to have left-sided chronic subdural hematoma.	Burr hole and craniotomy	Deceased

(Contd...)

Table 1: (Continued).

Year	First Author	Age	Sex	Location	Time Course	Description	Treatment	Outcome
2018	Merchant ^[10]	18	M	Bilateral, frontoparietal convexities	20 Days	Eighteen-year-old male with years of chronic headaches presented with acute exacerbation associated with nausea and vomiting.	Transfusion and hydroxyurea	Several weeks after initiating therapy: Improvement in headache severity and radiographic reduction in masses.
2018	Merchant ^[10]	17	M	Right parieto-occipital calvarial thickening	6 Months	Seventeen-year-old male presented with chronic headaches.	Transfusion and hydroxyurea	Several weeks after initiating therapy: Improvement in headache severity and radiographic reduction in masses.
1969	Polliack ^[13]	0.75	M	Diffuse nodules along left hemisphere	Not Stated	Nine-month-old male presented with generalized weakness and uncontrollable diarrhea, progressed to comatose state.	Transfusions	Deceased
2011	Tabesh ^[15]	34	M	Left occipital horn	4 Months	Thirty-four-year-old male presented with chronic headaches associated with rapid vision loss and disequilibrium found to have a lobulated mass near the left occipital horn.	Surgery	At 4 months follow-up: headaches resolved residual vision loss.
2012	Tayari ^[16]	34	M	Left parietal, paraventricular	10 Months	Thirty-four-year-old male presented with 10 months of headache, nausea, and worsening vision loss. Left parietal intra-axial lesion was discovered on MRI.	Surgical biopsy	Not stated

EMH: Extramedullary hematopoiesis

traumatic brain injury such as cerebral edema, contusions, microscopic hemorrhages, or signs of brain compression or midline shift. The marrow signal on susceptibility weighted imaging was consistent with iron deposition. The extra-axial lesions were noted to be located within the dura and demonstrated minimal enhancement on post contrast imaging, distinguishing them from multiple meningiomas with calcification [Figure 2]. The clinical presentation and MRI findings were highly suggestive of multiple pseudotumors secondary to intracranial EMH. Confirmatory

diagnosis through biopsy or Tc99m labeled sulfur colloid was considered, however, due to patient being clinically stable and having consistent follow-up with an outside hospital, we thought that it would be unnecessary. Hematology was consulted and recommended that no thalassemia intervention was indicated. The remainder of the patient's hospital course was uncomplicated. Intracranial EMH was a newly observed phenotype in this patient, as he had no prior neurological symptoms or head imaging. The patient was discharged home in good condition.

DISCUSSION

Emergency management of space-occupying and extra-axial hematomas is a critical and necessary skill for all neurosurgeons. Our case of intracranial EMH highlights the importance of clinical correlation and entertaining a broad differential when the presentation is uncommon or the patient's history is suggestive of an alternative etiology. The initial presumed diagnosis for this patient with beta-thalassemia and head trauma was of traumatic extra-axial hematomas. The patient's neurological examination was good and additional radiographic stigmata of such a significant head injury were absent. This, combined with the patient's medical history of beta-thalassemia, prompted further investigation for an alternative diagnosis.

The patient's clinical presentation and diagnostic MRI were highly suggestive of the pseudotumors secondary to intracranial EMH. This altered the patient's management and was critical to avoiding prolonged neuromonitoring and unnecessary interventions for this patient. According to Singer and Quencer, confirmatory diagnosis is made by biopsy or Tc99m labeled sulfur colloid; however, considering the patient was clinically stable so we opted for no further testing.^[14] In addition, the appearance of intracranial EMH as multiple lesions that are isodense to grey matter has also been reported, further strengthening the importance of obtaining an MRI.^[7] Interestingly, we observed an apparent 4 h interval increase in the size of the patient's bifrontal convexity extra-axial lesions. This may suggest that pseudotumors have the potential to acutely worsen despite a generally chronic course. However, given mild expansion (2–3 mm in either dimension), we also cannot rule out the possibility that this was within the error of the scan given that the slice thickness was a standard 5 mm, rather than a thin-slice CT.

Mehta *et al.* have reported the only other case of head trauma and intracranial EMH in a patient with beta-thalassemia. The authors described the case of a 67-year-old female who presented 4 days after a mechanical fall with an altered level of consciousness and a chronic appearing subdural hematoma treated with burr-hole evacuation.^[9] The patient subsequently had episodes of symptomatic re-accumulation requiring repeated evacuation. During one of the evacuations, thickened skull and dura matter were encountered, as well as a gelatinous membrane encasing thick hemosiderin-stained material overlying the brain. The authors concluded that intracranial hematopoiesis may develop acutely after traumatic brain injury or multiple surgical manipulations. They further argued that immunohistochemical staining confirmed the diagnosis of EMH with positive glycophorin C in erythropoietic islands, neutrophil elastase, and CD42b. It remains unclear if this reported case truly represented intracranial EMH or merely chronic subdural hematoma membranes with findings related to angiogenesis within

those membranes.^[8] Additional cases of intracranial EMH in patients with beta-thalassemia without head trauma have been reported [Table 1].^[3,4,6,16]

Neuroaxis extramedullary pseudotumors can be managed nonoperatively or operatively. Several authors have reported acceptable outcomes after surgical resection.^[5,9,12,15] Radiation, either as primary or adjuvant therapy, has been used to treat EMH pseudotumors across various myeloproliferative disorders.^[2,11] Finally, medical management with transfusions has proven to be effective in reducing pseudotumor burden.^[1,10,13] Our patient presented with mild post-concussive headaches that improved during his hospital course. The authors agreed that the patient's pseudotumors were ultimately minimally symptomatic and nonoperative management was the most appropriate.

No written consent could be obtained for this publication. The first author received verbal consent from the patient on two separate occasions; however, attempts to receive a signed consent from the patient were unsuccessful. We believe that our manuscript does not have personal identifiers which would jeopardize the patient's confidentiality.

CONCLUSION

Intracranial extramedullary hematopoietic pseudotumor is a rare clinical phenotype and should be considered in the differential diagnosis for a space-occupying extra-axial lesion in a patient with history of beta-thalassemia and head trauma.

Declaration of patient consent

Patient's consent not required as patient's identity is not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

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