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Case Report Open Access

Compressive Optic Neuropathy in Thalassemia: A Rare Ophthalmic Consequence of Extramedullary Hematopoiesis

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Abstract

Extramedullary hematopoiesis (EMH) is a compensatory physiological proliferation of hematopoietic elements outside the bone marrow as a result of insufficient bone marrow erythropoiesis. It is found in various hematologic disorders (e.g., as sickle cell anemia, thalassemia, myelofibrosis) especially those with chronic anemias. It can affect in any organs, thus producing numerous complications. However, compressive optic neuropathy has been rarely reported. The authors present a case report of an 18-year-old man who was known to be beta thalassemia/Hb E disease with the presentation of compressive optic neuropathy with an excellent response to combination treatment of blood transfusions and low-dose radiotherapy. These findings reflect that beta thalassemia/Hb E or thalassemia intermedia patients should have periodic comprehensive ophthalmic assessment especially those with inadequate blood transfusions. Moreover, favorable visual outcome can be achieved with early recognition and prompt management with blood transfusions combined with low-dose radiotherapy.

Keywords: Extramedullary hematopoiesis; Thalassemia; Optic neuropathy; Compression; Visual loss

Introduction

Extramedullary hematopoiesis (EMH) is a compensatory physiological proliferation of hematopoietic elements outside the bone marrow as a result of insufficient bone marrow erythropoiesis [1]. It is found in various hematologic disorders (e.g., as sickle cell anemia, thalassemia, myelofibrosis) especially those with chronic anemias [1]. EMH is typically seen in areas producing fetal hemoglobin, such as spleen, liver and lymph nodes [2]. However, intracranial, middle ear, intrathoracic, adrenal gland, paravertebral and pelvic cavity have also been reported [1,3]. Regarding neurological complications, spinal cord compression from vertebral canal EMH is the most common sequela [1]. Compressive optic neuropathy is an extremely rare complication. Here we present a rare case of visual impairment as a consequence of anterior visual pathway compression due to EMH in a patient with beta thalassemia/Hb E disease.

Case Report

An 18-year-old Thai man presented with slowly progressive, painless visual loss of his right eye over a month. He denied seeing double vision. His past medical history was significant for beta thalassemia/Hb E disease. He received recent blood transfusion at the age of 3 years and his hematocrit was stable at 26 since then.

Ophthalmic examination revealed visual acuity of 20/80 right eye, and 20/20 left eye. Relative afferent pupillary defect was present in the right eye. Anterior segment of both eyes were unremarkable. Fundus examination of both eyes showed normal appearance of optic discs with presence of spontaneous venous pulsations. Neither proptosis nor limitation of ocular motility was observed. Systemic neurological examination was otherwise unremarkable.

Computerized static visual field test using Humphrey SITA 30-2 program of right eye showed diffused visual field defect with inferonasal quadrant sparing (Figure 1A). Visual field test of the left eye using the same program was normal. Color vision test using Ishihara pseudoisochromatic plate and Farnsworth panel D-15 of both eyes were normal. Despite the accurate arrangement of total 15 colored discs in Farnsworth panel D-15 test and correct identification of all plates in Ishihara pseudoisochromatic plate, slower performance was observed when his right eye was tested. Optical coherence tomography (OCT) examination using StratusOCT (Carl Zeiss Meditec, Dublin, CA, software version 6.0.0 (0599)) showed average peripapillary retinal nerve fiber layer of 102 micrometers, 82 micrometers for right eye and left eye respectively.

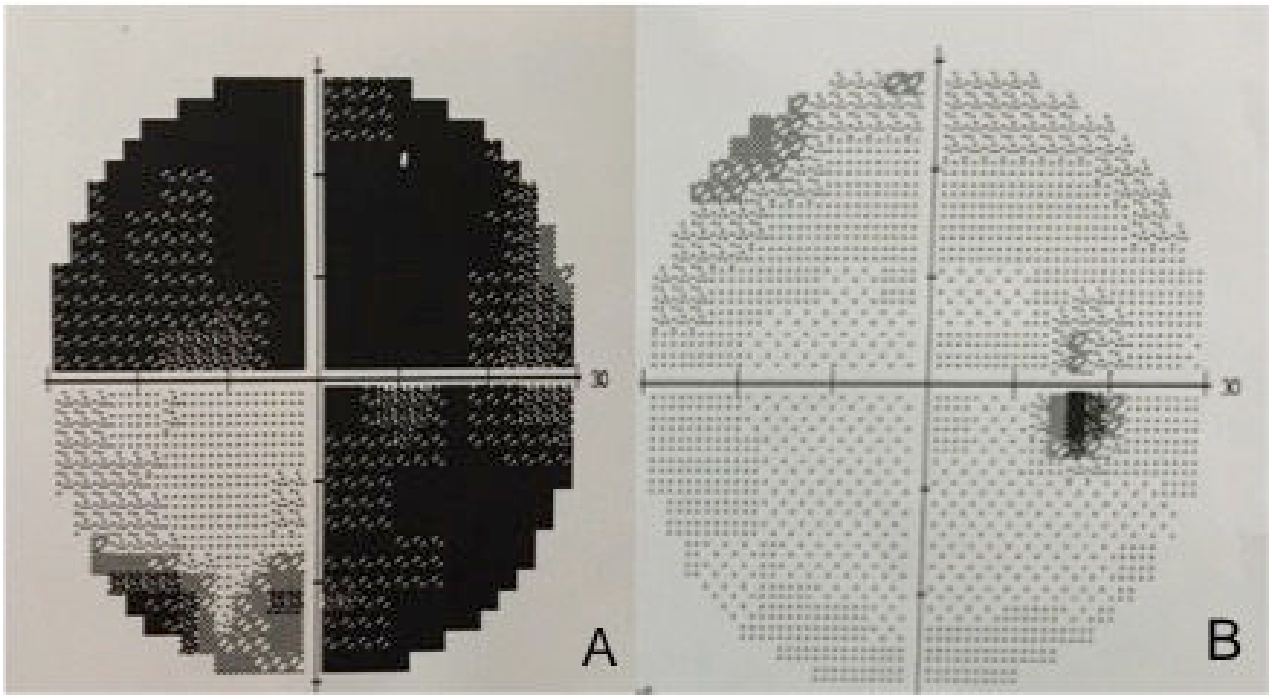

Figure 1. Humphrey visual field 30-2 of the right eye at initial presentation (A) and one month after treatment (B).

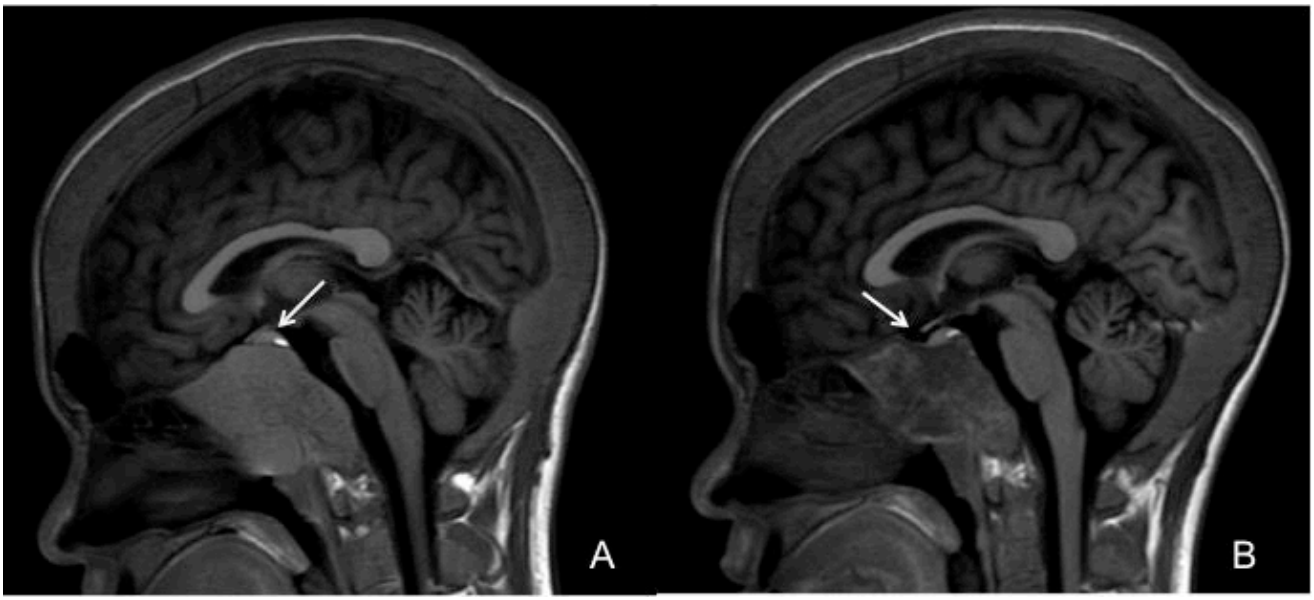

Figure 2: MRI of the orbit and brain. (A) Sagittal T1-weighted showing massive expansion of marrow originating from clivus, obliterating bilateral sphenoid sinuses and pituitary fossa. Pituitary gland is also displaced upward from the tumor-like expansion of marrow (arrow). Enlargement of the diplopic space of calvarium is also depicted. (B) Sagittal T1-weighted showing reduction in the size of tumor-like expansion with visible pituitary fossa (arrow).

Complete blood count showed hemoglobin of 7.5 g/dL (normal: 13-18 g/dL), hematocrit of 26.1 (normal: 40-54), with anisocytosis, microcytosis, hypochromia, and nucleated red blood cells (940 per 100 white blood cells).

Magnetic resonance imaging (MRI) of the orbit and brain revealed enlargement of the diplopic space of calvarium, massive expansion of marrow at the clivus obliterating bilateral sphenoid sinuses and pituitary fossa (Figure 2A). Moreover, narrow bilateral optic canals,

compression and stretching of prechiasmatic optic nerves and optic chiasm were detected (Figure 3A). Hyperintense T2 of prechiasmatic, intracanalicular and intraorbital optic nerves with right side predominance were revealed which consisted with bilateral optic neuropathy (Figure 4). No enhancement of bilateral optic nerves was shown from the study. Additional orbital computed tomography (CT) showed significant enlargement of diplopic space of sphenoid bone resulting in bilateral narrow optic canals (Figure 5).

The diagnosis of compressive optic neuropathy due to extramedullary hematopoiesis was made. Subsequently, treatment was begun with monthly blood transfusions. A course of 10-day radiotherapy (total dose of 20 Gy in 10 fractions) was also performed.

One month later, he reported significant improvement of his vision. Relative afferent pupillary defect was no longer present. Visual acuity was 20/20 both eyes. No pallor of both optic discs was found. Visual field test of both eyes using the same program as previous mentioned was perfectly unremarkable (Figure 1B). OCT examination of average peripapillary retinal nerve fiber layer remained stable compared to initial result. Complete blood count showed hemoglobin of 9.9 g/dL (normal: 13-18 g/dL), hematocrit of 33.4 (normal: 40-54). Follow-up MRI also showed marked resolution of extramedullary hematopoietic tissue along with improvement of compression and stretching of bilateral optic nerves (Figures 2B and 3B).

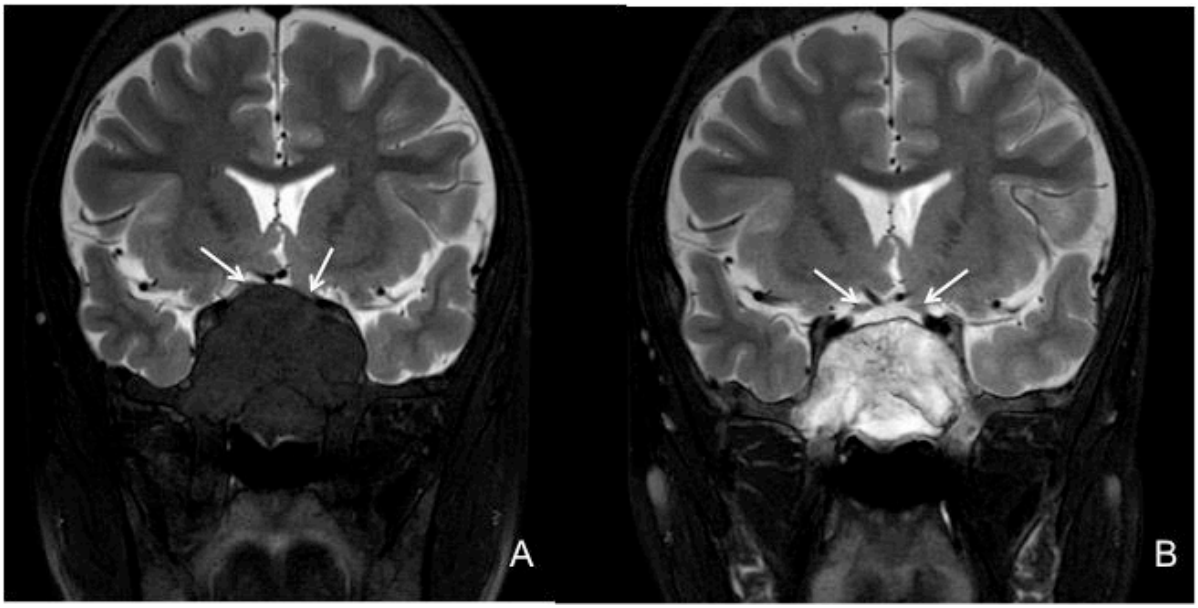

Figure 3: MRI of the orbit and brain. **(A)** Coronal T2-weighted showing compression and stretching of bilateral prechiasmatic optic nerves (arrows). **(B)** Coronal T2-weighted showing reduction in the size of the tumor-like expansion along with improvement of compression and stretching of bilateral prechiasmatic optic nerves (arrows).

Publication	Age (y), sex	Phenotype	Hb (g/dL)	Previous BT	VA	VF defect	Optic disc appearance	Treatment	Final VA	Final VF	Follow-up period (months)
[6]	21, M	Homozygous B-thal	7.5	Age of 4 y (monthly)	CF1m CF0.5m	Constriction and superior bitemporal quadrantanopia BE	Pale BE	BT,RT,C,SX	CF2m CF1m	Same	96
[5]	NA	B-thal intermedia	NA	NA	20/20 20/40	NA	Pale BE	BT,C,EPO,H	20/20 20/40	NA	NA
[4]	13, F	B-thal/HbE	7.5	Age of 5 y (every 3 months)	2/60 5/60	Tunnel vision with constriction BE	Pale BE	BT,RT	6/36 6/24	NA	at least 1 week
[7]	21, M	B-thal intermedia	8.3	Age of 4 y (intermittent)	CF2m HM	NA	Chronic papilledema BE	BT,ACE	CF2m CF0.5m	NA	13

M: Male; F: Female; y: Years; B-thal: Beta Thalassemia; HbE: Hemoglobin E; Hb: Hemoglobin; BT: Blood Transfusions; VA: Visual Acuity; CF: Finger Count; m: Meter; HM: Hand Motions; VF: Visual Field; BE: Both Eyes; RT: External Radiation; C:Corticosteroids; SX: Partial Excision of Intrasellar Mass (Transphenoidal Approach); EPO: Erythropoietin; H:Hyperbaric oxygen; ACE: Acetazolamide; NA: Not Applicable.

Table1: Overview of compressive optic neuropathy due to extramedullary hematopoiesis in thalassemia in the current literature.

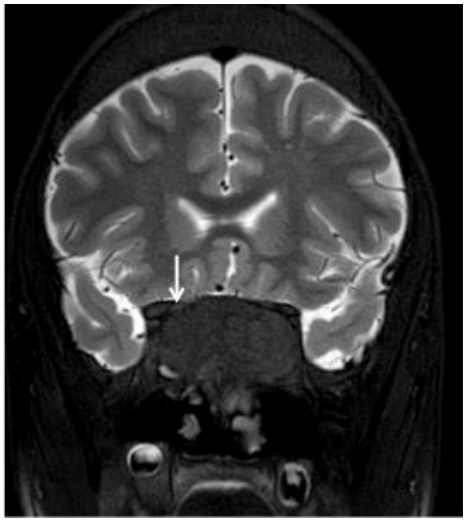

Figure 4: MRI of the orbit and brain. Coronal T2-weighted showing hyperintense T2 of intracanalicular optic nerve of the right eye (arrow) with close proximity to the tumor-like expansion of marrow.

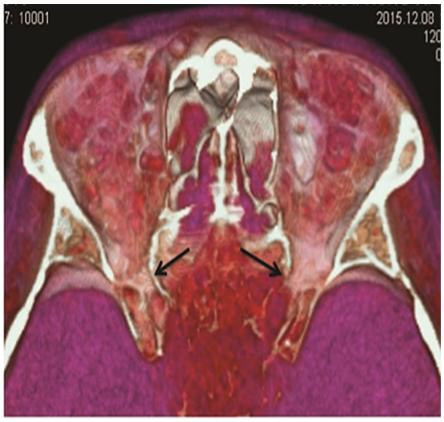

Figure 5: CT of the orbit showing expansion of sphenoid bone resulting in bilateral narrow optic canals (arrows).

Discussion

Only 4 patients of compressive optic neuropathy due to extramedullary hematopoiesis in thalassemia have been reported [4-7], (Table 1). Of all 4 patients, initial assessment of fundus examination showed optic disc pallor in the affected eyes. To our knowledge, our patient was the first patient reporting the best visual outcome regarding treatment of compressive optic neuropathy secondary to extramedullary hematopoiesis in thalassemia given the initial normal appearance of optic discs without any pallor in our patient.

Regular blood transfusions were the first-line and main treatment among previous published reports. Regular blood transfusions combined with low-dose radiotherapy have been reported to be efficacious [4]. Since extramedullary hematopoietic tissue is highly radiosensitive, shrinkage of ectopic marrow and reduction of compressive effect on adjacent structures can be achieved with low-dose radiotherapy [8]. Ittipunkul et al. [4] reported a 13-year-old girl with beta thalassemia/Hb E disease who developed visual loss in both eyes from optic nerve compression caused by extramedullary hematopoiesis. Visual acuity was 2/60 right eye, and 5/60 left eye. Fundus examination revealed optic disc pallor in both eyes. Improvement of vision to 6/36 right eye, and 6/24 left eye following blood transfusion and radiation (13 Gy) was noted.

Sorcinelli et al. [5] reported a patient with thalassemia intermedia who presented with bilateral optic atrophy resulting from compressive optic neuropathy due to extramedullary hematopoietic tissue. The patient received various modalities of treatment including corticosteroids, erythropoietin and hyperbaric oxygen in addition to blood transfusions. Visual acuity was stable at 20/20 right eye, and 20/40 left eye.

Aarabi et al. [6] described a patient with homozygous beta thalassemia complaint of dimness of vision. Bilateral optic atrophy with visual acuity of 1 meter finger count right eye, and one-half meter finger count left eye were documented. In addition to regular blood transfusions, partial resection of the tumor combined with low-dose radiation (30 Gy) was underwent. Final visual acuity of 2 meter finger count right eye, and 1 meter finger count left eye were achieved.

The last patient was reported by Pakdel et al. [7]. Pakdel et al. described a 21-year-old man known to be beta-thalassemia intermedia who presented with blurred vision and chronic papilledema. Spontaneous venous pulsations were not seen. Visual acuity was 2 meter finger count right eye, and hand motions left eye. The expansion of hematopoietic tissue resulted in compression of both optic nerves. Moreover, hydrocephalus due to compression of sylvian aqueduct was also noted. Regular blood transfusions with acetazolamide were initiated with final visual acuity of 2 meter finger count right eye, and one-half meter left eye.

Significant improvement of visual functions both visual acuity and visual field in our patient following regular blood transfusion and low-dose radiotherapy was achieved owing to two reasons. First, our patient was diagnosed at the early stage of the disease. He reported progressive loss of his vision only a month. Second, his initial assessment of fundus examination showed neither pallor nor absence of spontaneous venous pulsations of both optic discs in contrast to the previous published reports [4-7].

In conclusion, although compressive optic neuropathy secondary to extramedullary hematopoiesis is extremely rare. Beta thalassemia/Hb

E or thalassemia intermedia patients should have periodic comprehensive ophthalmic assessment especially those with inadequate blood transfusions. Favorable visual outcome can be achieved with early recognition and prompt management with blood transfusions combined with low-dose radiotherapy.

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