

R Muhamad-Amin^{1,2,3}, Nur
Hasnida Gani^{1,2,3}, AH Zamli³
AT Liza-Sharmini^{1,2}

Optic Nerve Infiltration in Adult Acute Lymphoblastic Leukaemia (ALL)

¹Department of
Ophthalmology, School of
Medical Sciences, Universiti
Sains Malaysia, Health
Campus, 16150 Kubang
Kerian, Kelantan, Malaysia

²Hospital Universiti Sains
Malaysia, 16150 Kubang
Kerian, Kelantan, Malaysia

³Hospital Tengku Ampuan
Afzan Pahang, Jalan Tanah
Putih, 25100 Kuantan,
Pahang

*Corresponding author:
Muhamad Amin Ramli
E-mail:
muhamadaminramli@gmail.com

Received 23 July 2018.
Revised 30 Nov 2018.
Accepted 25 Dec 2018.
Published Online 08 Jan 2019

Abstract— Acute lymphoblastic leukemia (ALL) is the most common childhood leukaemia. It is a malignant neoplasm caused by the proliferation of poorly differentiated precursors of the lymphoid cells. It is relatively uncommon in adult. In adult ALL, central nervous system (CNS) involvement is associated with poor prognosis. The incidence of CNS involvement has been reported between 7% and 15 %. We report a case of optic nerve infiltration in ALL in a 49 years old gentleman. He was diagnosed with precursor-B ALL. He was treated with chemotherapy and CNS prophylactic regime. He presented with sudden left eye loss of vision for one-day duration with history of right eye inferior visual field loss for the past three months. His visual acuity was no perception to light on the left eye and 6/9 on the right eye. There was marked left relative afferent pupillary defect. The right eye showed decreased in optic nerve function with inferior visual field defect. Anterior segment examination was unremarkable in both eyes. Left optic disc appeared normal but the right optic disc was pale. Blood investigation showed no sign of infection or haemoconcentration. Cerebral spinal fluids examination revealed abundant of white cells and blast cells. Magnetic resonant imaging showed bilateral optic nerve enhancement suggesting of bilateral optic nerves infiltration. He was started on a new regime of chemotherapy followed by cranial radiotherapy. Unfortunately, he succumbed to death due to septicaemia. There are variations in clinical presentation of optic nerve infiltration in leukaemic patients. Normal appearance of optic disc may not exclude the possibility of infiltration by malignancy. Assessment of the optic nerve function and imaging is helpful for the detection of leukaemic infiltration. Early detection of optic nerve infiltration is important for initiation or change of therapy to prevent mortality.

Keywords— acute lymphoblastic leukaemia, optic nerve infiltration.

1 INTRODUCTION

Acute lymphoblastic leukaemia (ALL) is a malignant neoplasm caused by proliferation of poorly differentiated precursors of lymphoid cells [1]. The estimated worldwide annual incidence of ALL in adult is about one in 100,000 [2]. Contrary to childhood ALL, overall survival rate with modern therapeutic modalities is lower with 80% survival after 5 years of treatment [3].

Ocular involvement is not uncommon in ALL. It can be classified into two major categories: primary or direct leukemic infiltration of the ocular structures; and secondary or indirect involvement. These secondary involvements are due to hematologic abnormalities; anaemia, thrombocytopenia, leukopenia, and hyperviscosity [1]. Any part of ocular and orbital structures can be affected. Optic nerve infiltration can be part of early presentation of ALL or early sign of relapse after remission [4]. There are

reported variations in clinical presentation of optic nerve infiltration that may delay the diagnosis.

We reported a case of ALL in an adult who presented with different clinical presentation of bilateral optic nerve infiltration. Thorough investigation was conducted to confirm the central nervous system (CNS) involvement in this uncommon type of leukaemia in adult.

2 CASE REPORT

A 49 years old gentleman presented to us with a complaint of left eye vision loss. He was previously diagnosed with precursor-B ALL for one year duration, and was then on German Multicentre Study Group for Adult Acute Lymphoblastic Leukaemia (GMALL) regime. Prophylactic central nervous system (CNS) treatment was included in this regime. He was diagnosed with ALL after multiple episodes of high grade fever, marked weight loss, generalized

lymphadenopathy, splenomegaly and gum bleeding.

At 22 weeks of treatment with chemotherapy, he complained to us of left eye vision loss for one-day duration. It was associated with minimal left eye pain. However, there were no symptoms of increased intracranial pressure. He also noticed that he had difficulty in climbing up stairs for the past 3 months. He had difficulty in seeing the steps of the stairs which he regarded as part of the side effects of treatment. However, there was no history of a fall.

On examination, left relative afferent pupillary defect (RAPD) was present. Visual acuity on left eye was no perception to light (NPL) and right eye best corrected vision was 6/9. There was desaturation of red colour on the right eye but with normal intensity in light brightness. Anterior segment examinations were unremarkable for both eyes. Fundus examination showed pale optic disc on the right eye (Figure 1). Left eye showed well defined margin and pink optic disc with cup to disc ratio of 0.4. There was no sign of optic disc swelling or any changes in the retinal and the vessels were normal (Figure 1). Intraocular pressure was within normal limits. Humphrey Visual Field (HVF) of the right eye showed inferior altitudinal vision loss (Figure 2). Optical coherence tomography (OCT) of the optic nerve head and central macula was essentially normal bilaterally (Figure 4 and 5). His colour vision was also defective based on the 100 Hue test.

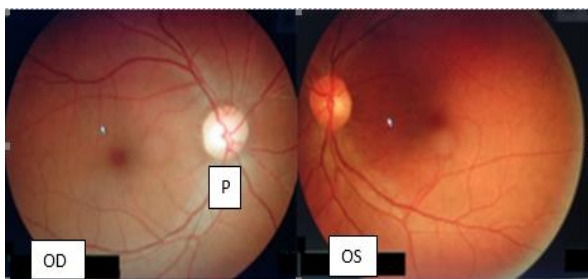


Figure 1: Right fundus showing optic disc pallor and normal appearance of left optic disc. OD: right eye, OS: left eye, P: pale optic disc

Full blood count showed haemoglobin level at 10.7 g/dl, packed cell volume of 31.6%, platelet count of $238 \times 10^9/L$, and total white blood cell count of $14.59 \times 10^9/l$. Full blood picture showed no increase of blast cell. The patient showed elevated erythrocyte sedimentation rate (ESR) of

41 mm/hr. Magnetic resonance imaging (MRI) of brain and orbit showed marked enhancement of the bilateral optic nerve sheath (Figure 3). Lumbar puncture was also conducted and abundant white blood cells (65 per microliter) and blast cells were detected on the cerebrospinal fluid (CSF) examination. The opening pressure was normal. There was no organism seen in the CSF. Bone marrow aspiration Trepine (BMAT) showed acellular with heterogeneous population mostly by erythroid cells and there was no increase in blast cells.

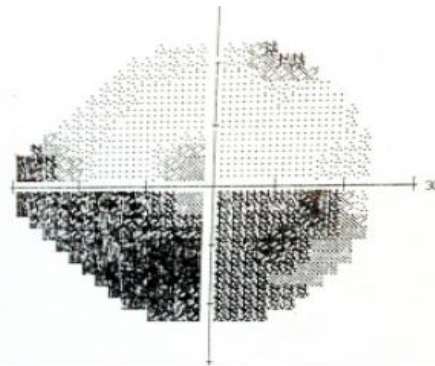


Figure 2: Humphrey visual field analysis of right eye showed loss of inferior half of visual field.

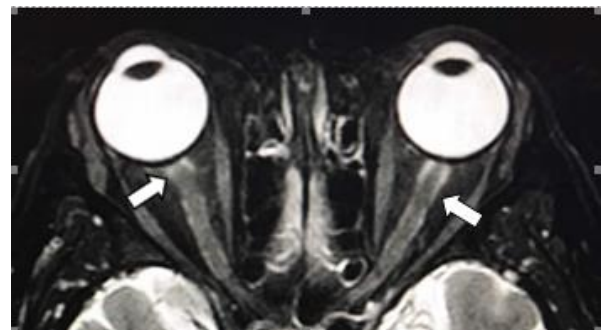


Figure 3: Contrast-enhanced MRI showing marked enhancement of the bilateral optic nerve sheath on axial view replicating the tram track sign.

Based on the clinical presentation and investigations, he was diagnosed with CNS infiltration through optic nerve involvement. Intravenous methylprednisolone 1 gram once daily for three days was started as a trial treatment for optic neuritis. However, there was no improvement in optic nerve function and visual acuity. Due to aggressiveness of the disease, intrathecal methotrexate was administered and cranial irradiation was conducted. Unfortunately,

there was not much improvement; he succumbed to the disease due to complications with septicaemia three month later.

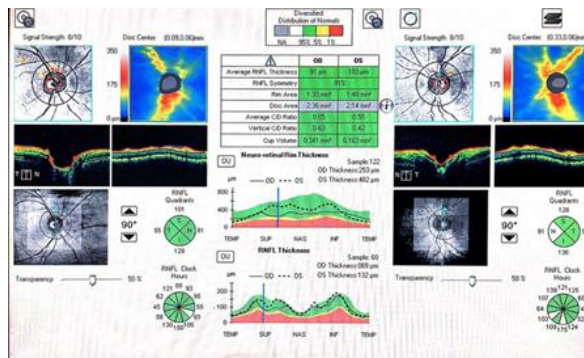


Figure 4: Normal retinal nerve fibre layer thickness of both optic nerve head on ocular coherence tomography imaging. OD: right eye, OS: left eye.

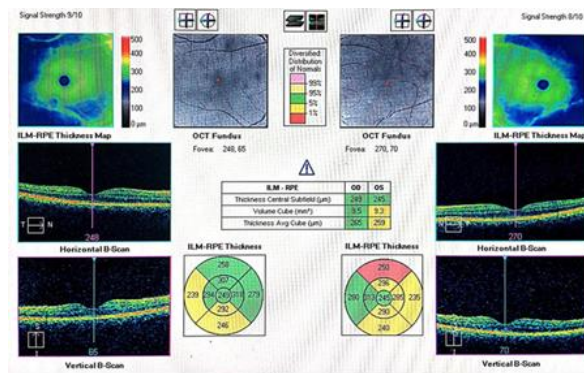


Figure 5: Normal central macula thickness of both eyes on ocular coherence tomography imaging. OD: right eye, OS: left eye

3 DISCUSSION

Ocular involvement is the third-most-frequent extramedullary presentation of acute leukaemia after the meninges and testicles [5]. Ocular involvement is associated with higher frequency of bone marrow relapses and central nervous system involvement. Optic nerve infiltration is caused by direct infiltration of the tumour cells and various inflammatory reactions secondary to the tumour.

We reported a case of bilateral optic nerve infiltration in an adult with ALL that occurred during the chemotherapy treatment. The incidence of the optic nerve infiltration has been reported from 13 to 18 % of all type of leukaemias. It has been reported to occur either during evolution of ALL [1] or as extramedullary

relapse after remission. It is not uncommon; due to the blood-ocular and blood-brain barriers, the chemotherapy drugs failed to reach the eye and brain [6]. The optic nerve is considered a pharmacologic sanctuary from leukaemia therapy [6]. In the present case, he was treated with CNS prophylactic chemotherapy as part of the GMALL regime.

However, clinical presentations of optic nerve infiltration varies. Optic disc elevation or swelling with evidence of optic nerve dysfunction, optic disc elevation or swelling with no evidence of optic nerve dysfunction and normal appearance of optic disc associated with evidence of dysfunction have been reported [7]. Optic disc swelling is the most frequent sign of optic nerve infiltration [1]. Optic disc swelling can be due to direct infiltration of the nerve by leukaemic cells, increased intraocular pressure, or swelling because of retro lamellar leukaemic invasion. Leukaemic infiltration features also include retinal haemorrhages, vitreous haemorrhage and retinal detachment [8].

In this present case, there was normal appearance of optic disc of the left eye without any changes in the fundus finding. While in the right eye, optic disc showed sign of atrophy (figure 1). Most likely, the right eye was affected earlier (even may have occurred during initial presentation) but he was not aware due to essentially good vision of the left eye. Another possible explanation is non-arteritic anterior ischemic optic neuropathy (NAION) in the right eye. NAION is due to small vessel infarction in optic nerve head and in this case most likely due to inflammatory cells or leukaemic infiltration. Inferior altitudinal visual field defect (figure 2) and optic nerve dysfunction is the classical finding of NAION. Majority of the cases maintained good visual acuity and persistent visual field defect after the initial episode of vision loss in NAION [9]. However, the age is rather young for classical NAION.

MRI findings further strengthen the argument of bilateral optic nerve infiltration caused by inflammation of neural sheath rather than NAION. Involvement of the retrobulbar inflammation of neural sheath may provide an explanation of normal retinal nerve fiber layer (RNFL) thickness of optic nerve head in this patient. Right RNFL thickness was still within normal range in the presence of optic atrophy was likely due to short duration post postulated optic nerve infiltration [10]. Blood investigation and CSF findings further supported the CNS

involvement in this case. An isolated CNS relapse is classically defined as the presence of five or more white blood cells (WBCs) per microliter in the cerebral spinal fluid (CSF) associated with the presence of leukemic blasts and no morphologic evidence of marrow relapse [11] as shown in this case.

Poor prognostic factor for survival in ALL include age and CNS infiltration [12]. In spite of the aggressive treatment given, he succumbed to death due to septicaemia. Perhaps, if the initial presentation of right eye infiltration was detected earlier, chances of survival would be better. However, detection is a challenge due to variations of clinical presentations. Even in the same patient, presentation may differ between the two eyes as observed in this patient.

4 CONCLUSION

There are variations in clinical presentation of optic nerve infiltration in leukaemic patients. Normal fundus appearance in leukemic patient does not rule out infiltration. Symptoms of visual disturbance is an early indicator of optic nerve infiltration. Early detection of optic nerve infiltration in ALL patients by assessment of the optic nerve function and imaging is helpful for the detection of leukaemic infiltration and important to improve the survival. Variation of clinical presentation make the diagnosis challenging and sometimes delay the detection of optic nerve infiltration.

CONFLICT OF INTEREST

The authors declare no conflict of interests. The authors alone are responsible for the content and writing of the paper.

REFERENCES

- [1] Mateo J, Ascaso FJ, Núñez E, Peiro C, González G, Cristóbal JA. Ophthalmological manifestations in acute lymphoblastic leukemia. *Novel Aspects in Acute Lymphoblastic Leukemia: InTech*; 2011.
- [2] Abbasi S, Maleha F, Shobaki M. Acute lymphoblastic leukemia experience: epidemiology and outcome of two different regimens. *Mediterranean journal of hematology and infectious diseases*. 2013; 5(1).
- [3] Pui C-H, Robison LL, Look AT. Acute lymphoblastic leukaemia. *The Lancet*. 2008; 371(9617):1030-43.
- [4] Bandyopadhyay S, Das D, Das G, Gayen S. Unilateral optic nerve infiltration as an initial site of relapse of acute lymphoblastic leukemia in remission. *Oman journal of ophthalmology*. 2010; 3(3):153-4.
- [5] Charif Chefchaouni M, Belmekki M, Hajji Z, Tahiri H, Amrani R, El Bakkali M, et al. Ophthalmic manifestations of acute leukemia. *Journal francais d'ophtalmologie*. 2002; 25(1):62-6.

- [6] Nikaido H, Mishima H, Ono H, Choshi K, Dohy H. Leukemic Involvement of the Optic Nerve. *American Journal of Ophthalmology*. 1988; 105(3):294-8.
- [7] Miller NR, Walsh FB, Hoyt WF. *Walsh and Hoyt's clinical neuro-ophthalmology*: Lippincott Williams & Wilkins; 2005.
- [8] Hsuen-Fu Lin., Ming-Shen Dai., Woei-Yau Kao., Chao. T-Y. Unilateral Optic Nerve Leukemic Infiltration with Sudden Vision Loss Heraldng a Systemic Relapse of Acute Lymphoblastic Leukemia. *J Med Sci*. 2005; 25(2):097-100.
- [9] Anthony C. Arnold M, M. Tariq Bhatti M, Leah Levi M, Valerie A. Purvin M. Case Studies in Optic Disc Edema *EyeNet Magazine* 2015. 43-8]. Available from: <https://www.aao.org/eyenet/article/case-studies-of-optic-disc-edema>.
- [10] Byon IS, Jung JH, Choi JH, Seo JH, Lee JE, Choi HY. Evaluation of Retinal Nerve Fiber Layer in Patients with Idiopathic Optic Perineuritis using Optical Coherence Tomography. *Neuro-ophthalmology*. 2015; 39(1):34-8.
- [11] Jacobs JE, Hastings C. Isolated extramedullary relapse in childhood acute lymphocytic leukemia. *Current hematologic malignancy reports*. 2010; 5(4):185-91.
- [12] Rowe JM. Prognostic factors in adult acute lymphoblastic leukaemia. *British journal of haematology*. 2010; 150(4):389-405.