Malaysian Journal of Ophthalmology

© Malaysian Journal of Ophthalmology 2019; 1:60-65

Case report

Reversal of impending central retinal vein occlusion secondary to hyperleukocytosis in chronic myeloid leukemia by leukapheresis: a case report

Logesvaran Murugan, Aida Zairani Mohd Zahidin, Wan Haslina Wan Abdul Halim

Department of Ophthalmology, Hospital Canselor Tuanku Muhriz, Universiti Kebangsaan Malaysia Medical Center (UKMMC), Cheras, Kuala Lumpur, Malaysia

Abstract

We report an uncommon case of bilateral impending central retinal vein occlusion (CRVO) in a young girl with newly diagnosed chronic myeloid leukaemia (CML) and its successful reversal with leukapheresis. A young girl presented with vomiting and fever. Examination revealed hepatosplenomegaly and multiple enlarged lymph nodes. Investigations show severe hyperleukocytosis and anaemia. Bone marrow aspirate and trephine biopsy confirmed CML in the chronic phase. She was promptly referred to the ophthalmology team for assessment of vasculopathy. Bilateral fundus showed swollen and hyperaemic optic discs. There were dilated and tortuous retinal venules with perivascular white cell extravasation, scattered intraretinal haemorrhages, and Roth spots at mid-periphery. She received four cycles of leukapheresis and, consequently, her leukocytes reduced dramatically with associated significant improvement in fundus findings.

Correspondence: Aida Zairani Mohd Zahidin, MS Ophthal (UKM), Department of Ophthalmology, Universiti Kebangsaan Malaysia Medical Centre, Jalan Yaacob Latiff, Bandar Tun Razak, 56000 Cheras, Kuala Lumpur, Malaysia.
E-mail: aidazahidin2@gmail.com

This case highlights uncommon impending CRVO in a young girl and the dramatic improvement in fundus signs following leukapheresis that halted and reversed the progression of impending CRVO.

Keywords: central retinal vein occlusion, chronic myeloid leukaemia, leukapheresis

Pemulihan semula oklusi vena retinal utama ekoran daripada hiperleukositosis dalam leukemia myeloid kronik melalui rawatan leukapheresis

Abstrak

Kami melaporkan kes luar biasa berlaku pada seorang gadis muda, pengidap leukemia myeloid kronik (CML) yang hampir mengalami oklusi vena retinal utama (CRVO) pada kedua-dua belah mata, dan berjaya dipulihkan semula melalui rawatan leukapheresis. Seorang gadis muda mengalami demam dan muntah. Pemeriksaan mendedahkan hepatosplenomegali dan pembengkakan beberapa nodus limfa. Penyiasatan menunjukkan hyperleukocytosis yang teruk dan anemia. Pemeriksaan sumsum tulang dan biopsi trephine mengesahkan CML dalam fasa kronik. Beliau segera dirujuk kepada oftalmologi untuk pemeriksaan lanjut. Fundus pada kedua-dua mata menunjukkan cakera optik yang bengkak dan hiperemik. Terdapat venul retina yang mengembang dan bergelung-gelung serta limpahan sel putih perivascular dengan pendarahan intraretinal, dan bintik Roth pada fundus di bahagian antara pusat dan pinggiran. Beliau menerima empat kitaran leukapheresis dan hasilnya jumlah leukosit berkurangan secara ketara, seterusnya menunjukkan pemulihan yang ketara pada fundus.

Kes CRVO pada seorang gadis muda ini bukanlah kes yang lazim berlaku di mana pemulihan ketara pada fundus berikutan rawatan leukapheresis , yang akhirnya merencatkan dan memulihkan semula CRVO yang hampir berlaku.

Kata kunci: oklusi vena retinal utama, leukemia myeloid kronik, leukapheresis

Introduction

Venous occlusive disease of the retina is the second most common retinal vascular disorder after diabetic retinopathy.[1] Central retinal vein occlusion (CRVO) represents a large subset of venous occlusive disease of the retina and one of the major causes of severe vision impairment. It occurs due to thrombosis of the central retinal vein at

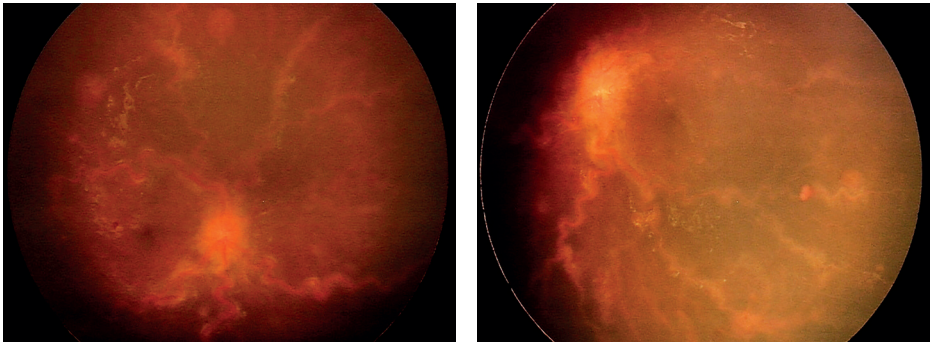

Fig. 1. Fundus pictures of both eyes taken with RetCam showing bilateral dilated, tortuous retinal veins, intraretinal haemorrhages, and a few preretinal haemorrhages. There is also marked optic disc swelling and perivascular white cell extravasation near to optic disc.

the level of the lamina cribrosa. CRVO can be divided into non-ischemic and ischemic varieties based on clinical and fluorescein angiography features.[1] Impending CRVO (also known as incipient, partial, or incomplete CRVO) is an arbitrary term used to describe asymptomatic patients or patients with amaurosis fugax with mild dilated, tortuous retinal veins and few widely scattered retinal haemorrhages.[2] Common risk factors for the development of CRVO include aging, smoking, obesity, atherosclerosis, hypertension, diabetes mellitus, hyperlipidaemia, raised intraocular pressure, and autoimmune disorders. In young patients, uncommon risk factors such as myeloproliferative disorders, congenital or acquired hypercoagulable states, and inflammatory disease associated with occlusive periphlebitis should be considered.[1]

Methods

Case report.

Results

A previously healthy 13-year-old Malay girl was referred to eye casualty with vomiting for two days and fever. There was no altered bowel habit, abdominal pain, appetite loss, nor weight loss. There is no history of malignancy in family. Past ocular history and social history were insignificant.

Upon general examination, there was pallor and multiple enlarged lymph nodes at supraclavicular and inguinal region. Systemic examination revealed normal lungs and cardiovascular system. However, abdominal examination showed presence of

Table 1. Pertinent blood investigation results

Investigations	Results
WBC	728.1 x 10^9/L
HB	6.9 g/dl
Platelet	265 x 10^9/L
C-reactive protein	0.62 mg/dl
Liver function test	Normal
Renal profile Sodium Potassium Urea Creatinine	 137 mmol/L 2.7 mmol/L 3.5 mmol/L 74.9 mmol/L
WBC after 4 cycles of leukapheresis	163.6 umol/L

massive hepatosplenomegaly. At presentation, she was having tachycardia with a heart rate of 130 beats/minute and temperature of 38.8°C.

A battery of tests was conducted and early results raised suspicion of haematological malignancy. She was promptly referred to the ophthalmology team for assessment of retinopathy or vasculopathy associated with haematological malignancy. She denied any visual symptoms and her visual acuity was 6/6 OU with no relative afferent pupillary defect. Her anterior segment examination and intraocular pressure were unremarkable. Bilateral fundus showed swollen and hyperaemic optic discs. There were markedly dilated and tortuous retinal venules with peculiar perivascular white cell extravasation, scattered intraretinal haemorrhages, and Roth spots at mid-periphery. The macula was normal and there was no neovascularization either on the retina or iris (Fig. 1).

Bone marrow aspirate and trephine biopsy confirmed chronic myeloid leukaemia (CML) in the chronic phase. Other investigation results are tabulated in Table 1. She was immediately started on cytoreduction therapy with hydroxyurea, cytarabine, and four cycles of leukapheresis. Subsequently, her leukocytes reduced dramatically to normal levels with accompanying significant improvement in fundus findings. The retinal vessels became progressively less tortuous and dilated, with resorption of perivascular leukocytes and improvement in optic disc swelling.

One month later, the retinal vessels were no longer dilated and tortuous, with complete resolution of retinal haemorrhages and marked reduction of optic disc swelling (Fig. 2). The impending CRVO was completely reversed with rapid instigation of treatment.

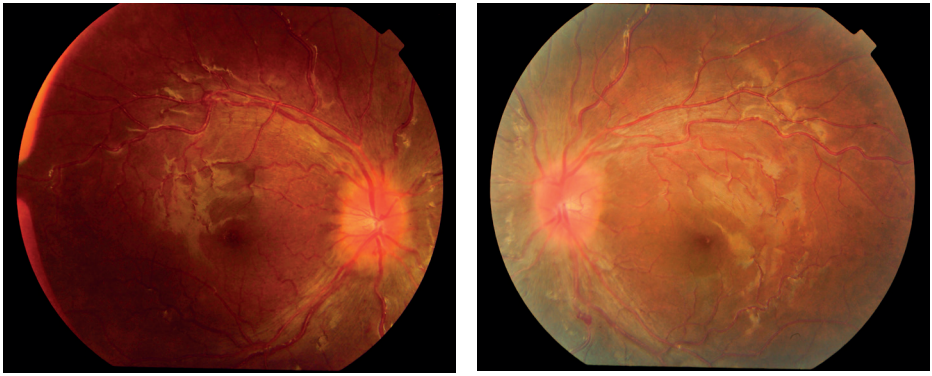

Fig. 2. Fundus pictures of the right eye (*right*) and left eye (*left*) taken two weeks post-leukapheresis shows complete resolution of retinal veins and marked reduction in optic disc swelling. Macula is normal and retinal haemorrhages have mostly resolved.

Discussion

CRVO is an important cause of painless visual impairment. It commonly presents as unilateral in 90% of cases and may later involve the fellow eye to become bilateral in 10% of cases if there is no intervention on the risk factors. Simultaneous bilateral CRVO is a rare clinical entity, presenting in less than 1% of cases.[1] It is commonly associated with elderly patients. However, it may occur in young people with haematological malignancy, as highlighted in this case.

CML is a myeloproliferative disorder characterized by increased proliferation of the granulocytic cell line in bone marrow and spill over into the blood stream. CML has three phases, increasing in severity: chronic phase, accelerated phase, and blast crisis.[3] This patient presented with CML in the chronic phase, which is early-phase in CML. Hyperleukocytosis, which is a feature of CML, is defined as a white blood cell (WBC) count of more than > 100 x 10^9/L. Critical hyperleukocytosis can cause leukostasis, a life-threatening condition with disturbed microcirculation caused by occlusion of small vessels due to elevated blast cell count, endothelial adhesion of myeloid blasts, and tissue infiltration.[4] Leukostasis leads to decreased tissue perfusion, especially in the brain and lungs, leading to a high fatality rate.[5] In view of this, a rapid reduction of WBC is thought to be the mainstay of treatment. This is achieved by cytoreduction through combination of chemotherapy and leukapheresis.

Leukapheresis is a therapeutic procedure that separates WBC from blood and reduces the leukocyte count in patients with symptomatic or threatening leukostasis until induction chemotherapy works.[6] This procedure rapidly reduced the leukocyte count and improved leukostasis in our patient. Consequently, this improved blood flow throughout the body, including the retina, thus restoring normal perfusion.

Eventually, the progression of CRVO was successfully arrested and reversed, hence preventing visual impairment.

Conclusion

This case highlights the dramatic improvement in fundus with swift cytoreduction and remedial measures that halted and reversed the progression of impending CRVO. In view of the restricted availability of leukapheresis treatment, early referral to a centre with leukapheresis facility would save the patient's life and vision.

References

1. Goldman DR, Shah CP, Morley MG, Heier JS. Venous occlusive disease of the retina. In: Yanoff M, Duker JS, eds. Ophthalmology. 4th ed. Philadelphia, PA: Elsevier Saunders; 2014. Chapter 6; p. 526-530.
2. Gass JD. Stereoscopic atlas of macular diseases: diagnosis and treatment. 4th ed. St Louis: Mosby; 1997. p. 546–555.
3. Besa EC. Chronic Myelogenous Leukemia (CML). [Online] Medscape, June 23, 2017. [Cited: Sept 27, 2017.] http://emedicine.medscape.com/article/199425-overview.
4. Stucki A, Rivier AS, Gikic M, et al. Endothelial cell activation by myeloblasts: molecular mechanisms of leukostasis and leukemic cell dissemination. Blood. 2001;97:2121–2129.
5. Dutcher JP, Schiffer CA, Wiernik PH. Hyperleukocytosis in adult acute nonlymphocytic leukemia: impact on remission rate and duration, and survival. J Clinical Oncol. 1987;5:1364–1372.
6. Hölig K, Moog R. Leukocyte depletion by therapeutic leukocytapheresis in patients with leukemia. Transfus Med Hemother. 2012;39(4):241-245.