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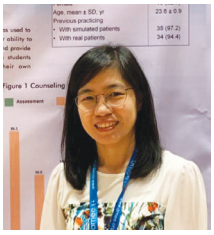
Case Report/รายงานผู้ป่วย

Simultaneous Bilateral Central Retinal Vein Occlusion as an Initial Presentation of Hematologic Disease: Two Cases Reports

รายงานผู้ป่วยที่มาด้วยภาวะโรคหลอดเลือดดำใหญ่จอประสาทตาอุดตัน 2 ข้าง นำไปสู่การวินิจฉัยโรคเลือด



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แผนกจักษุวิทยา ศูนย์แพทย์ศาสตร์ศึกษาชั้นคลินิก โรงพยาบาลสุรินทร์ 68 ถนนหลักเมือง ตำบลในเมือง อำเภอเมือง จังหวัดสุรินทร์ 32000

Abstract

Bilateral central retinal vein occlusion (CRVO) is uncommon presentation. The author reported two cases (30-year-old, 73-year-old) of bilateral CRVO. The patients came to hospital with ophthalmic problems which required medical and laboratory investigations. They were newly diagnosed with hematological disorders. Early treatment of underlying diseases should be performed to save life and improve visions. The visual prognosis and clinical outcomes depend on hematologic disease.

Keywords: bilateral central retinal vein occlusion, hematologic disease

บทคัดย่อ:

ภาวะโรคหลอดเลือดดำใหญ่จอประสาทตาอุดตัน 2 ข้างพบได้ไม่บ่อย ผู้วิจัยรายงานผู้ป่วย 2 รายที่มาโรงพยาบาลด้วยโรคหลอดเลือดดำใหญ่จอประสาทตาอุดตัน 2 ข้าง และได้ทำการตรวจร่างกาย วินิจฉัยทางห้องปฏิบัติการสืบค้น นำมาซึ่งการวินิจฉัยความผิดปกติทางเลือด การรักษาที่ทันท่วงทีช่วยป้องกันการเสียชีวิต และพิการทางตาที่อาจเกิดขึ้นได้ พยากรณ์โรคและผลการรักษาของผู้ป่วยขึ้นกับภาวะโรคเลือดที่เป็นอยู่

คำสำคัญ: โรคหลอดเลือดดำใหญ่จอประสาทตาอุดตัน 2 ข้าง, โรคเลือด

Introduction

Retinal vein occlusion (RVO) is a common ocular presentation especially in people older than 50 years. Predisposing conditions include diabetes mellitus, hypertension, opened angle glaucoma and hyperviscosity syndrome. The most frequent clinical manifestation is acute unilateral painless visual loss. In fact, the prevalence for CRVO was lower than BRVO in all ethnic populations. In recent meta-analysis, the global prevalence of any RVO in people aged 30-89 years was 0.77% (BRVO 0.64% and CRVO 0.13%).[1] BRVO was more common than CRVO, ranging from 3 to 10 times more prevalent. Bilateral RVO is rare, affecting fewer than 10% of individuals with RVO.[2] A study at Lamphun hospital, CRVO was more predominant than BRVO may be from selection bias.[3] However, simultaneous bilateral CRVO is a rare condition. The author reported two cases of concurrent bilateral central retinal vein occlusion. This study was approved by the Research Ethics Committee of Surin Hospital with the reference number of 71/2564.

Case 1

A 30-year-old male presented with one week of bilateral blurred vision. He had fever, sore throat, productive cough for one week and history of fatigue for one month. His visual acuity was 6/60 in right eye, finger count three feet in left eye, intraocular pressure was 15 mmHg in the right eye and 16 mmHg in the left eye. Anterior segment was normal. There was no relative afferent pupillary defect. The fundus showed generalized flame shape hemorrhage, white-centered hemorrhages, mild tortuous venous and macula edema in both eyes. Preretinal hemorrhage was seen in the right eye. (Figure 1) Optical coherence tomography (OCT) findings showed macula edema with foveal

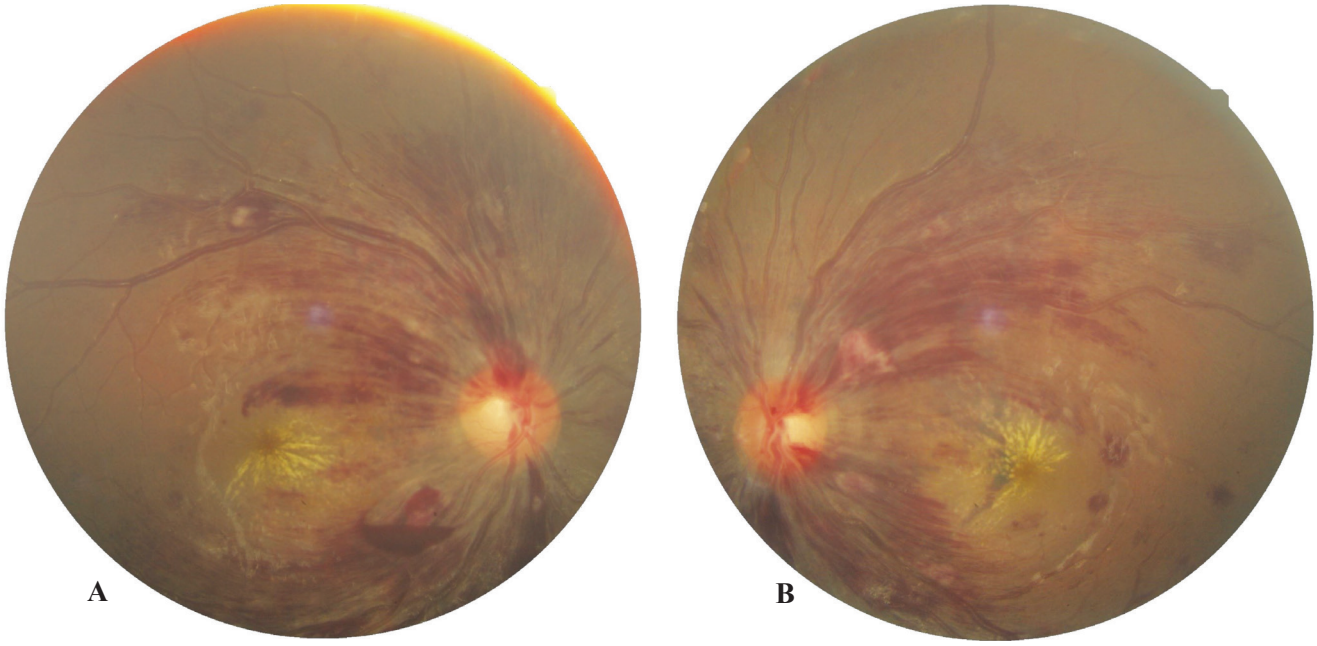

Figure 1 Fundus photograph of the right eye (1A) and the left eye (1B) demonstrating flame-shaped hemorrhages, macular edema, mild dilated and tortuous retinal veins.

thickness of 550 μ (right eye) and 790 μ (left eye).

The patient was admitted with initially a diagnosis of upper respiratory tract infection and bilateral nonischemic central retinal vein occlusion. The vital signs were as following: body temperature was 36.3 ˚C, pulse rate was 118 /minute, respiratory rate was 20/minute and blood pressure was 123/69 mmHg. Conjunctival pallor and tonsillar enlargement were seen. Other examinations were unremarkable.

The lab results are shown in Table 1. Bone marrow examination by immunophenotyping revealed strong positive for CD 13, CD 33, CD 15, CD 64, CD 117 and myeloperoxidase. The chromosome study showed translocation between chromosome1,4 and translocation between chromosome15,17. Acute promyelocytic leukemia (APL or AML-M3 subtype) was diagnosed. He received induction therapy with all-trans retinoic acid (ATRA; tretinoin). Five days after induction, the visual acuities improved to 6/18 in both eyes and OCT showed reduction in central macular thickness of 293 μ (right eye) and 318 μ (left eye). He developed sepsis from deep neck abscess and parotid abscess after 12 days of admission. The empirical treatment with intravenous meropenem 1 g 8 hourly, vancomycin 1 g 12 hourly, fosfomycin 4 g 8 hourly and amphotericin B 50 mg once daily were administered. He had coagulopathy and disseminated intravascular coagulation (DIC). He received pack red cell, fresh frozen plasma, platelets, cryoprecipitate transfusions. The patient later developed klebsiella pneumonia and intracerebral hemorrhage and then deceased 24 days after hospitalization.

Table 1 Case 1 Lab results on admission

Hematology			
Analyte (S)	Result (S)	Ref. range	Units
RBC	1.19	4.2-5.5	$\times 10^6/\mu L$
HGB	3.8	12-16	g/dL
HCT	11.4	40.3-51.9	%
MCV	96.2	80-100	fl
MCH	31.7	26-34	pg
MCHC	32.9	31-37	g/dL
RDW-CV	16.9	11.5-14.5	%
PLATELET	15	140-400	$\times 10^3/\mu L$
WBC	4.60	4.5-10	$\times 10^3/\mu L$
Blasts	51		%
Neutrophils	4	40-70	%
Lymphocytes	44	20-50	%
Monocyte	1	2-6	%
Eosinophils	0	0-6	%
Basophils	0	0-1	%
BUN	13	8-20	mg/dL
Creatinine	0.99	0.72-1.18	mg/dL
Total bilirubin	0.64	0.3-1.2	mg/dL
AST	12	< 50	U/L
ALT	4	< 50	U/L
ALP	46	30-120	U/L
Albumin	3.8	3.5-5.2	g/dL
LDH	385	208-378	U/L
Prothrombin time	14.7	9.6-12.3	sec
INR	1.39		
Partial thromboplastin time	28	22.2-31.1	sec

RBC: red blood cell count; HGB: hemoglobin; HCT: hematocrit; MCV: mean cell volume; MCH: mean cell hemoglobin; MCHC: mean cell hemoglobin concentration; RDW-CV: red cell distribution width-coefficient variation; WBC: white blood cell count; BUN: blood urea nitrogen; AST: aspartate aminotransferase; ALT: alanine aminotransferase; ALP: alkaline phosphatase; LDH: lactate dehydrogenase; INR: international normalized ratio.

Case 2

A 74-year-old female presented with two weeks of bilateral blurred vision. She had a history of palpitation and syncope for one month. She had essential hypertension and diabetic mellitus type II. On examination Snellen visual acuities were 6/60 in both eyes. Intraocular pressure was 17 mmHg in both eyes. The anterior segment examination showed bilateral moderate nuclear sclerosis. Dilated fundus examination revealed the cup to disc ratio were 0.4, diffuse retinal hemorrhage, mild engorged retinal veins, and exudate on macula in both eyes. (Figure 2) Optical coherence tomography (OCT) findings showed macula edema with foveal thickness of 724 µ (right eye) and 616 µ (left eye). Bilateral nonischemic central retinal vein occlusion with macula edema was diagnosed and she was admitted for systemic work up.

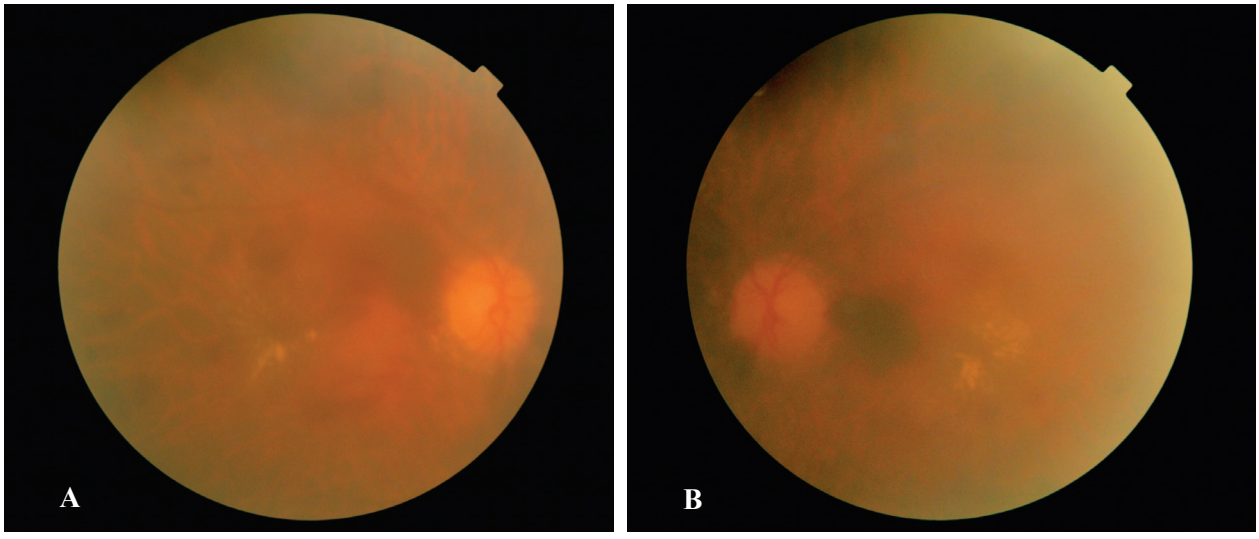

Figure 2 Fundus photograph of the right eye (2A) and the left eye (2B) showed scattered retinal hemorrhages, macular exudate and mild engorged retinal vein (2A)

Complete blood count showed bicytopenia (anemia and thrombocytopenia) (Table 2). Bone marrow aspiration and biopsy showed moderately hypercellular trilineage marrow, markedly decreased megakaryocytes with dysplasia, dysplastic erythroid cells and no evidence of increased blasts consistent with myelodysplastic syndrome (MDS). She received pack red cell, platelets transfusions, oxymethalone and supportive care. She had intravitreal 1.50 mg (0.06 ml) bevacizumab injection three times with an interval one month. The examination revealed improvement of visual acuity and fundus appearance. The visual acuities at 4 months follow-up visit were 6/15 in both eyes. Central retinal thickness was 230 µ (right eye) and 251 µ (left eye). (Figure 3)

Table 2 Case 2 Lab results on admission

Hematology			
Analyte (S)	Result (S)	Ref. range	Units
RBC	1.33	4.2-5.5	$\times 10^6/\mu L$
HGB	4.9	12-16	g/dL
HCT	15.1	40.3-51.9	%
MCV	113.3	80-100	fl
MCH	36.5	26-34	pg
MCHC	32.2	31-37	g/dL
RDW-CV	16.5	11.5-14.5	%
PLATELET	14	140-400	$\times 10^3/\mu L$
WBC	4.9	4.5-10	$\times 10^3/\mu L$
Neutrophils	63.3	40-70	%
Lymphocytes	25	20-50	%
Monocyte	10.3	2-6	%
Eosinophils	0.7	0-6	%
Basophils	0.7	0-1	%
BUN	19	8-20	mg/dL
Creatinine	0.81	0.72-1.18	mg/dL
Total bilirubin	1.23	0.3-1.2	mg/dL
AST	28	< 50	U/L
ALT	16	< 50	U/L
ALP	78	30-120	U/L
Albumin	3.9	3.5-5.2	g/dL
FBS	115	76-106	mg/dL
Prothrombin time	13.6	9.6-12.3	sec
INR	1.25		
Partial thromboplastin time	28.3	22.2-31.1	sec
ESR	156	0-10	mm/hr
CRP	3.67	0-6	mg/L

RBC: red blood cell count; HGB: hemoglobin; HCT: hematocrit; MCV: mean cell volume; MCH: mean cell hemoglobin; MCHC: mean cell hemoglobin concentration; RDW-CV: red cell distribution width-coefficient variation; WBC: white blood cell count; BUN: blood urea nitrogen; AST: aspartate aminotransferase; ALT: alanine aminotransferase; ALP: alkaline phosphatase; FBS: Fasting blood sugar; INR: international normalized ratio; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein

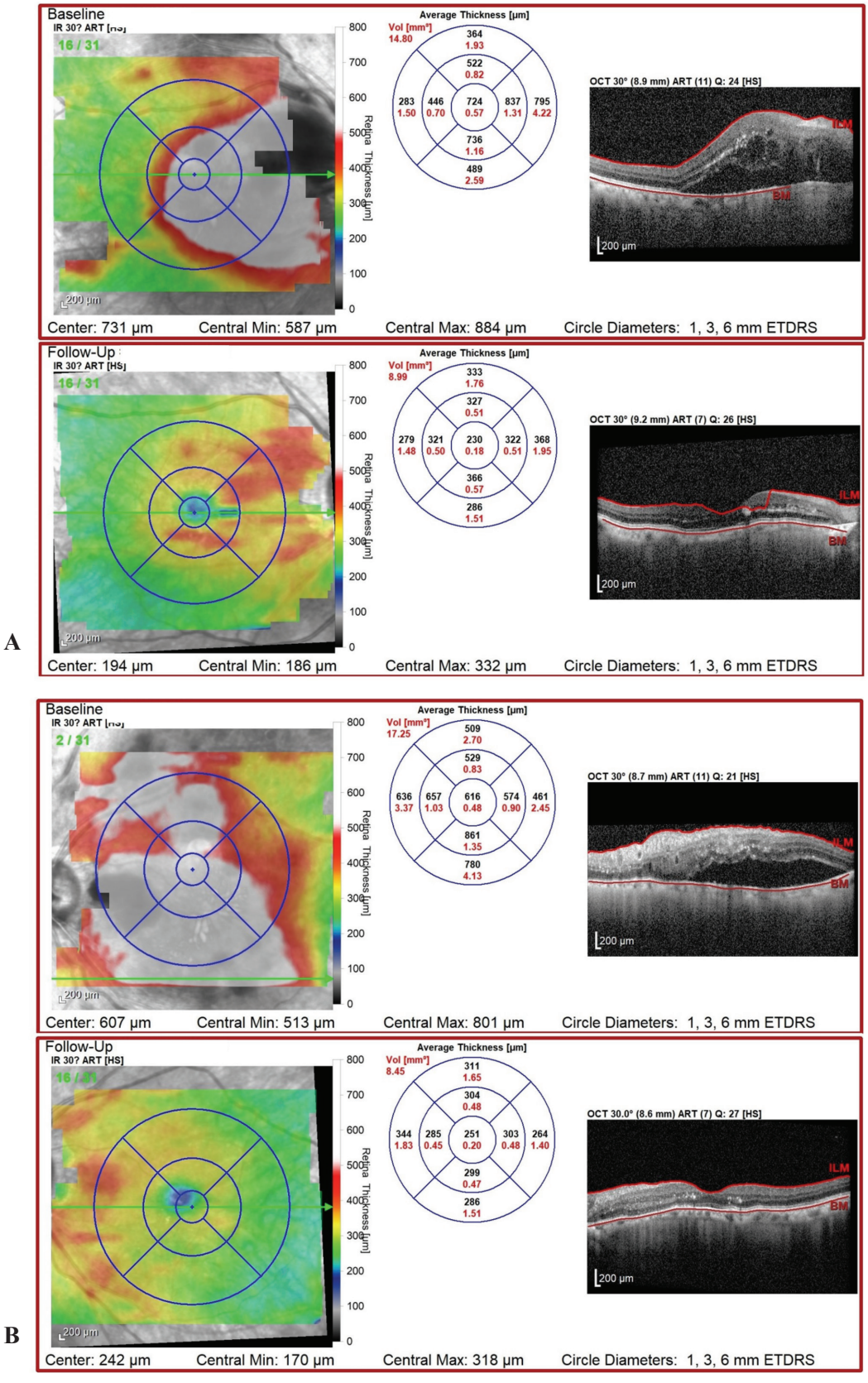

Figure 3 Optical coherence tomography (OCT) showing resolution of macula edema secondary to central retinal vein occlusion of right eye (3A) and left eye (3B)

Discussion

Bilateral CRVO is an uncommon manifestation which required systemic work up to rule in hyperviscosity syndrome or inflammatory condition. Ocular involvement in leukemia varies from 9% to 90% including leukemic infiltrates (preretinal white masses), intraretinal hemorrhage, white-centered retinal hemorrhages related to anemia or thrombocytopenia, ophthalmic finding in hyperviscosity state, and retinal abnormality from opportunistic infection or neurological involvement.[4] Commonly CRVO is a complication from hyperviscosity state. Bilateral CRVO represented early hematologic diseases such as, acute myeloid leukemia (AML), polycythemia, chronic myeloid leukemia (CML), acute lymphoblastic leukemia (ALL), and Waldenstrom's macroglobulinemia.[5-9] The results of previous studies associated with leukemia are summarized (Table 3).

CML is an abnormal proliferative of myeloid stem cells resulting from translocation of *ABL1* on chromosome 9 to the region of the *BCR* gene on chromosome 22. Patients with CML usually present with fatigue, bleeding and weight loss. Twenty percents of them are incidental diagnosis. Common laboratory findings are leukocytosis, anemia and thrombocytosis.[10]

AML is the most common leukemic form in adults. Symptoms and signs of AML are resulting from bone marrow failure such as anemia, infection and bleeding. These symptoms develop in a few weeks. Bone marrow examination, immunophenotype and cytogenetic study are essential for diagnosis, classification AML subtype and assessing prognosis. Acute promyelocytic leukemia (APL) is found in 10 percent of acute myeloid leukemia. The pathogenesis of coagulopathy in APL includes hypercoagulability, primary hyperfibrinolysis and endothelial cell damage.[11] Promyelocyte cells can produce three types of procoagulants (tissue factor, cancer procoagulant, and microparticles) which generate thrombus formation, decrease coagulation time, resulting in hypercoagulable state. Promyelocyte cells also release inflammatory cytokine that induce endothelial cell damage. Coagulopathy and disseminated intravascular coagulation (DIC) are main cause of death in APL patients.

Our cases presented with bilateral nonischemic CRVO. It is characterized with visual acuity better than 20/400, mild dilatation tortuous venous and less cotton wool spot in all quadrant of retina. Nonischemic CRVO patients have better visual prognosis than ischemic CRVO. The first case gained vision after induction therapy. The accumulation of leukemic cells and hyperviscosity were considered to be cause of venous obstruction in this case.

In our second case, we found that advanced age, hypertension and diabetes were risk factors of CRVO. Due to limitations in our setting, we cannot provide fluorescein angiography. Eventhough this test is helpful for interpretating retinal perfusion. Therefore, the author has considered from all available data and findings that venous tortuosity and dilatation would be from vein obstruction rather than diabetic retinopathy (DR). This patient did not show any signs of microaneurysm, that is one of the sign of patient with DR. Possible role of hemostatic factors in bilateral CRVO should be considered in this case. Myelodysplastic syndrome (MDS) is abnormal blood cells forming in bone marrow and resulting in low count of red blood cells, platelets, and white blood cells. MDS is related to transformation to acute myeloid leukemia. The most common lab findings are anemia

Table 3 Summary reported cases of bilateral central retinal vein occlusion and leukemia

Reference	Age (year)	Sex	Visual acuity (RE, LE)	Diagnosis	Treatment	Outcome	Final visual outcome
Tseng, et al[3]	30	male	6/60, 6/60	Acute myeloid leukemia (M1 Subtype)	Chemotherapy, bone marrow transplantation		6/9,6/18
Goel, et al[4]	14	boy	3/60, 3/60	Chronic myeloid leukemia with massive retinal infiltrate	Aggression hydration, chemotherapy, bone marrow transplantation		6/12, 6/12
Narang, et al[5]	50	male	6/38, 6/60	Chronic myeloid leukemia	Chemotherapy, panretinal photocoagulation, intravitreal bevacizumab both eyes	Neovascularization of disc of both eyes	6/24, 6/12
Al-Abdulla, et al[7]	65	male	6/60, 6/9	Chronic myeloid leukemia, open-angle glaucoma, Anticardiolipin phospholipid autoantibodies	Chemotherapy, panretinal photocoagulation, trabeculectomy	Neovascularization glaucoma of left eye	N/A
Uhr, et al[6]	23	female	6/27, 6/15	Acute lymphoblastic leukemia	Chemotherapy		N/A
Our first case	30	male	6/60, finger count three feet	Acute promyelocytic leukemia (M3 subtype)	Chemotherapy	Died 24 days later	
Our second case	74	female	6/60, 6/60	Myelodysplastic syndrome	Oxymethalone, intravitreal bevacizumab both eyes		6/15, 6/15

and thrombocytopenia. The risk of thrombosis in MDS patients is low due to anemia and thrombocytopenia. Incidence of deep vein thrombosis was 0.04 % of MDS patients and associated with central venous catheter placement and red blood cell transfusion.[12] Berry and Fekrat reported a case of 18 year-old woman with MDS who developed a unilateral CRVO.[13] We hypothesized that MDS might be a possible cause of bilateral CRVO

in our patient and her multiple risk factors might work synergistically to create a prothrombotic state.

Bilateral CRVO can be a clinical manifestation in hematologic diseases. Prognosis of disease depends on early diagnosis and treatment. Previous studies showed ocular improvement after systemic disease control. However, treatment with intravitreal anti-vascular endothelial growth factor (VEGF) injection in macular edema from CRVO may be required combine with systemic remission by chemotherapy.[7]

Conclusion

We presented unusual cases of bilateral CRVO. Systemic work up revealed hematologic disorder. Early management is important to save life and visions.

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Footnotes and Financial Disclosures

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Disclosure(s)
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