

A patient with Multiple Myeloma presenting with bilateral retinal vein thrombosis: A case report

Abstract

Central retinal vein occlusion is a cause of acute unilateral painless visual loss in the elderly, while bilateral central retinal vein occlusion in a young patient is a rare presentation.

We present a case of a 41-year-old gentleman, without previously identified risk factors, coming with bilateral retinal vein occlusion. His evaluation revealed multiple myeloma with type 1 cryoglobulinaemia as the underlying cause for hypercoagulability.

Our patient's story illustrates that myeloma should be considered as a differential for bilateral retinal vein occlusion especially when it occurs in the absence of other underlying risk factors.

Key words

Retinal vein occlusion, multiple myeloma, cryoglobulinaemia

Case presentation

41-year-old previously healthy gentleman presented with 5 days history of painless visual loss of both eyes. His previous medical history was unremarkable, without diabetes mellitus, hypertension, or hypercholesterolemia. He experienced some undue tiredness for 3 months prior to the presentation; however, it didn't interfere with his day-to-day activities so he was able to continue his employment as a pump attendant in a petrol station. His visual symptoms develop about 5 days prior to presentation, which was of sudden onset. His visual impairment made him unable to continue his occupational activities. He didn't have constitutional symptoms including loss of weight, loss of appetite, fever, or night sweats. He couldn't recall any trauma or falls. He never had joint pains, rashes, or any features of connective tissue disorders or other thromboembolic manifestations.

He was an ex-smoker with 2 pack years of tobacco consumption. He used to consume alcohol occasionally during social gatherings. He never used other illicit drugs, and never was on long-term medications including complementary and ayurvedic medications. He never had high-risk sexual behaviors.

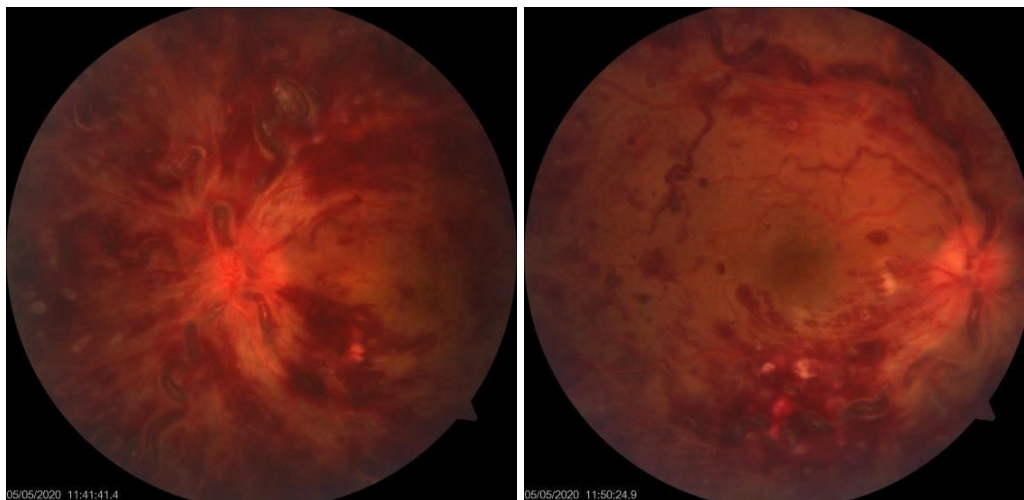
Examination revealed an averagely-built male with a body mass index of 23kg/m^2 . Clinically he was afebrile, and pale, but not icteric. He didn't have lymphadenopathy, rashes, or edema.

The patient only had the ability to count fingers at a 2 feet distance from the right eye, while the left eye could identify hand motions only. Visual fields and color vision couldn't be assessed properly due to low visual acuity. Pupil sizes were bilaterally 3 mm with sluggish pupillary reactions. Fundoscopic examination revealed optic disc swelling and blurring of the margins, with hyperemia and diffuse hemorrhages in all quadrants. Extra-ocular movements were full in both eyes. Other cranial nerves examination was unremarkable as well as the neurological examination of the limbs.

He had regular pulses, with good volume, and had similar normal pulses in all extremities. There were no carotid or renal bruits. He was normotensive with both supine and erect blood pressure values of 110/80mmHg. Both heart sounds were normal without audible murmurs.

His respiratory rate was 18 breaths per minute with oxygen saturation of 98% at room air, and the rest of the respiratory examination too was unremarkable. Abdominal examination was normal without organomegaly, masses, or bruits.

Fundal photography (Figure 1) visualized dilated and tortuous retinal veins bilaterally, with multiple dot and blot and flame-shaped intraretinal hemorrhages involving all quadrants, which confirmed bilateral central retinal venous occlusion. Fluorescein angiography (Figure 2) demonstrated areas of non-perfusion with blockage of venous fluorescein.



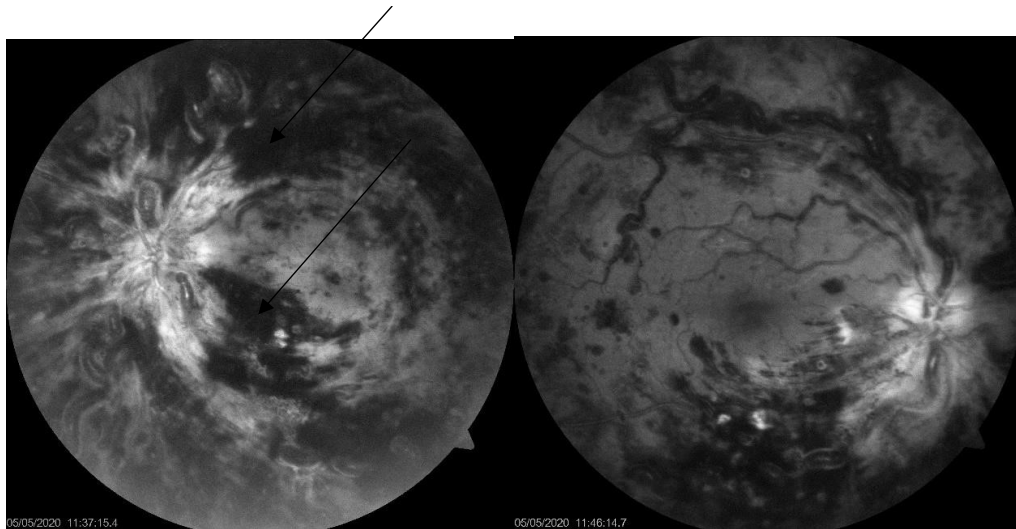
A

B

Figure 1:

A-Right eye, B-left eye

Colour Fundus photography showing bilateral central retinal vein occlusion



A

B

Figure 2:

A-Right eye, B-left eye

Fundal Fluorescein angiogram.

Hypo-perfused areas depicted in arrows correspond with hemorrhages

A summary of his investigations is given below in table 1

His basic hematological investigations revealed normocytic anemia, elevated erythrocyte sedimentation rate, and mildly elevated C-reactive proteins. He had acute renal impairment with raised serum creatinine. An ultrasound scan of the abdomen confirmed acute renal parenchymal disease as evidenced by bilateral increased cortical echogenicity with altered cortico-medullary demarcation. His urine analysis didn't reveal active sediments and his output remained satisfactory. His serum protein was low with a reversal of albumin to globulin ratio. Albumin-corrected Calcium was elevated.

His electrocardiogram (ECG) was normal with sinus rhythm, transthoracic echocardiogram showed mild left ventricular hypertrophy without regional wall motion abnormalities. The ejection fraction was 60%.

Non-contrast computed tomography (CT) of the brain was reported as normal which was followed by Magnetic Resonance Imaging (MRI) of the brain and orbits.

MRI revealed bilateral retinal hemorrhages and protruded optic discs with mild contrast enhancement. There was no evidence of retinal detachment. MRI brain was normal other than some non specific T2W/FLAIR high signal foci in the medial temporal and right frontal lobes.

Laboratory Parameter		Value	Reference Range
Full Blood Count	WBC	8.2×10^3	4×10^3 - 10×10^3 /micro litre
	N%	37.3	50-70%
	L%	53.4	20-40%
	Haemoglobin	7 g/dL	11-16mg/dL
	MCV	96.6	80-100fL
	MCH	34.6	27-34 pg
	MCHC	343	320-360g/L
	Platelets	167×10^3	150×10^3 - 450×10^3 /micro litre
Inflammatory Markers	CRP	10	<6 mg/L
	ESR	100	<15 mm/1 st hour
Renal Functions	Creatinine	2.02	0.5-1.1mg/dL
	Sodium	140	135-140mmol/L
	Potassium	3.5	3.5-5.1mmol/L
	AST	75	10-40U/L
	ALT	68	9-55U/L
	ALP	103	40-150U/L
	GGT	219	10-50U/L
	Total Protein	5.1	6.4-8.3g/dL
	Albumin	2.2	3.2-5.2g/dL
	Globulin	2.9	2.8-3.4g/dL
Coagulation Profile	INR	1.4	0.8-1.3
	PT	15	11-13.5s
	APTT	31	20-35s
Serum lipids	Total Cholesterol	132	<200mg/dL
	TG	63	<150mg/dL

	LDL	65	<100mg/dL
	HDL	54	40-60mg/dL
Serum corrected Calcium levels		11.3	8.5-10.5mg/dL
Fasting blood sugar		92	100-126mg/dL

Table 1

WBC=White Blood Cells, N%= Neutrophils percentage, L%=Lymphocyte percentage, MCV=Mean Corpuscular Volume, MCH=Mean Corpuscular Haemoglobin, MCHC=Mean Corpuscular Haemoglobin Concentration, CRP= C Reactive Protein, ESR=Erythrocyte Sedimentation Rate, INR=International Normalized Ratio, PT=Prothrombin Time, APTT=Activated partial Thromboplastin Time, TG=Triglycerides, LDL=Low density lipoprotein levels, HDL=High density lipoprotein levels.

Examination of his blood film showed normocytic normochromic red blood cells with marked rouleaux formation with red cell agglutination and normal reticulocyte count. However, white blood cells were normal in number and morphology, without abnormal cells and platelets number was also normal with some large platelets and platelet clumps.

There were cryoglobulins in the blood picture with Leishman stain. Marked rouleau and agglutination were also attributed to the presence of cryoglobulins. The workup of investigations was directed at the evaluation of the etiology of cryoglobulinemia.

Bone marrow examination confirmed clonal plasma cells of 15% (Figure 3). With the presence of end organ damage, a diagnosis of multiple myeloma was made.

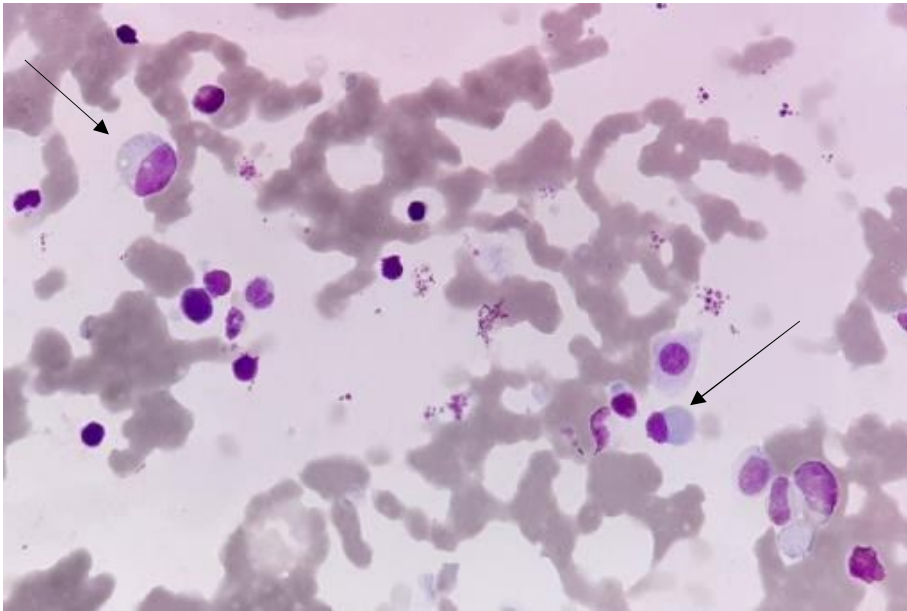


Figure 3:

Bone Marrow examination showing marked rouleaux formation and abundant plasma cells (arrowed)

Ophthalmological assessment further revealed macular edema, secondary to central retinal vein occlusion, for which anti-vascular endothelial growth factors (anti-VEGF) treatment was commenced.

Definitive management was started with the consultant hematologist's input. Meanwhile, therapeutic plasma exchange was attempted, which failed thrice due to the hyperviscosity of blood. Chemotherapy with bortezomib started and the patient showed clinical improvement.

At the same time, his visual acuity improved to 1/6 in both eyes.

Patient was followed up with a long-term plan of bone marrow transplantation.

Discussion

This previously healthy male, presented with a sudden painless bilateral visual loss with the fundoscopic appearance of swollen disc and hemorrhages.

Differential diagnoses considered at that point were papilloedema, vitreous hemorrhage, retinal detachment, ischaemic optic neuropathy, acute hypertensive retinopathy, and central retinal venous occlusion. Occipital stroke too was considered however the possibility was remote, given the evidence of bilateral involvement. It was ruled out with brain imaging including CT and MRI.

Detailed ophthalmological evaluation including fluorescein angiogram confirmed bilateral central retinal vein occlusion. The rest of the systemic examination in this patient was unremarkable except for clinically detectable anemia.

Bilateral retinal vein occlusion itself is a rare clinical manifestation among the population so an underlying risk factor evaluation was a necessity.

Strong risk factors for retinal vein occlusion include hypertension, diabetes mellitus, hypercholesterolemia, cigarette smoking, and glaucoma (1, 2). All the above common risk factors were not elicited in this patient except for past history of cigarette smoking. Therefore, it was prudent to consider alternative aetiologies in this young patient.

His peripheral blood film showed evidence of cryoglobulinemia which directed our evaluation further, especially to exclude a monoclonal gammopathy. Cryoglobulins are immunoglobulins in circulation which precipitate in cold temperatures, while Type 1 cryoglobulinemia refers to the presence of monoclonal immunoglobulins (3). Type 1 cryoglobulinemia is associated with hematological diseases such as monoclonal gammopathy

of indeterminate significance, smoldering multiple myeloma, multiple myeloma, Waldenström's macroglobulinemia and chronic lymphocytic leukemia (4)

Multiple myeloma is a disorder of clonal plasma cell proliferation with abnormal monoclonal immunoglobulins, which is usually prevalent among elderly individuals (5). It is a known cause of hyperviscosity secondary to paraproteinaemia. Among the different presentations of myeloma, which include anemia, pathological fractures, renal impairment, and infections, hyperviscosity remains a relatively infrequent presenting feature. (6,7)

In this patient, the diagnosis of multiple myeloma was made with the demonstration of 15% clonal plasma cell proliferation in bone marrow with the concomitant presence of myeloma-related organ impairment, as evidenced by hypercalcemia (serum calcium >11 mg/dL), renal insufficiency (serum creatinine >2 mg/dL) and anemia (Hb <10g/dL). (8) However, his skeletal X-rays didn't show osteolytic lesions.

With the commencement of chemotherapy, the patient showed a considerable improvement in his visual impairment, as well as his well-being. The patient was re-referred to the ophthalmology team for anti-VEGF treatment because anti-VEGF has proven benefits in improving visual impairment in central retinal vein occlusion (9).

Autologous stem cell transplantation remains the definitive treatment for myeloma (10), so our patient was included in the transplant workup.

Conclusion

This young gentleman's story illustrates an interesting and rare presentation of myeloma.

Therefore, in young patients with retinal vein occlusion, without other systemic risk factors, paraproteinemias including multiple myeloma should be considered as a differential for the underlying etiology, which would lead to a timely referral to a haematologist and early treatment commencement.

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