Case study

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

Abstract

Central retinal vein occlusion is a cause for acute unilateral painless visual loss in 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 a rare presentation of myeloma with bilateral retinal vein occlusion. Multiple myeloma should be considered in young patients presenting with retinal vein occlusion especially in the absence of other underlying risk factors.

Key words

Retinal vein occlusion, multiple myeloma, cryoglobulinaemia

Introduction

Multiple myeloma is a neoplasm characterized by the proliferation of plasma cells producing monoclonal immunoglobulins. While the presentation is often subacute or chronic, a small proportion of patients will present acutely. Patients may present with bone pain

secondary to lytic lesions, an increased serum protein concentration, unexplained anemia, hypercalcemia, or acute renal failure [12,13]. Multiple myeloma is a neoplasm characterized by the proliferation of plasma cells producing monoclonal immunoglobulins. While the presentation is often subacute or chronic, a small proportion of patients will present acutely [14-16]. Patients may present with bone pain secondary to lytic lesions, an increased serum protein concentration, unexplained anemia, hypercalcemia, or acute renal failure.

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 hypercholesterolaemia. He experienced some undue tiredness for 3 months prior to presentation; however, it didn't interfere 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 behaviours.

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

Patient only had the ability to count fingers at a 2 feet distance from right eye, while the left eye could identify hand motions only. Visual fields and colour vision couldn't be assessed properly due to low visual acquity. Pupil sizes were bilaterally 3 mm with sluggish pupillary reactions. Fundoscopic examination revealed optic disc swelling and blurring of the margins, with hyperaemia and diffuse haemorrhages in all quadrants. Extra-occular 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 haemorrhages involving all quadrants, which confirmed bilateral central retinal venous occlusion. Fluoroscein angiography (Figure 2) demonstrated areas of non-perfusion with blockage of venous fluorescein.

A summary of his investigations is given below in table 1

His basic haematological investigations revealed normocytic anaemia, elevated erythrocyte sedimentation rate and mildly elevated C reactive proteins. He had acute renal impairement with raised serum creatinine. Ultrasound scan of the abdomen confirmed acute renal parenchymal disease as evidenced by bilateral increased cortical echogenicity with altered corticomedullary 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. Ejection fraction was 60%.

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

MRI revealed bilateral retinal haemorrhages, protruded optic discs with mild contrast enhancement. There was no evidence of retinal detachment. MRI brain was normal other than some non specificT2W/FLAIR high signal foci in 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/1st 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

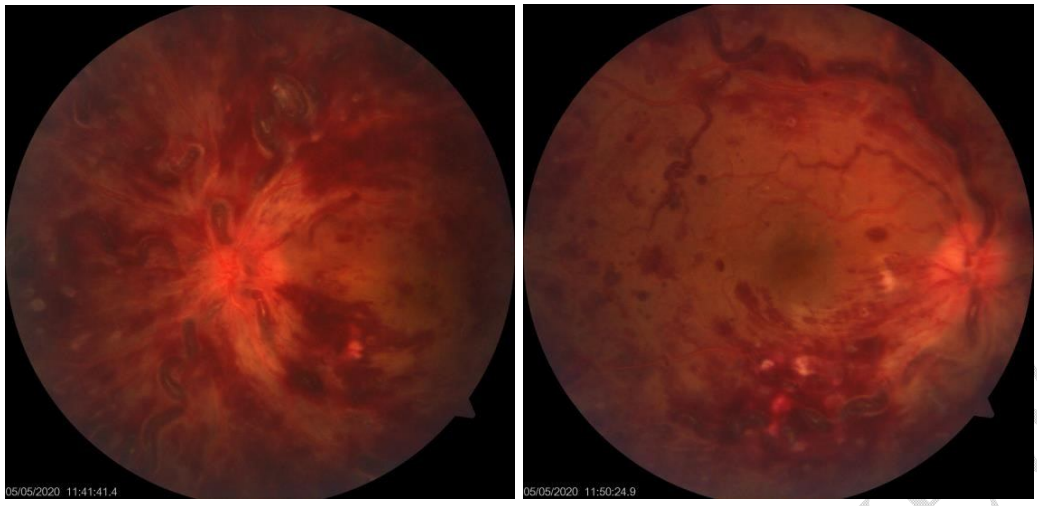

Figure 1:

Fundoscopy showing bilateral central retinal vein occlusion

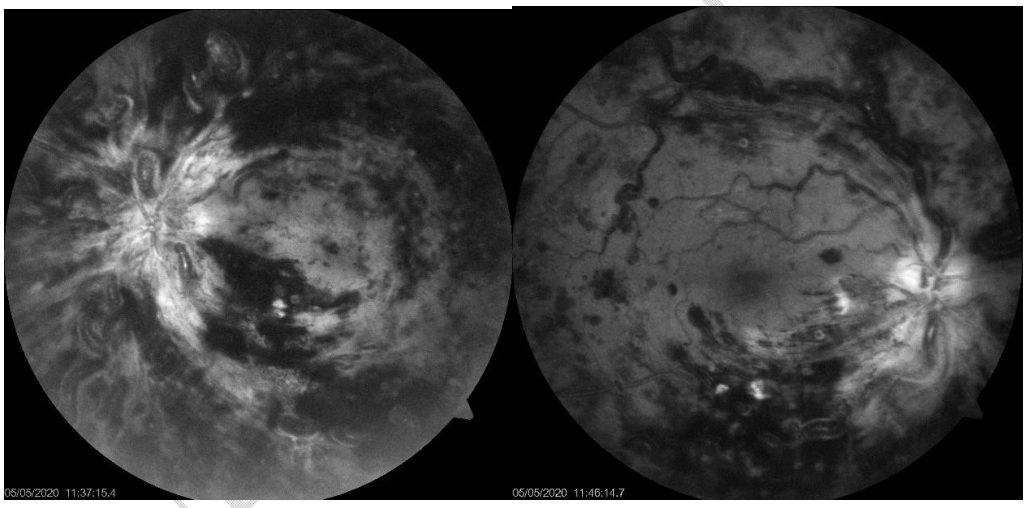

Figure 2:

Fluorescein angiogram.

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 blood picture with Leishman stain. Marked roulaeux and agglutination were also attributed to the presence of cryoglobulins. Workup of investigations were directed on evaluation of aetiology of cryoglobulinaemia.

Bone marrow examination confirmed clonal plasma cells of 15% (Figure3). With the presence of end organ damage, a diagnosis of multiple myeloma was made.

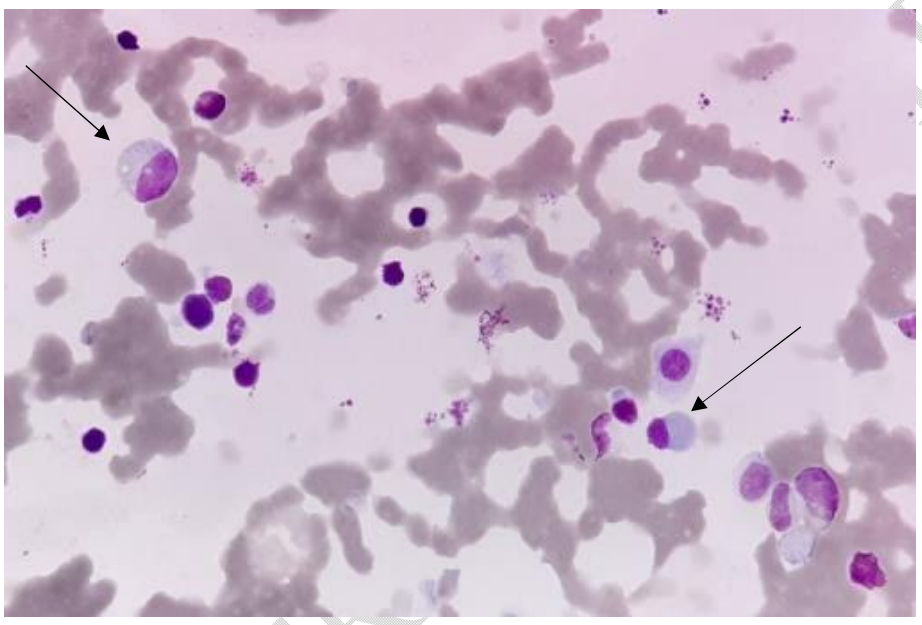

Figure 3:

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

Definitive management was started with the consultant haematologist's input. Meanwhile, therapeutic plasma exchange was attempted, which was failed thrice due to hyperviscocity of blood. Chemotherapy with bortezomib started and patient showed clinical improvement. Patient was followed up with a long-term plan of bone marrow transplantation.

Discussion

This previously healthy, gentleman presented with sudden painless bilateral visual loss with fundoscopic appearance of swollen disc and haemorrhages.

Differential diagnoses considered at that point were papilloedema, vitreous haemorrhage, 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 the brain imaging including CT and MRI.

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

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

Strong risk factors for retinal vein occlusion includes hypertension, diabetes mellitus, hypercholesterolemia, cigarette smoking and additionally glaucoma for central retinal vein occlusion. (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 cryoglobulinaemia which directed our evaluation further, especially to exclude a monoclonal gammopathy. Cryoglobulins are immunoglobulins in circulation which precipitate in cold temperature while Type 1 cryoglobulinaemia refers to the presence of monoclonal immunoglobulins (3). Type 1 cryoglobulinaemia is associated with haematological diseases such as monoclonal

gammopathy of indeterminant significance, smoldering multiple myeloma, multiple myeloma, Waldernstromes 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 for hyperviscocity secondary to paraproteinaemia. Among the different presentations of myeloma, which includes anaemia, pathological fractures, renal impairement and infections, hyperviscocity remains a relatively infrequent presenting feature. (6,7)

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

With commencement of chemotherapy, patient showed a considerable improvement of his visual impairement, as well as his wellbeing. Patient was re referred to ophthalmology team for anti-vascular endothelial growth factors (anti VEGF) treatment because anti VEGF has proven benefit 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 to the transplant workup.

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, multiple myeloma should be considered as a differential for the underlying aetiology, which would lead for timely referral to haemotologist and early treatment commencement.

References

1. Hayreh SS, Zimmerman B, McCarthy MJ,Podhajsky P,Syatemic diseases associated with various types of retinal vein occlusion.Am J Ophthalol 2001;131:61-77
2. Rath EZ, Frank RN,Shin DH,Kim C.Risk factors for retinal vein occlusions: a case control study. Ophthalmology 1992;99:509-14
3. Terrier B, Karras A, Kahn JE, et al. The spectrum of type I cryoglobulinemia vasculitis: new insights based on 64 cases. Medicine (Baltimore) 2013;92(2):618
4. Harel S, Mohr M, Jahn I, et al. Clinico-biological characteristics and treatment of type I monoclonal cryoglobulinaemia: a study of 64 cases. Br J Haematol. 2015;168(5):671–678
5. Röllig C, Knop S, Bornhäuser M. Multiple myeloma. Lancet. 2014:385
6. Riccardi A Gobbi PG Ucci G et al. Changing clinical presentation of multiple myeloma.*Eur J Cancer.* 1991; 27: 1401-1405
7. Kyle RA, Gertz MA, Witzig TE, Lust JA, Lacy MQ, Dispenzieri A, et al. Review of 1027 patients with newly diagnosed multiple myeloma. Mayo Clin Proc. 2003;78:21-33
8. Rajkumar SV, Dimopoulas MA, Palumbo A,et al.International Myeloma Working Group updated vriteria for the diagnosis of multiple myeloma. Lancet Oncol 2014;15:e538
9. Ho M, Liu DT, Lam DS, Jonas JB. Retinal vein occlusions, from basics to the latest treatment. Retina. 2016 Mar;36(3):432–48
10. Barlogie B, Shaughnessy J, Tricot G, et al. Treatment of multiple myeloma. Blood. 2004; 103:20–32
11. Wong TY, U. Scott IU. Retinal-Vein Occlusion. N Engl J Med 363;22: 2135-2144

12. Borgman CJ. Concomitant multiple myeloma spectrum diagnosis in a central retinal vein occlusion: a case report and review. Clinical and Experimental Optometry. 2016 Jul 1;99(4):309-12.

13. Spicka I. Advances in multiple myeloma therapy during two past decades. Comp Struct Biotech J 2014; 10: 38–40

14. Gozzetti A, Candi V, Papini G, Bocchia M. Therapeutic advancemens in multiple myeloma. Front Oncol 2014; 4: 1–5

15. Hameed A, Brady JJ, Dowling P, Clynes M, O'Gorman P. Bone disease in multiple myeloma: pathophysiology and management. Cancer Growth Metastasis 2014; 7: 33–42

16. Fonseca R, Monge J, Dimopoulos MA. Staging and prognostication of multiple myeloma. Expert Rev Hematol 2014; 7: 21–31