

# Combined Central Retinal Artery & Central Retinal Vein Occlusion in Secondary APS

Harish Prabhu<sup>a</sup>, Vishnu S Chandran<sup>a</sup>, K K Velayudhan<sup>a</sup>

a. Department of Internal Medicine, Amritha Institute of Medical Sciences and Research Centre, Edapally, Cochin\*

## ABSTRACT

Published online on 30<sup>th</sup> December 2015

Antiphospholipid syndrome (APS) is an autoimmune disorder characterized by either vascular thrombosis (arterial or venous) or pregnancy morbidity due to the presence of abnormal antibodies circulating in the blood. It is a hypercoagulable condition & systemic features of the syndrome can be varied depending upon the organ affected. Ocular Involvement occurs in upto 80- 90 % of APS in the form of amaurosis Fugax, retinal artery occlusion, retinal vein occlusion, optic neuropathy etc. Even though central retinal arterial obstruction (CRAO) and central retinal venous obstruction (CRVO) have been noted independently in APS (primary and secondary), combined CRAO and CRVO is one of the rarest presentation in APS. We are presenting a case of combined CRAO & CRVO as the initial presenting complaint in a 38yr old lady with secondary APS.

**Keywords:** Anti Phospholipid Syndrome, Central Retinal Artery Occlusion, Central Retinal Vein Occlusion, Combined CRAO & CRVO

\*See End Note for complete author details

## INTRODUCTION

The AntiPhospholipid Syndrome (APS) is an autoimmune disorder characterized by either a history of vascular thrombosis (one or more clinical episodes of arterial, venous, or small vessel thrombosis in any tissue or organ) or pregnancy morbidity in association with the presence of antiphospholipid (aPL) antibodies. These antibodies namely, anticardiolipin (aCl) antibodies, lupus anticoagulant (LA), or antibodies against beta2-glycoprotein I (anti-b2GPI) either of IgG or IgM isotype have been recently established as the laboratory criteria for the diagnosis of definite APS. APS is prevalent in 2-4% of general population and 50% of them are due to primary etiology. Among the secondary causes the most common one is SLE & 23% of cases with systemic lupus erythematosus (SLE) develop APS. It is a hypercoagulable condition & thrombosis can occur anywhere in the body including nervous system, renal, liver skin & eye. Almost all cases of APS have bilateral ocular involvement while monocular presentation can also occur. Studies on ocular manifestations as the initial presentation in APS have not been done, as only a few cases have been reported worldwide in which patient presents with eye manifestation as the initial complaint. Among ocular manifestations retinal artery or venous occlusion has been well described. But combined arterial and venous obstruction as an initial

presentation in APS is very rare.

Combined central retinal arterial obstruction (CRAO) and central retinal venous obstruction (CRVO) is an uncommon retinal vascular disease that leads to relatively sudden loss of visual acuity. This combined entity includes the clinical features and characteristic retinal changes of both CRAO and CRVO. It is well distinguished from isolated CRAO or CRVO. The pathophysiology of the disease and thrombosis as the cause of the obstruction is not well defined. Affected eyes typically have a poor outcome and tend to develop severe complications, such as rubeosis iridis and neovascular glaucoma. Unfortunately no treatment capable of reversing the visual loss has been described.

## CASE REPORT

38 yr old, house wife from Kochi presented to us with complaints of painless loss of vision of her left eye as she got up from sleep. She did not have any history of eye pain, trauma to eye, redness or watering, fever, symptoms of raised intracranial tension, no focal neurological deficits, rashes, joint pain, alopecia, recurrent oral ulcers or genital ulcerations, edema, cough, palpitation or breathlessness. No hematuria or frothy urine. No h/o animal bite. She gives history of 3 abortions. 1<sup>st</sup> pregnancy she had a spontaneous abortion at 7<sup>th</sup> month

### Corresponding Author:

Dr. Harish Prabhu, Postgraduate Trainee, Department of Internal Medicine, Amritha Institute of Medical Sciences and Research Centre, Edapally, Cochin. Phone: 09995107927. Email: harishprules@gmail.com



Figure 1. Right Eye Fundoscopic Image

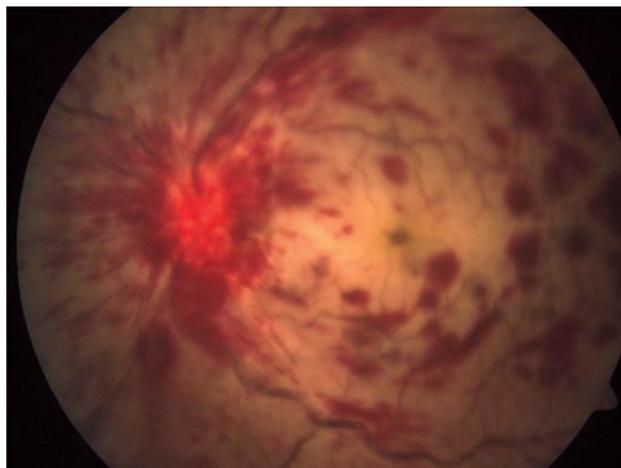


Figure 2. Left Eye Fundoscopic Image

of pregnancy, during 3<sup>rd</sup> pregnancy she had an intrauterine death at 6<sup>th</sup> & 4<sup>th</sup> pregnancy she had spontaneous abortion at 2<sup>nd</sup> month. In her 2<sup>nd</sup> pregnancy she gave birth to a live male child.

On initial examination she was anemic, her right eye was normal (**Figure 1**) and Left eye was completely blind with absent light perception & Direct Light reflex (Indirect Reflex was present). Left fundus showed a ‘splashed tomato’ appearance with multiple superficial & deep hemorrhages involving all the quadrants, disc margins were not clear with dilated & tortuous veins. All these features suggested of a CRVO. In addition to the above mentioned findings, retina was very pale & there was presence of Cherry red spot which was suggestive of CRAO (**Figure 2**). Ophthalmology evaluation and florescent fundus angiogram which showed delayed arterial filling & choroidal ischemia (suggestive of CRAO) & retinal capillary non-perfusion (suggestive of CRVO) confirming our clinical findings.

Initial blood Investigations showed Pancytopenia. (Hb-7.14, PCV- 22.8, Total WBC count- 3.01, Platelet-21300) & raised ESR (62), aPPT was 50/32, which was not corrected even after mixing study suggestive of no factor deficiency. PT – INR was normal.

VDRL was positive, TPHA was negative. Anti Cardiolipin was positive IgM positive – 13.8 (0-11 MPLu/ml), IgG positive – 97.4 (0-23 GPLu/ml), LUPUS anticoagulant – positive,  $\beta$ 2 Glycoprotein-negative 3.42 (0-5 ). Her ANA (IFA) showed speckled pattern and Anti-ds DNA – positive 51 (0-30 IU/ml)

When both clinical and laboratory parameters were combined we arrived at a final diagnosis of APS based on criteria in **Table 1**. But only 3 out of 11 criteria of SLE (Pancytopenia, ANA, Anti-ds DNA) were present. So a final diagnosis of APS secondary to probable SLE

was considered

She was initially pulsed with steroids (Methyl prednisolone) for 5 days & then changed to Oral steroids (Prednisolone). Along with that she was anticoagulated with LMWH (low molecular weight heparin-Enoxaparin) which was followed by oral anticoagulation with warfarin (INR strictly maintained between 2-3). At the time of discharge her left eye was still completely blind. She was advised regular follow up in Medical and Ophthalmology Departments.

Table 1. Clinical and laboratory criteria for diagnosis of antiphospholipid syndrome

Clinical criteria
1. Vascular thrombosis
2. Pregnancy morbidity
a. One or more deaths of normal fetus at or beyond 10th week of gestation
b. One or more premature births of normal neonate before 34th week of gestation from eclampsia, pre-eclampsia or placental insufficiency
c. Three or more consecutive spontaneous abortions before the 10th week of gestation with maternal anatomic or hormonal abnormalities and paternal and maternal chromosomal causes excluded
Laboratory criteria
1) Lupus anticoagulant
2) Elevated anticardiolipin antibody
3) Elevated anti- $\beta$ 2Glycoprotein antibody

Note. At least 1 of both criteria is need for definitive classification. Laboratory results must be present on 2 or more occasions separated by no less than 12 weeks but no more than 5 years.

After 3 months antibodies were repeated again which showed Anti cardiolipin Positive, IgG 63.2 (0-23GPLu/ml), Lupus anticoagulant positive & even anti- $\beta$ 2Glycoprotein which was negative initially was also positive 26.0 (0-15) and diagnosis of APS was confirmed. Her vision in the left eye is gradually improving. She was able to perceive finger movements by 3 months & visual acuity improved to 6/60 by 7 months.

## DISCUSSION

Antiphospholipid syndrome is an acquired thrombophilic disorder in which autoantibodies are produced to a variety of phospholipids and phospholipid-binding proteins. These antibodies include anticardiolipin antibodies, b-2-glycoprotein-1 antibodies, and lupus anticoagulant. The characteristic pathologic finding in the APS is a bland thrombosis with minimal vascular or perivascular inflammation. This change is not specific for the APS, as it also occurs in a variety of other disorders including the hemolytic-uremic syndrome/thrombotic thrombocytopenic purpura, systemic sclerosis (scleroderma), and malignant hypertension. Larger vessels, both arteries and veins, may develop in situ thrombosis or be sites from or into which emboli originate or lodge.

The diagnostic criteria require one clinical event, i.e. thrombosis or pregnancy complication, and two positive blood tests spaced at least 3 months apart. These antibodies are: lupus anticoagulant, anti-cardiolipin and anti- $\beta_2$ -glycoprotein-I.

The term “primary antiphospholipid syndrome” is used when APS occurs in the absence of any other related disease. APS however also occurs in the context of other autoimmune diseases, such as systemic lupus erythematosus (SLE), in which case the term “secondary antiphospholipid syndrome” is used. In rare cases, APS leads to rapid organ failure due to generalized thrombosis; this is termed “catastrophic antiphospholipid syndrome” (CAPS) and is associated with a high risk of death.

Ocular manifestations as already mentioned occur in 90% cases of APS. Unlike other autoimmune disorders APS is more of hypercoagulable condition. Therefore the ocular manifestations are mainly due to Thrombosis rather than vasculitis which is more common in other autoimmune disorders like Rheumatoid arthritis, Sjogren’s syndrome etc.. It can affect choroid, retina & optic nerve. According to a multicenter study done in Europe, including 100 APS patients the most common ocular manifestations included Amaurosis Fugax, Retinal artery & retinal vein thrombosis, isolated retinal hemorrhages and cotton wool spots, and retinal neovascularization & optic neuropathy. APS can affect any part of eyes (**Table 2**).

These conditions typically occur in the elderly, APS patients may experience them earlier in life.

Usually either CRAO & CRVO occur separately. But combined CRAO & CRVO is very rare presentation

**Table 2** Title Eye Manifestations in Antiphospholipid Antibody Syndrome

Symptoms	unclear vision, transient diplopia, transient field loss, amaurosis fugax, photopsia
Conjunctiva	telangiectasias, aneurysms, episcleritis
Cornea	keratoprecipitates, limbal keratitis
Vitreous	haemorrhage, cells
Optic nerve	disc oedema, anterior ischemic optic neuropathy
Retina	arterial or venous occlusion, venous tortuosity, aneurysms, cotton-wool spots, vasculitis, vascular sheathing, macular serous detachment, acute retinal necrosis

of APLA. Only 3 cases have been reported worldwide. The 1<sup>st</sup> one was 27 yr old described by Fitzpatrick in English Medical Literature in whom SLE & APS was detected only after the initial ocular event. The 2<sup>nd</sup> Patient was reported by Durukan which was a 23 yr old female who was already a diagnosed case of SLE & APS developed 5 days postpartum. She had stopped Prophylactic heparin 3 weeks before the event. The 3<sup>rd</sup> case was reported by Chang from School of Medicine, Taipei which was a case of 35yr old female who was already a diagnosed case of SLE on prophylaxis (poor compliance) & reported with sudden unilateral loss of vision. What we have in our case is a 38 year old who has presented with combined CRAO & CRVO, who fits into the criteria of APLA. APLA can be primary or secondary. Among secondary SLE is the most common cause. Our patient only satisfies 3 out of 11 criteria for SLE. But SLE is an evolving disease, so in future she may develop other manifestations of SLE

In the above reported cases 1 & 2 there was complete loss of vision and no recovery at all. While in case 3 there was almost complete recovery of vision only to have subsequent similar episodes. While in our case there is slow recovery that too after 7 months of the event & her visual acuity improved to 6/60 from being completely blind.

The reason for the ocular manifestations in APS with SLE can be due to both Thrombosis & Vasculitis. But APS is more of a hypercoagulable state & most of the systemic manifestations or presentations are due to thrombotic phenomenon. Also it is very unlikely for a vasculitis to cause unilateral loss of vision as it has been reported in all the 4 cases.

The main treatment is anticoagulation. We started our patient on Low molecular Weight heparin & were later bridged with Oral Anticoagulant-Warfarin. Anticoagulation is of utter most importance because these individuals are prone for recurrent thrombotic events in future. And as in our case there can additional benefit in the form of gradual improvement in vision.

Even though she might not regain her total vision, at least her quality of life has improved.

The occurrence of ocular events is very common in APS. So APS should always be ruled out in individuals who present with sudden loss of vision secondary to a vascular phenomenon in which no definite cause can be identified. Even though combined CRAO & CRVO is a very rare presentation of APS, the possibility should always be kept in mind as it is a treatable condition & can improve one's vision like in our case. But more studies are required in this field for final acceptance. Also as the studies have already showed, 23 % of SLE patients develop APS in future, always rule out APS antibodies in patients with SLE, as early diagnosis and initiation of anticoagulant therapy can prevent such thrombotic vascular complications.

The long-term prognosis for APS is determined mainly by recurrent thrombosis, which may occur in up to 29% of patients, sometimes despite antithrombotic therapy

## END NOTE

### Author Information

1. Dr. Harish Prabhu, Postgraduate Trainee, Department of Internal Medicine, Amritha Institute of Medical Sciences and Research Centre, Edapally, Cochin. Phone: 09995107927. Email: harishprules@gmail.com
2. Dr. Vishnu S Chandran, Assistant Professor, Department of Internal Medicine, Amritha Institute of Medical Sciences and Research Centre, Edapally, Cochin. Phone: 9497336625. Email: vishnuschandran@aims.amritha.edu
3. K K Velayudhan, Professor, Department of Internal Medicine, Amritha Institute of Medical Sciences and Research Centre, Edapally, Cochin.

Phone: 9446141810.

Email: kkvelayudhan@amis.amritha.edu

**Conflict of Interest:** None declared

**Cite this article as:** Prabhu H, Chandran VS, Velayudhan KK. Combined Central Retinal Artery & Central Retinal Vein Occlusion in Secondary APS. Kerala Medical Journal. 2015 Dec 14;8(4):35–8

## REFERENCES

1. Asherson RA, Khamashta MA, Ordi-Ros J, Derksen RH, Machin SJ, Barquinero J, et al. The "primary" antiphospholipid syndrome: major clinical and serological features. *Medicine (Baltimore)*. 1989 Nov;68(6):366–74.
2. Castañón C, Amigo MC, Bañales JL, Nava A, Reyes PA. Ocular vaso-occlusive disease in primary antiphospholipid syndrome. *Ophthalmology*. 1995 Feb;102(2):256–62.
3. Glacet-Bernard A, Bayani N, Chretien P, Cochard C, Lelong F, Coscas G. Antiphospholipid antibodies in retinal vascular occlusions. A prospective study of 75 patients. *Arch Ophthalmol*. 1994 Jun;112(6):790–5.
4. Hughes GR. The antiphospholipid syndrome: ten years on. *Lancet*. 1993 Aug 7;342(8867):341–4.
5. Kleiner RC, Najarian LV, Schatten S, Jabs DA, Patz A, Kaplan HJ. Vaso-occlusive retinopathy associated with antiphospholipid antibodies (lupus anticoagulant retinopathy). *Ophthalmology*. 1989 Jun;96(6):896–904.
6. Klok AM, Geertzen R, Rothova A, Baarsma GS, Kijlstra A. Anticardiolipin antibodies in uveitis. *Curr Eye Res*. 1992;11 Suppl:209–13.
7. Nojima J, Suehisa E, Akita N, Toku M, Fushimi R, Tada H, et al. Risk of arterial thrombosis in patients with anticardiolipin antibodies and lupus anticoagulant. *Br J Haematol*. 1997 Mar;96(3):447–50.
8. Oosting JD, Derksen RH, Bobbink IW, Hackeng TM, Bouma BN, de Groot PG. Antiphospholipid antibodies directed against a combination of phospholipids with prothrombin, protein C, or protein S: an explanation for their pathogenic mechanism? *Blood*. 1993 May 15;81(10):2618–25.
9. Pulido JS, Ward LM, Fishman GA, Goodwin JA, Froelich CJ, Sanghvi JP. Antiphospholipid antibodies associated with retinal vascular disease. *Retina (Philadelphia, Pa)*. 1987;7(4):215–8.
10. Rafuse PE, Canny CL. Initial identification of antinuclear-antibody-negative systemic lupus erythematosus on ophthalmic examination: a case report, with a discussion of the ocular significance of anticardiolipin (antiphospholipid) antibodies. *Can J Ophthalmol*. 1992 Jun;27(4):189–93.