Central retinal vein occlusion with depot medroxyprogesterone acetate use – an extremely rare complication

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Abstract

A 35-year old woman developed bilateral central retinal vein occlusion secondary to 3 years of DMPA use. The results of the investigations for inherited/acquired thrombophilia, diabetes and connective tissue disorders were normal. She was treated by a private ophthalmologist with aspirin, 100 mg daily. She made a complete recovery from bilateral central retinal vein occlusion.

She was referred by a general practitioner to our gynaecology outpatient department clinic for decision on non-hormonal, contraceptive choices and she underwent laparoscopic sterilization procedure.

Key words: central retinal vein occlusion (CRVO), depot medroxyprogesterone acetate (DMPA).

Introduction

Despite DMPA having a 34-year history as a safe and effective contraception for the vast majority, there were only two possible causal associations with retinal vein occlusion reported. This is most probably the third reported case.

Central retinal vein occlusion (CRVO) is a common retinal vascular disorder. CRVO presents with variable visual loss. In females the contraceptive pill is the most common underlying association. Although it is well-established that oestrogen-containing contraception has prothrombotic potential in women over 35 years of age, particularly in women who smoke, low dose progesterone-containing contraception, both oral and parenteral, has not been conclusively linked to prothrombotic events. The association with retinal venous thrombosis is less well defined.

However, the use of progestogens including medroxyprogesterone has been associated with vision disorders. Events reported by less than 1% of subjects included thrombophlebitis and deep vein thrombosis.

Case report

Ms. DK had been using DMPA since January 2006. She suddenly developed blurring of vision in February 2009. After ophthalmological assessment and investigations, she was diagnosed with bilateral central retinal vein occlusion.

Ms. DK had two uncomplicated pregnancies and spontaneous normal vaginal deliveries.

She never had any thrombotic episodes. She had epilepsy between the ages of 18-23. She is currently not on any antiepileptic treatment or any follow-up. She does not have hypertension or diabetes mellitus.

She does not have any significant surgical or gynaecological history.

She smokes about 20 cigarettes a day. She does not have any family history of DVT/thrombophilia or any connective tissue disorders.

On examination, her BMI is 30kg/sq.m. Her general, cardio vascular, respiratory systems were clinically normal. Her abdomen was soft and unremarkable. Per vaginal examination was normal. She had normal vision. Her neurological examination was normal.

All the blood investigations, including the SLE and the thrombophilia screen are normal.

She was treated by a private ophthalmologist with aspirin 100 mg daily. She had a complete recovery from bilateral central retinal vein occlusion. She has completed her three monthly and six monthly ophthalmological follow up. She underwent laparoscopic sterilization procedure.

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Discussion

Central retinal vein occlusion (CRVO) is a common retinal vascular disorder. Clinically, CRVO presents with variable visual loss; the fundus may show retinal haemorrhages, dilated tortuous retinal veins, cotton-wool spots, macular oedema, and optic disc oedema.

Retinal vein occlusion occurs when the circulation of a retinal vein becomes obstructed by an adjacent blood vessel, causing haemorrhages in the retina. Swelling and ischemia (lack of oxygen) of the retina as well as glaucoma are fairly common complications.

There were two possible causal associations of DMPA with retinal vein occlusion reported in the British Journal of Ophthalmology in 2007 by Byron F Deen, R Keith Shuler, Jr and Sharon Fekrat.

Should the patient experience pulmonary embolism, cerebrovascular disease or retinal thrombosis while receiving Depo-Provera, the drug should not be readministered.

Detection and diagnosis: Vein occlusion is diagnosed by examining the retina with an ophthalmoscope. Fluorescein angiography may be performed in some cases to study the circulation of the retina and to determine the extent of macular oedema or swelling.

Broadly, CRVO can be divided into 2 clinical types, ischemic and nonischemic. Nonischemic CRVO is the milder form of the disease. It may present with good vision, few retinal haemorrhages and cotton-wool spots, no relative afferent pupillary defect, and good perfusion to the retina. Nonischemic CRVO may resolve fully with good visual outcome or may progress to the ischemic type.

Ischemic CRVO is the severe form of the disease. Usually, ischemic CRVO presents with severe visual loss, extensive retinal hemorrhages and cotton-wool spots, presence of relative afferent pupillary defect, poor perfusion to retina, and presence of severe electoretinographic changes. In addition, patients may end up with neovascular glaucoma and a painful blind eye.

The visual symptoms can vary in severity from one person to the next, and are dependent on whether the central retinal vein or a branch retinal vein is involved. Patients who experience a branch vein occlusion often notice a gradual improvement in their vision as the haemorrhage resolves.
The exact pathogenesis of the thrombotic occlusion of the central retinal vein is not known. Various local and systemic factors play a role in the pathological closure of the central retinal vein\textsuperscript{5,6,7}. Thrombotic occlusion of the central retinal vein can occur as a result of various pathologic insults, including compression of the vein (mechanical pressure due to structural changes in lamina cribrosa, e.g., glaucomatous cupping, inflammatory swelling in optic nerve, orbital disorders); hemodynamic disturbances (associated with hyperdynamic or sluggish circulation); vessel wall changes (e.g., vasculitis); and changes in the blood (e.g., deficiency of thrombolytic factors, increase in clotting factors)\textsuperscript{1}.

The central retinal artery and vein share a common adventitial sheath as they exit the optic nerve head and pass through a narrow opening in the lamina cribrosa. Because of this narrow entry in the lamina cribrosa, the vessels are in a tight compartment with limited space for displacement. This anatomical position predisposes to thrombus formation in the central retinal vein by various factors, including slowing of the blood stream, changes in the vessel wall, and changes in the blood\textsuperscript{1}. The prognosis of CRVO depends upon the reestablishment of patency of the venous system by recanalization, dissolution of clot, or formation of optociliary shunt vessels\textsuperscript{1}.

**Frequency**

**United States**

CRVO and branch retinal vein occlusion constitute the second most common retinal vascular disorder. The nonischemic type is more common than the ischemic type\textsuperscript{1}.

In a recent publication, it is reported that the 15-year cumulative incidence of CRVO to be 0.5\%\textsuperscript{8}.

**International**

A large population-based study in Israel reported a 4-year incidence of retinal vein occlusion of 2.14 cases per 1000 of general population older than 40 years and 5.36 cases per 1000 of general population older than 64 years\textsuperscript{1}. In Australia, the prevalence of vein occlusion ranges from 0.7\% in patients aged 49-60 years to 4.6\% in patients older than 80 years\textsuperscript{9,11}.

**Morbidity**

- In more than 90\% of patients with ischemic CRVO, final visual acuity may be 20/200 or worse. Anterior segment neovascularization with associated neovascular glaucoma develops in more than 60\% of cases. This can happen within a few weeks and up to 1-2 years afterward\textsuperscript{1}.

- It has been reported that the fellow eye may develop retinal vein occlusion in about 7\% of cases within 2 years. In another report, the 4-year risk of developing second venous occlusion is 2.5\% in the same eye and 11.9\% in the fellow eye. Neovascular glaucoma may result in a painful blind eye\textsuperscript{1}.

CRVO does not have any particular racial preference\textsuperscript{1}.

CRVO occurs slightly more frequently in males than in females\textsuperscript{1}.

More than 90\% of CRVO occurs in patients older than 50 years, but it has been reported in all age groups\textsuperscript{1}.

Central retinal vein obstruction has been associated with various systemic pathological conditions, although the exact cause and effect relationship has not been proven.

Some of the conditions in which CRVO has been associated include the following (1):

- Systemic vascular disease
  - Hypertension
  - Diabetes mellitus
  - Cardiovascular disease

- Blood dyscrasias
  - Polycythemia vera
  - Lymphoma
  - Leukemia

- Clotting disorders
  - Activated protein C resistance
  - Lupus anticoagulant
  - Anticardiolipin antibodies
  - Protein C
  - Protein S
  - Antithrombin III

- Paraproteinemia and dysproteinemias
  - Multiple myeloma
  - Cryoglobulinemia

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• Vasculitis
  o Syphilis
  o Sarcoidosis

• Autoimmune disease – Systemic lupus erythematosus

• Oral contraceptive use in women

• Other rare associations
  o Closed-head trauma
  o Optic disc drusen
  o Arteriovenous malformations of retina

The risk of CRVO is decreased with increasing levels of physical activity and increasing levels of alcohol consumption.

It is reported that a decreased risk of CRVO with the use of postmenopausal estrogens and an increased risk with higher erythrocyte sedimentation rates in women.

Learning points

• Central retinal vein occlusion (CRVO) is a common retinal vascular disorder, presents with variable visual loss.

• CRVO has been reported in all age groups

• The use of progestogens including medroxyprogesterone has been associated with vision disorders.

• Should the patient experience visual loss or retinal thrombosis while receiving Depo-Provera, the drug should not be readministered.

• However, low dose progesterone-containing contraception, both oral and parenteral, has not been conclusively linked to prothrombotic events.

References


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