CASE REPORT

Association between clomiphene citrate and central retinal vein occlusion

A case report

Maria I Viola, MB ChB, MMed, FCOG (Argentina)
Department of Obstetrics and Gynaecology, Reproductive Medicine Unit, Stellenbosch University, Tygerberg, W Cape, and Vincent Pallotti Hospital, Cape Town

David Meyer, MB ChB, FCFP (SA), Hons BSc (Pharm), MMed, FCOphth (SA), PhD
Division of Opthalmology, Stellenbosch University

Thabo Matsaseng, MB ChB, MMed, FCOG (SA)
Thinus Kruger, MD, FRCOG
Department of Obstetrics and Gynaecology, Reproductive Medicine Unit, Stellenbosch University, and Vincent Pallotti Hospital, Cape Town

Central retinal vein occlusion (CRVO) is a common retinal vascular disorder associated with cardiovascular disorders and other related risk factors. A case of CRVO secondary to clomiphene citrate has been reported. We present a case that also illustrates the association between clomiphene citrate and CRVO, and hope that it will serve to increase awareness among physicians who use the drug.

Central retinal vein occlusion (CRVO) is a common retinal vascular disorder that has been associated with various systemic pathological conditions, although the exact cause is unknown. A case of CRVO secondary to clomiphene citrate has been reported.[1] The Beaver Dam Eye Study Group recently reported a 0.5% incidence of CRVO in the USA.[2]

CRVO is not often seen by gynaecologists, but they should be aware of the condition in fertility patients undergoing induction of ovulation, especially with clomiphene citrate. In our research we found one report on CRVO in the English literature.[1]

Case report

A 38-year-old woman, gravida 0 para 0, presented with primary infertility and a 2-year history of uterine fibroids. She had irregular menses associated with dysmenorrhoea and had never used any contraceptives. A spermiogram was normal.

The patient had had hypertension and dyslipidaemia for 10 years and was on perindopril 4 mg/d and simvastatin 20 mg/d. She had undergone a laparotomy myomectomy followed by laparoscopy (adhesiolysis). A year later the findings on hysteroscopy had been normal. There was no relevant family history.

On examination her blood pressure was 130/80 mmHg, with a normal pulse rate. Her body weight was 87.3 kg, her height 1.68 m and her body mass index 31. Systemic examination revealed no abnormalities.

In vitro fertilisation was planned and ovulation induced with clomiphene citrate 100 mg per day and human menopausal gonadotropin (Menopur) 225 IU on day 1 followed by 150 IU daily. The patient developed visual symptoms in her right eye on day 4 of the above medication. These included black spots and flashes initially, followed by moderate loss of acuity.

The medication was stopped and she was referred to her ophthalmologist after visual acuity dramatically worsened. Her initial recorded acuity was 6/60 in the right eye. The initial fundoscopic features were suggestive of a central retinal vein occlusion, and oral acetazolamide 250 mg 6-hourly and prednisone 60 mg/d were commenced. However, her vision deteriorated to count fingers vision (near) in the right eye, in which there was a dense central scotoma. The corrected visual acuity in the left eye was normal. Both anterior segments were normal, and a right relevant afferent pupil defect of 0.9 log units was present. Dilated examination of the right fundus revealed distorted veins, a few haemorrhages and a few cotton wool spots. A large central serous elevation of the macula and a swollen disc were present. Ocular motility was normal. Optical coherence tomography of the right fundus confirmed a large serous detachment/elevation of the neurosensory retina and possibly also the retinal pigment epithelium.

A full screen for hyperviscosity conditions including plasma homocysteine levels, anti-DNA antibodies, cardiolipin antibodies, protein C and protein S, factor V Leiden and prothrombin 20210A was normal, as were the blood glucose level and a lipogram. A full blood count revealed microcytic hypochromic anaemia with a haemoglobin concentration of 8.6 g/dl, a platelet count of 534×10^9/l and a normal erythrocyte sedimentation rate.

Results

A week later the patient's vision had only minimally improved, but the serous retinal detachment had flattened significantly. The prednisone was stopped and the diagnosis of central retinal vein occlusion was confirmed. She was advised to increase her fluid intake and take 150 mg aspirin per day.

Discussion

CRVO is a common retinal vascular disorder. Clinically it presents with variable visual loss. The exact pathogenesis is not certain. Various local and systemic factors play a role in the pathological closure of the central retinal vein. More than 90% of cases occur in patients older than 50 years, but it has been reported in all age groups.

CRVO has been associated with various systemic pathological conditions and medications, including the following:[3]

- systemic vascular disease – hypertension, diabetes mellitus, cardiovascular disease
- blood dyscrasias – polycythaemia vera, lymphoma, leukaemia
- clotting disorders – activated protein C resistance, lupus anticoagulant, anticardiolipin antibodies, protein C, protein S, antithrombin III
- paraproteinaemia and dysproteinaemias – multiple myeloma, cryoglobulinaemia
- vasculitis – syphilis, sarcoidosis
- auto-immune disease – systemic lupus erythematosus
- oral contraceptive use in women
- other rare associations – closed head trauma, optic disc drusen, arteriovenous malformations of the retina.

Although CRVO is a rare condition in fertility patients care should be exercised, especially in patients with associated risk factors who undergo ovulation induction with clomiphene citrate.

Clomiphene citrate is an orally administered, non-steroidal ovulation stimulant that has been demonstrated to be a useful therapy for the anovulatory patient desiring pregnancy. The first endocrine event in response to a course of clomiphene therapy is an increase in the release of pituitary gonadotrophins followed by an increase in thrombogenic oestradiol. Thrombo-embolic complications have been reported in patients receiving clomiphene, including deep-vein thrombosis, myocardial infarction and central retinal vein occlusion.[1,4,5] No association between Menopur and visual disorders has been reported in spite of the fact that the drug raises oestradiol levels.

Patients receiving clomiphene should be advised to report visual symptoms such as blurring, spots or flashes that occur during therapy. These symptoms increase in incidence with increasing total dose or duration of therapy.[6]

Physicians should be aware of the potential risk of clomiphene, especially in patients with associated risk factors for CRVO. Should visual disturbances occur, therapy should be terminated and the patient referred for specialist ophthalmic care.

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