

# Central retinal vein thrombosis as an initial manifestation of heterozygous protein C deficiency - Case Report

*Trombose da veia central da retina como manifestação inicial da deficiência de proteína C na forma heterozigótica - Relato de Caso*

Rodrigo Pessoa Cavalcanti Lira<sup>1</sup>  
Gustavo Araújo Covolo<sup>2</sup>  
Wilson Nadruz Júnior<sup>3</sup>  
Carlos Eduardo Leite Arieta<sup>4</sup>

## ABSTRACT

The purpose of this paper is to report a case of central retinal vein thrombosis associated with isolated heterozygous protein C deficiency. Acute occlusion of the central retinal vein presents as one of the most dramatic pictures in ophthalmology. It is often a result of both local and systemic causes. A rare systemic cause is heterozygous protein C deficiency, and it usually occurs in combination with other thrombophilic conditions. This case highlights that isolated heterozygous protein C deficiency may be the cause of central retinal vein thrombosis and underscores the importance of its screening in young patients with this ophthalmologic disease.

**Keywords:** Retinal vein thrombosis; Protein C deficiency; Case report

Thrombophilic conditions may be associated with retinal vein thrombosis. The most common is activated protein C resistance, but its deficiency is also described in some patients. We report a case of central retinal vein thrombosis associated with isolated heterozygous protein C deficiency.

## CASE REPORT

A 34-year-old white woman was admitted to our institution with a sudden decrease of visual acuity in the right eye. She did not present ocular pain, photophobia, fever or any other local or systemic complaint. The patient had no personal or familial history of eye disease, systemic hypertension, diabetes mellitus, thrombophilia, malignancy or use of oral contraceptive pills. At examination, blood pressure measurement was 114 x 73 mmHg. Visual acuity in the right eye (OD) was 20/25 and left eye (OS) was 20/20 with best correction. In both eyes, slit-lamp biomicroscopic findings were normal, without pupillary defects, and intraocular pressure was 15 mmHg. Ophthalmoscopy of the right eye revealed occlusion of the central retinal vein with venous engorgement, few flame-shaped hemorrhages, blurring of optic disc margins and rare cotton-wool spots. In the left eye, ophthalmoscopy was normal. Angiography of OD showed a nonischemic central retinal vein occlusion (Figure 1), and of OS was normal. Biochemistry and hematology tests were otherwise normal. Erythrocyte sedimentation rate was 7 mm/h. Immunological tests for rheumatoid factor, lupus anticoagulant, as well as tests for nuclear, DNA, phospholipid and neutrophil cytoplasmic antibodies were negative. A DNA analysis showed no mutation for factor V, prothrombin or MTHFR genes. Plasma levels of protein S and antithrombin III were normal. Plasma level of protein C was 58% (normal 70-140%), compatible

<sup>1</sup> Doutor em Ciências Médicas pela Universidade Estadual de Campinas - UNICAMP

<sup>2</sup> Pós-graduando nível Mestrado do Curso de Pós-graduação em Ciências Médicas da Universidade Estadual de Campinas - UNICAMP

<sup>3</sup> Pós-graduando nível Doutorado do Curso de Pós-graduação em Clínica Médica da Universidade Estadual de Campinas - UNICAMP

<sup>4</sup> Professor Assistente Doutor do Departamento de Oftalmo-Otorrinolaringologia da UNICAMP

**Endereço para correspondência:** Rua Afonso Celso n.66 apt.1502 - Recife (PE) CEP 52060-110  
E-mail: rodrigopclira@hotmail.com

Recebido para publicação em 24.07.2001

Aceito para publicação em 05.08.2002

**Nota Editorial:** Pela análise deste trabalho e por sua anuência na divulgação desta nota, agradecemos ao Dr. Ayrton Roberto Branco Ramos.

with the diagnosis of heterozygous protein C deficiency. Heparin anticoagulation was promptly instituted and warfarin then introduced. One month later, visual acuity of the right eye was 20/20 and complete improvement in ophthalmoscopic findings was noted. Neither parents nor children were available for ocular and systemic examination.

#### COMMENT

Acute occlusion of the central retinal vein is one of the most dramatic pictures in ophthalmology. It is often a result of both local and systemic causes<sup>(1-2)</sup>. An increased risk for central retinal vein occlusion is found in patients with systemic hypertension, diabetes mellitus, open-angle glaucoma, and thrombophilic conditions<sup>(1-3)</sup>.

Although there is no consensus, referring patients younger than 50 years old with central retinal vein occlusion to thrombophilia screening seems to be appropriate<sup>(1-4)</sup>. A cost-effective approach would be to screen initially for activated protein C resistance, because the test for this disease is relatively easy to perform and provides good differentiation between normal and resistant subjects. If this test is negative, then the patient should be screened for lupus anticoagulant, anticardiolipin antibody, protein C, protein S, and antithrombin III deficiencies<sup>(1-2)</sup>.

Activated protein C resistance is the most common inherited hypercoagulable state associated with venous thrombosis. It is usually caused by a single point mutation in the factor V gene referred to as factor V Leiden<sup>(1,4-5)</sup>. This condition has been frequently associated with central retina vein occlusion<sup>(1-2,5)</sup>. In contrast, protein C deficiency is an uncommon cause of venous thrombosis<sup>(6-8)</sup>. Its inherited deficiencies are either heterozygous or homozygous, with levels of protein C around 50% and 1%, respectively (normal 70-140%). Although homozygous deficiencies of protein C tend to result in severe neonatal thrombotic disease, heterozygous deficiencies result in milder thrombotic tendencies<sup>(1,6-7)</sup>. Patients with the heterozygous form who have already suffered an episode of thrombosis may be treated with long-term anticoagulation, but each patient should be considered on an individual basis<sup>(8)</sup>. This disorder seems to represent an autosomal dominant trait, although its penetrance is variable<sup>(4,6)</sup>.

There are few reports of central retinal vein occlusion associated with protein C deficiency<sup>(3,9-10)</sup>, and they usually occur in combination with other thrombophilic conditions. This case highlights that isolated heterozygous protein C deficiency may be the cause of central retinal vein thrombosis and underscores the importance of its screening in young patients with this ophthalmologic disease.

#### RESUMO

O objetivo deste estudo é relatar um caso de trombose da veia central da retina associada à deficiência isolada de proteína C

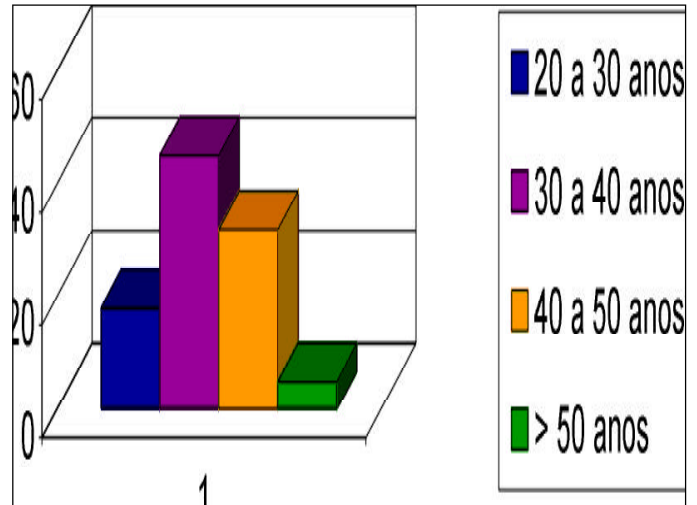


Figure 1 - Fluorescein angiography of the right eye at late phase showed a nonischemic central retinal vein occlusion. Perfusion of retinal capillary bed is good. Retinal edema is minimal, and flame-shaped hemorrhages are few in number

na forma heterozigótica. Oclusão aguda da veia central da retina é um dos mais dramáticos quadros oftalmológicos. Geralmente resulta tanto de fatores locais como sistêmicos. Uma causa sistêmica rara é a deficiência de proteína C na forma heterozigótica, ocorrendo usualmente associada a outras trombofilias. Este caso mostra que deficiência isolada de proteína C na forma heterozigótica pode ser a causa da trombose da veia central da retina e reforça a importância de sua investigação em pacientes jovens com esta doença ocular.

**Descritores:** Trombose venosa retiniana; Deficiência proteínica C; Relato de caso

#### REFERENCES

- Vine AK, Samama MM. The role of abnormalities in the anticoagulant and fibrinolytic systems in retinal vascular occlusions. *Surv Ophthalmol* 1993; 37:283-92.
- Greiner K, Hafner G, Dick B, Peetz D, Prellwitz W, Pfeiffer N. Retinal vascular occlusion and deficiencies in the protein C pathway. *Am J Ophthalmol* 1999;128:69-74.
- Tekeli O, Gursel E, Buyurgan H. Protein C, protein S and antithrombin III deficiencies in retinal vein occlusion. *Acta Ophthalmol Scand* 1999;77:628-30.
- Rosendaal FR. Venous thrombosis: a multicausal disease. *Lancet* 1999; 353:1167-73.
- Willianson TH, Rumley A, Lowe GD. Blood viscosity, coagulation, and activated protein C resistance in central retinal vein occlusion: a population controlled study. *Br J Ophthalmol* 1996;80:203-8.
- Reitsma PH. Protein C deficiency: from gene defect to disease. *Thrombosis and haemostasis* 1997;78:344-50.
- Nizzi FA Jr, Kaplan HS. Protein C and S deficiency. *Semin Thromb Hemost* 1999;25:265-72.
- Sanson BJ, Simioni P, Tormene D et al. The incidence of venous thromboembolism in asymptomatic carriers of a deficiency of antithrombin, protein C, or protein S: a prospective cohort study. *Blood* 1999;94:3702-6.
- Bertram B, Remky A, Arend O, Wolf S, Reim M. Protein C, protein S, and antithrombin III in acute ocular occlusive diseases. *Ger J Ophthalmol* 1995; 4:332-5.
- Krüger K, Anger V. Occlusion ischémique de la veine centrale de la rétine et déficit en protéine C. *J Fr Ophthalmol* 1990;13:369-71.