

Metabolic syndrome and central retinal artery occlusion

Natalija Kosanović-Jaković*, Lidija Petrović[†], Dijana Risimić*,
Svetislav Milenković*, Danica Matić[‡]

Clinical Center of Serbia, *Institute for Ophthalmology, Belgrade; Clinical
Hospital Center „Zvezdara“[†] Clinic for Ophthalmology „Prof. dr Ivan
Stanković“, Belgrade; Clinical Center of Serbia,
[‡]Institute for Cardiology, Belgrade

Background. The accumulation of risk factors for central retinal artery occlusion can be seen in a single person and might be explained by the metabolic syndrome. **Case report.** We presented the case of a 52-year-old man with no light perception in his right eye. The visual loss was monocular and painless, funduscopy showed central retinal artery occlusion and the laboratory investigation showed the raised erythrocyte sedimentation rate of 105 mm/h and the raised C-reactive protein of 22 mg/l. Specific laboratory investigations and fluorescein angiography excluded the presence of vasculitis, collagen vascular diseases, hypercoagulable state and antiphospholipid syndrome. **Conclusion.** The patient met all the five of the National Cholesterol Education Program (NCEP) criteria for the metabolic syndrome: hypertension, abnormal lipid profile, abnormal glucose metabolism, obesity and hyperuricemia. Measurement of C-reactive protein is useful for the assessment of therapeutic systemic effect on any abnormality in the metabolic syndrome. Individual therapy for all risk factors in the metabolic syndrome is necessary to prevent complications such as cardiovascular, retinal vascular diseases and stroke.

Key words: metabolic syndrome X; retinal artery;
retinal artery occlusion; visual acuity.

Background

The metabolic syndrome, or the so-called syndrome X, or the insulin resistance syndrome is characterized by abdominal obesity, diabetes, glucose intolerance, dyslipidemia, high blood pressure and hyperuricemia (1). According to the National Cholesterol Education Program (NCEP) criteria, an individual may be diagnosed to have the metabolic syndrome if he/she has three or more of the following findings: abdominal obesity, triglycerides > 1.7 mmol/l, HDL cholesterol < 1.0 mmol/l, blood pressure > 130/85 or antihypertensive medication and fasting glucose > 6.1 mmol/l (insulin or hypoglycemic agents) (2, 3). The results of many studies suggest that arteriosclerosis and insulin resistance share a common inflammatory basis by showing that the raised C-reactive protein has direct harmful effects on vessel walls (4). Furthermore, these metabolic disorders are closely linked to each other, and thus the primary patho-

genesis of this syndrome is difficult to determine in each patient. It also remains to be determined which metabolic disorders should be the primary therapeutic targets to prevent cardiovascular diseases (CVD) and stroke, and which metabolic disorders should be monitored to follow therapeutic effects (2, 5, 6).

Central retinal artery occlusion (CRAO) is one of the most sudden and dramatic events seen by the ophthalmologist and was described as early as in 1859 (7). Patients usually present with a sudden painless loss of vision. The appearance of a cherry-red spot in the fundus was the main characteristic (8). The cherry-red spot appears because soon after the obstruction of the blood flow to the inner retina, the normally transparent retina becomes opaque and blocks the brownish-red color from the underlying choroid, which is still supplied by blood. Because the retina overlying the foveola is relatively thin, however, the normal color of the choroid is still visible in this area (9). It is not known how

long this cherry-red spot takes to appear, but in a primate model, it appears as early as 30 minutes after the obstruction (10). The difference in the etiology of CRAO depends on the age of patients presenting with an obstruction. The CRAO in patients 30 years of age or younger tends to be associated with migraine, coagulation disorders, intraocular abnormalities, and trauma (11).

Possible risk factors for the development of CRAO are arteriosclerosis, chronic atrial fibrillation, congestive heart failure, cerebrovascular accident, systemic hypertension, myocardial infarction, diabetes mellitus, primary open angle glaucoma and rheumatic heart diseases (10, 12).

Case report

We presented the case of a 52-year-old man who suddenly observed severe painless visual loss with no light perception in his right eye. Our assessment showed that the best corrected visual acuity in the left eye was 6/6 by Snellen chart. Intraocular pressure was 16 mm Hg in both eyes measured by applanation tonometry. Both anterior segments were normal. An afferent pupil defect was present in the right eye.

The CRAO diagnose was based on the abrupt visual loss accompanied by one or more of the following signs as observed by slit lamp biomicroscopy with a +78 diopter lens, fundus photography and fluorescein angiography (FA): sluggish, thinned retinal artery flow; the fragmentation of the blood column in retinal arterioles; retinal opacification combined with sluggish retinal blood flow; and the presence of a cherry red spot (Figures 1–2). These findings were compared with the fellow uncompromised eye. The left fundus was normal.

Standard laboratory investigations revealed: the raised erythrocyte sedimentation rate 105 mm/h, the raised C-reactive protein 22 mg/l, and fibrinogen 6 g/l. The serum uric acid level was high, 650 $\mu\text{mol/l}$ (normal < 420 $\mu\text{mol/l}$). The full blood count (red cell count 4.03, hemoglobin 11.3 g/dl, packed cell volume (PCV) 0.33, platelet count 298, and white blood count 6.6), prothrombin time 89% and the activated partial thromboplastin time 29 s, serum creatinine 144 $\mu\text{mol/l}$, serum urea 11.9 mmol/l, fasting glucose 4.55–6.9 mmol/l, HbA1c 7.6%, serum lipid levels: total cholesterol 7.9 mmol/l, high-density lipoprotein (HDL) 1.04 mmol/l, and triglycerides 3.98 mmol/l. The presence of rheumatoid factor antibodies, antinuclear antibodies, anti-neutrophil cytoplasmatic antibodies, immune complexes, antiphospholipid antibody and lupus anticoagulans were also analyzed. They were negative.

The patient had been only under hypertension treatment since 1993. During cardiologic examination, chest radiography was normal, and no anomaly of cardiac rhythm was found by Holter monitoring. Normal atrial and ventricular volumes, normal valvular function and normal coronary arteries (< 10% stenosis) were found on echocardiography. A color Doppler scan of the carotid arteries

showed bilateral stenosis of 30%. A urine test revealed microhematuria with urate crystals. We found nephrolithiasis of the right side by renal ultrasonography.

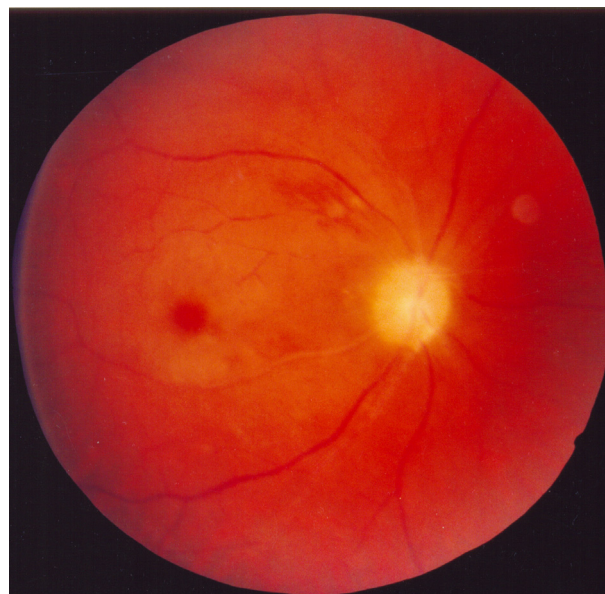


Fig. 1 – Fundus photograph of the right eye show central retinal artery occlusion (cherry-red spot)

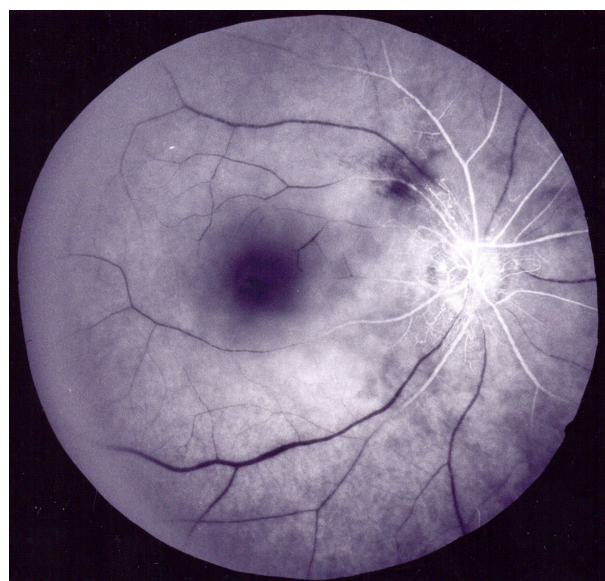


Fig. 2 – The early phase (23 s) of the fluorescein angiogram of the right eye shows complete failure of dye to enter the retinal circulation and retrograde filling close to the optic disc

Discussion

In this patient we could change the traditional attitude toward making a diagnosis by considering the examination findings first and then the history of a disease in an attempt to come to a differential diagnosis. Our third key point on examination allowed us to point out precisely the giant cell

arteritis (GCA). Visual loss was at first monocular and painless, then fundoscopy revealed CRAO, and then the laboratory investigation showed the raised ESR of 105 mm/h (normal 33 mm/h), and the raised CRP of 22 mg/l (normal 6 mg/l). We had those results available within the 2 hours. There was a high index of suspicion to GCA. The incidence of CRAO in GCA given in the literature was between 2% and 18% (13, 14). GCA is a potentially blinding disease, and its early diagnosis is the key to prevent the blindness in the fellow eye with the megadose therapy (1 000 mg prednisone i.v.) (14). To confirm a diagnosis, our patient underwent biopsy of the right temporal artery immediately, but histopathological examination was negative.

The nonspecific markers of immune system activation (CRP, ESR) were raised and it is our practice to search for anticardiolipin antibodies in cases of the clinical and fluorangiographic evidence of retinal vasculitis, vascular thrombosis, central retinal vein occlusion and CRAO. The prevalence of CRAO in antiphospholipid syndrome is uncertain, and is always assessed in relation to the associated syndrome (systemic lupus erythematosus) between 7% and 9% with red eye, diplopia and headache (15, 16). Specific laboratory investigations and FA showed that vasculitis, collagen vascular diseases, hypercoagulable state, and antiphospholipid syndrome were excluded.

Arteriosclerosis is probably the most commonly associated systemic condition with CRAO. In some cases, a cause of CRAO is relatively clear, such as a visible embolus. In other cases, however, especially those associated with systemic disorders such as diabetes, hypertension, CVD, the association is less clear (10). O'Farrell et al., (17) found no difference between stenosis in the ipsilateral and the contralateral carotid artery. This suggests that the cause of retinal artery occlusions may not be carotid artery steno-

sis – it may be simply associated with these occlusions. Merchut et al. (18) found no relation between the types of arterial occlusion branch or central, and the type of underlying carotid artery disease. Wijman et al. (19) found a high grade internal carotid stenosis of 70% or more in 73% of the patients with retinal ischemia that included transient ischemic attacks (TIAs), and arterial occlusions, both acute and chronic. Diabetes mellitus and CVD are probably the next two most common associated conditions (20, 21).

According to the recent literature, the most common risk factors for CRAO are present in the metabolic syndrome. The patient had all the five NCEP criteria for metabolic syndrome: hypertension, abnormal lipid profile, abnormal glucose metabolism, obesity and hyperuricemia. Each abnormality involved in the metabolic syndrome with the raised proinflammatory marker levels (CRP, fibrinogen) is also a classic risk factor for CVD and stroke (1–3).

Conclusion

Although there have been numerous clinical and experimental studies of the pathophysiology of CRAO, the disease still has multifactorial causes and relatively poor visual prognosis (blindness). Each abnormality involved in the metabolic syndrome is also a classic risk factor for the retinal obstructive diseases and CVD. Accumulation of such risk factors in a single person, younger than 55 years, can be the result of two mechanisms: the coincidence or the clustering. Unfortunately, there is no therapeutic strategy to treat this condition. The measurement of CRP is useful for the assessment of therapeutic systemic effect on each abnormality in the metabolic syndrome. Individual therapy is necessary to reveal any risk factor and to prevent complications such as CVD, stroke and retinal vascular diseases.

REFERENCES

1. Meigs JB. Invited commentary: insulin resistance syndrome? Syndrome X? Multiple metabolic syndrome? A syndrome at all? Factor analysis reveals patterns in the fabric of correlated metabolic risk factors. *Am J Epidemiol* 2000; 152(10): 908–11.
2. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA* 2001; 285(19): 2486–97.
3. Takahashi S, Moriwaki Y, Tsutsumi Z, Yamakita J, Yamamoto T, Hada T. Increased visceral fat accumulation further aggravates the risk of insulin resistance in gout. *Metabolism* 2001; 50(4): 393–8.
4. Rosenson RS. Assessing risk across the spectrum of patients with the metabolic syndrome. *Am J Cardiol* 2005; 96(4A): 8E–10E.
5. Grundy SM, Hansen B, Smith SC Jr, Cleeman JI, Kahn RA; American Heart Association, et al. Clinical management of metabolic syndrome: report of the American Heart Association/National Heart, drug, and Blood Institute/American Diabetes Association conference on scientific issues related to management. *Circulation* 2004; 109(4): 551–6.
6. Lakka HM, Laaksonen DE, Lakka TA, Niskanen LK, Kumpusalo E, Tuomilehto J, et al. The metabolic syndrome and total and cardiovascular disease mortality in middle-aged men. *JAMA* 2002; 288(21): 2709–16.
7. von Graefe A. Massive embolia of central retinal artery as a cause of sudden blindness. *Arch für Klin und experim Ophth* 1859; 5: 136. (German)
8. Karjalainen K. Occlusion of the central retinal artery and retinal branch arterioles. A clinical, tonographic and fluorescein angiographic study of 175 patients. *Acta Ophthalmol Suppl* 1971; 109: 1–95.

9. *Duke-Elder S, Dobree JH.* Diseases of the Retina. In: *Duke-Elder*, editor. System of Ophthalmology. Vol X. St. Louis: CV Mosby; 1967. p. 253–6.
10. *Mangat HS.* Retinal artery occlusion. *Surv Ophthalmol* 1995; 40(2): 145–56.
11. *Brown GC, Magargal LE, Shields JA, Goldberg RE, Walsh PN.* Retinal artery obstruction in children and young adults. *Ophthalmology* 1981; 88(1): 18–25.
12. *Rumelt S, Dorenboim Y, Rehany U.* Aggressive systematic treatment for central retinal artery occlusion. *Am J Ophthalmol* 1999; 128(6): 733–8.
13. *Hayreh SS.* Ophthalmic features of giant cell arteritis. *Baillieres Clin Rheumatol* 1991; 5(3): 431–59.
14. *Hayreh SS, Podhajsky PA, Zimmerman B.* Ocular manifestations of giant cell arteritis. *Am J Ophthalmol* 1998; 125(4): 509–20.
15. *Glacet-Bernard A, Bayani N, Chretien P, Cochard C, Lelong F, Coscas G.* Antiphospholipid antibodies in retinal vascular occlusion. A prospective study of 75 patients. *Arch Ophthalmol* 1994; 112(6): 790–5.
16. *Gelfand YA, Dori D, Miller B, Brenner B.* Visual disturbances and pathologic ocular findings in primary antiphospholipid syndrome. *Ophthalmology* 1999; 106(8): 1537–40.
17. *O'Farrell CM, FitzGerald DE.* Ultrasound morphology of carotid lesions in retinal ischaemia. *Br J Ophthalmol* 1992; 76(11): 656–9.
18. *Merchut MP, Gupta SR, Naheedy MH.* The relation of retinal artery occlusion and carotid artery stenosis. *Stroke* 1988; 19(10): 1239–42.
19. *Wijman CA, Babikian VL, Matjucha IC, Koleini B, Hyde C, Winter MR, et al.* Cerebral microembolism in patients with retinal ischemia. *Stroke* 1998; 29(6): 1139–43.
20. *Brown GC, Magargal LE.* Central retinal artery obstruction and visual acuity. *Ophthalmology* 1982; 89(1): 14–9.
21. *Hayreh SS, Weingeist TA.* Experimental occlusion of the central artery of the retina. IV: Retinal tolerance time to acute ischaemia. *Br J Ophthalmol* 1980; 64(11): 818–25.

The paper was received on June 6, 2005.

Apstrakt

Kosanović-Jaković N, Petrović L, Risimić D, Milenković S, Matić D. *Vojnosanit Pregl* 2005; 62(12): 935–938.

METABOLIČKI SINDROM I OKLUZIJA ARTERIJE CENTRALIS RETINE

Uvod. Prisustvo svih vodećih faktora rizika za okluziju arterije centralis retine mogu se videti kod jednog bolesnika u sklopu metaboličkog sindroma. **Prikaz bolesnika.** Prikazujemo slučaj 52-godišnjeg muškarca bez osećaja svetla na desnom oku. Gubitak oštrine vida bio je monokularan i bezbolan, fundoskopija je pokazala prisustvo okluzije arterije centralis retine, a laboratorijski nalazi su ukazali na povišenu sedimentaciju eritrocita od 105 mm/h i povišen C-reaktivni protein od 22 mg/l. Specifični laboratorijski nalazi, kao i fluoresceinska angiografija isključili su postojanje vaskulitisa, kolagenih vaskularnih bolesti, stanja hiperkoagulabilnosti i antifosfolipidnog sindroma. **Zaključak.** Bolesnik ima svih pet Nacionalni holesterol obrazovni program (NHOP) kriterijuma za postavljanje dijagnoze metaboličkog sindroma: hipertenzija, abnormalni lipidni status, poremećen metabolizam glukoze, gojaznost i hiperurikemija. Praćenje vrednosti C-reaktivnog proteina korisno je za praćenje efekta sistemske terapije na svaki pojedinačni poremećaj u metaboličkom sindromu kako bi se preveniralo nastajanje komplikacija poput kardiovaskularnih bolesti, vaskularnih bolesti retine i cerebrovaskularnog insulta.

Ključne reči: metabolični sindrom X; a. centralis retinae; okluzija; vid, oštrina.