

Case Report

Orbital Infarction Syndrome in Nephrotic Syndrome Patient with Extensive Carotid Arteries Occlusion

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Orbital infarction syndrome is defined as ischemia of global intraorbital structures such as extraocular muscles, optic nerves, and retina. The most common cause of this syndrome is carotid arterial occlusion. Other causes include vasculitis, vasospasm, and compression of intraorbital circulation.

There has never been reported a case of orbital infarction syndrome in nephrotic syndrome patient. We present a case of 42-year-old Thai man with underlying disease nephrotic syndrome presented with abrupt onset of headache at left temporal area, horizontal diplopia, limitation of eye movement in all directions, ptosis, and blurred vision on the left eye. He was treated with pulse methylprednisolone intravenously for 3 days. Leg edema was improved however, the eye symptoms persisted. There was no evidence of hypercoagulable state. Magnetic resonance imaging (MRI), magnetic resonance angiography (MRA) revealed loss of signal intensity at left internal carotid artery from base of skull to intracavernous part. Cerebral angiography demonstrated complete occlusion of left common carotid artery. After the anticoagulant treatment, his symptoms were gradually improved. The cause of extensive carotid arterial occlusion in this patient is most likely from hypercoagulable state. Although it was negative for hypercoagulable state evidence, the authors assume that the high dose steroid treatment could lead to remission of nephrotic syndrome and resulting in the resolution of hypercoagulable state.

Keywords: *Orbital infarction syndrome, Stroke, Cerebrovascular disease*

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Ischemia of global intraorbital structures is now recognized as orbital infarction syndrome. It is responsible for insufficiency or thrombosis of the carotid system, or orbital circulation in the ophthalmic, maxillary, facial, and superficial temporal arteries. There are several reported cases of orbital infarction syndrome in the past. A literature review showed this condition is quite rare in clinical practice. There has been no previous reported case of orbital infarction syndrome in a nephrotic syndrome patient. This case report presents the classical case of orbital infarction syndrome due to occlusion of the common carotid (CCA), internal carotid (ICA), and external carotid (ECA) arteries on the left side, in a nephrotic syndrome patient.

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Case Report

A 42-year-old man presented with left visual loss and drooping eyelid for 3 weeks prior to Siriraj Hospital admission. He had bilateral leg edema, oliguria, albuminuria, hypercholesterolemia, and hypoalbuminemia and had been diagnosed with nephrotic syndrome 6 years ago. He underwent kidney biopsy 2 years earlier. The pathological report revealed IgM nephropathy without chronicity. He had been treated with prednisolone 40 mg/day, enalapril 20 mg/day, and a diuretic agent since then. Five months ago, he discontinued all medications by himself.

Three weeks earlier, he experienced abrupt onset of stabbing headache over the left temporal area. The severity of pain was constant. The pain did not disturb his daily living activities and was not aggravated by sneezing or coughing, including straining. He denied numbness, motor weakness, double or

blurred vision, nausea, and vomiting. He went to a private clinic and was treated with an intramuscular analgesic agent and oral medications. However, the symptom did not improve.

On the following day, after awakening, he noticed drooping and complete visual loss on the left eye. Additionally, he could not move the left eye in any directions. These symptoms accompanied with dulled periorbital pain and numbness at the left cheek up to the forehead. He rushed to the hospital for proper management. Investigations revealed normal blood chemistry profiles except serum albumin 1.4 g/dL, serum cholesterol 390 mg/dL and triglyceride 3,107 mg/dL. CT brain (after onset of symptoms 3 days) showed no abnormality. He was treated with methylprednisolone 1 gm intravenously for 3 days then prednisolone 60 mg/day, gemfibrozil 600 mg/day were prescribed. Improvement of numbness as well as periorbital pain was observed but not the visual loss and limitation of eye movement. He was discharged and appointed for the follow up after 3 weeks. The ophthalmologist found a markedly pale disc in the left eye with hemorrhagic spots. Central retinal artery occlusion was suspected. Consequently, he was referred to Siriraj Hospital.

He denied a history of weight loss, loss of appetite, chronic cough, rash, headache, arthralgia, sinusitis, abnormal discharge per ears/nose, head or face injuries, preceding motor weakness, or numbness.

He has smoked 10 cigarettes per day for 30 years and drinks alcohol occasionally.

Examination revealed blood pressure of 160/90 mmHg, pulse rate of 75 beat per minute, respiration of 18/min and temperature of 37°C. He was sthenic, alert, afebrile, and not edematous. The left carotid pulse was absent. Left eye revealed no proptosis, no orbital bruit, and no light perception. Fundoscopic examination showed left disc swelling, small hemorrhagic spots around disc, slightly pale retina, fully dilated pupil with complete ptosis, and complete limitation of eye movement in all directions. The right eye was entirely normal. There was impairment of pinprick sensation over left ophthalmic distribution. Other cranial nerves were normal as well as motor system. The deep tendon and plantar reflexes were normal. Sensation was normal in all modalities. There were no signs of meningeal irritation.

All laboratory findings were normal including complete blood count (CBC), estimated sedimentation rate (ESR), antinuclear antibody, antinuclear cytoplasmic antibody, venereal disease research laboratory (VDRL), anticardiolipin, coagulogram, lupus anticoagulant 1 (LA1), protein C, protein S, antithrombin III except

cholesterol (282 mg/dL), triglyceride (149 mg/dL) and homocysteine (30 mg/dL normal range 5-12 mg/dL) were mildly elevated. Urine analysis, urine microprotein, urine creatinine were normal.

Magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA), 4 weeks after the onset, revealed thrombosis of the left ICA, which involved cavernous and supraclinoid segments. Loss of signal intensity at the left ICA from the base of the skull to the intracavernous part (Fig. 1).

Ultrasonography of the carotid artery demonstrated complete occlusion of left CCA, ECA, and ICA.

Cerebral angiography showed complete occlusion of left CCA just distal to the origin 5 cm, cross circulation from right ICA and basilar artery to left middle cerebral artery (MCA) and left anterior cerebral artery (ACA). There was no string sign demonstrated (Fig. 2).

He was treated with prednisolone 40 mg per day for 7 days then tapering off. Unfractionated heparin intravenously was prescribed then changing to warfarin. He was admitted for 21 days. Home medication included prednisolone 15 mg/day, warfarin 3 mg/day, and simvastatin 10 mg/day. The periorbital pain was improved. However, he still had limitation of left eye movement approximately 50% in all directions. However, he still had no light perception on the left eye. Otherwise, he remained constant.

Discussion

The orbital infarction syndrome is a rare condition that has been defined as ischemia of all intraorbital and intraocular structures⁽¹⁾. Etiologies were established and included thrombosis of carotid arteries, vasculitis, direct compression to the intra-orbital circulation, and vasospasm. Bogousslavsky J, et al⁽²⁾ reported a similar case as the authors presented, with isolated complete orbital infarction from CCA thrombosis with complete occlusion but not in a nephrotic syndrome patient. The possible mechanism for this condition could be explained from the absence of an orbital collateral supply from the contralateral ECA and muscular cervical arteries systems. The arterial orbital circulation may be more vulnerable than the blood supply to the brain parenchyma because the brain supply has several collateral circulations when compared to the orbital circulation. The blood supply for the orbit is derived from rich anastomoses between internal carotid artery (ophthalmic artery and its branches) and external carotid artery (maxillary, facial, superficial temporal arteries, and their branches)^(3,4).

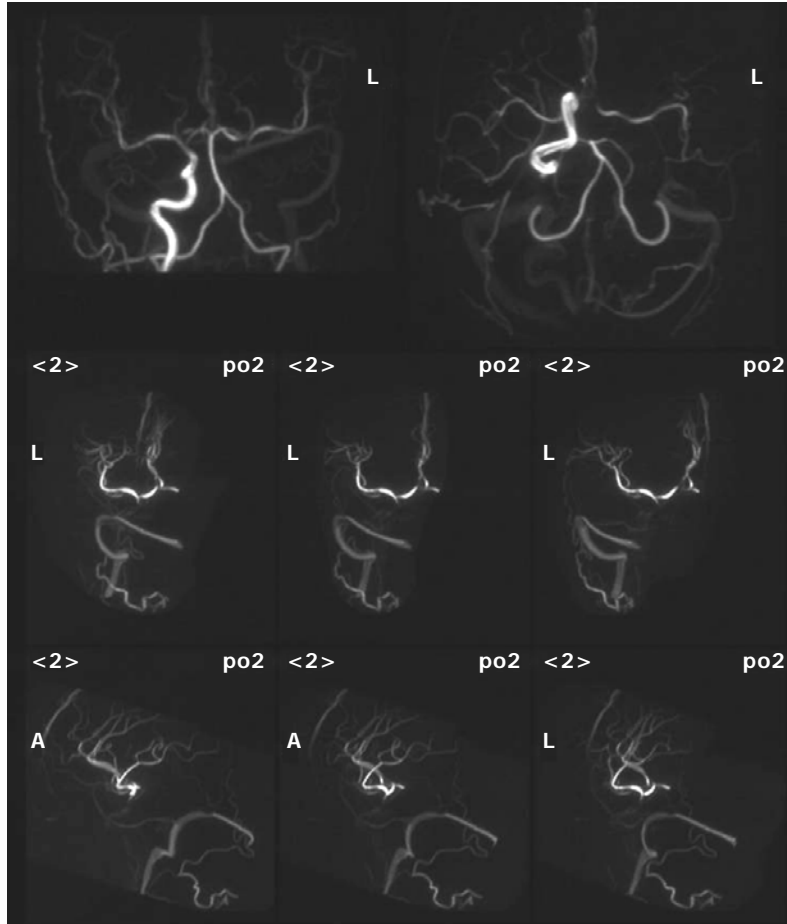


Fig. 1 MRA was performed at day 30th after the onset of symptoms demonstrated loss of signal intensity at left ICA from base of skull to intracavernous part



Fig. 2 Cerebral angiography (43 days after the onset) showed complete occlusion of left CCA just distal to the origin 5 cm, cross circulation from right ICA and basilar artery to left MCA and left ACA, there was no string sign demonstrated

Table 1. Previously reported cases of orbital infarct syndrome

| Author_year | Age | Sex | Clinical features | Diagnosis | Mechanism | Treatment |
|--|-----|-----|---|---|---|--|
| John P Blank et al 1981 ⁽⁷⁾ | 13 | M | Sickle cell anemia presented with eyelid swelling, limitation of upward gaze | Orbital cellulitis with bone infarction, sickle cell anemia | Vasculitis and inflammatory mass compressed microcirculation of intraorbital structures | Intravenous ampicillin |
| | 7 | F | Sickle cell anemia presented with frontal headache, swelling and tenderness | Orbital cellulitis with bone infarction, sickle cell anemia | Vasculitis and inflammatory mass compressed microcirculation of intraorbital structures | Intravenous ampicillin and nafcillin for 5 days |
| | 11 | F | of left eyelid Sickle cell anemia presented with fever, headache, leukocytosis | Orbital cellulitis with bone infarction, sickle cell anemia | intraorbital structures Vasculitis and inflammatory mass compressed microcirculation of intraorbital structures | Intravenous ampicillin and oxacillin for 7 days |
| MH Wolff et al 1985 ⁽⁶⁾ | 19 | M | Sickle cell anemia presented with fever, swelling right eyelid | Mucormycosis , sickle cell anemia | Vasculitis with intraosseous or subperiosteal pus under pressure compromises microcirculation leading to local ischemia | Blood transfusion, moxalactam 2.5 g q 6 hours |
| Francois-Xavier Bourruat et al 1993 ⁽¹⁾ | 51 | M | Transient left jaw pain, visual loss, ophthalmoplegia | Suspected giant cell arteritis | Vasculitis | Oral prednisolone 80 mg daily |
| | 85 | F | History of preceding left jaw claudication, left orbital pain, acute blindness | Giant cell arteritis | Vasculitis | Oral prednisolone 1 mg/kg |
| Carol F Zimmerman et al 1995 ⁽¹⁰⁾ | 36 | M | Postoperative ruptured anterior communicating artery aneurysm, operation time 18 hour, he developed ptosis, chemosis, fixed dilated pupil | Intraocular ischemia | Direct compression of the orbit due to head position | Topical levobunolo, systemic acetazolamide, methylprednisolone |

Table 1. Previously reported cases of orbital infarct syndrome (continue)

| Author_year | Age | Sex | Clinical features | Diagnosis | Mechanism | Treatment |
|---|-----|-----|--|---|---|---|
| | 29 | M | Post operative anterior communicating artery aneurysm, he developed ptosis, chemosis, ophthalmoparesis of left eye | Intraocular ischemia | Direct compression of the orbit due to head position | Supportive treatment |
| | 39 | F | Post operative ruptured anterior communicating artery aneurysm, immediate after surgery found ptosis, visual loss, ophthalmoplegia of left eye | Intraocular ischemia | Direct compression of the orbit due to head position | Topical levobunolol, systemic acetazolamide, methylprednisolone |
| | 56 | F | Post operative right middle cerebral artery trifurcation aneurysm, he developed right ptosis, proptosis, ophthalmoplegia within 3 hours and progressed to no light perception | Intraocular ischemia | Direct compression of the orbit due to head position | Systemic acetazolamide, timoptic, ocular paracentesis |
| Bryan P Arthurs et al 1999 ⁽⁵⁾ | 61 | F | SLE, hypothyroidism with sinusitis developed sudden loss of vision left eye | Intraocular ischemia | Vasospasm and direct compression of the orbit due to head position | Supportive treatment |
| Archana D Naran et al 2001 ⁽⁸⁾ | 16 | M | Sickle cell anemia presented with proptosis and periorbital soft tissue swelling of left eye | Orbital cellulitis with bone infarction, sickle cell anemia | Vasculitis and inflammatory mass compressed microcirculation of intraorbital structures | Intravenous antibiotic |
| Gregory P et al 2002 ⁽¹¹⁾ | 36 | F | Intranasal cocaine, heroine use with alcoholic consumption, she placed face and left orbit against desk for 3 hours then developed left orbital pain, left eyelid drooping, complete visual loss | Intraocular ischemia | Vasospasm and direct compression of the orbit due to head position | Supportive treatment |

Among the branches of the ophthalmic artery, only the central retinal artery and short posterior ciliary arteries are terminal vessels⁽³⁾.

The ocular manifestations of insufficiency or thrombosis of the carotid artery can be presented in various types. Systemic vasculitis such as giant-cell arteritis⁽¹⁾, systemic lupus erythematosus (SLE) can also cause this syndrome. There was a case report of orbital infarction and melting of the eyeball in a patient with SLE due to vasculitis⁽⁵⁾.

Bone infarction is a common complication of sickle cell disease, which can lead to intraorbital cellulitis and vasculitis that causes orbital infarction syndrome⁽⁶⁻⁸⁾.

Mucormycosis with orbital cellulitis and vasculitis^(1,9) has been reported as causing orbital infarction syndrome as well. The mechanism of orbital infarction of these patients was thought to be from vasculitis with occlusion of the blood vessels in the orbit.

Complications from the posture of surgical procedures have been established from serial case reports of post operation of intracranial aneurysm presented with orbital infarction syndrome⁽¹⁰⁾. According to the authors, the ocular vasculatures were in direct compression by the face and caused increase orbital pressure and collapse of the orbital arteries and veins. This resulted in orbital congestion and proptosis, decreased orbital perfusion pressure, and ischemia.

Drugs induced vasospasm can lead to orbital infarction, particularly, the potent sympathomimetic and vasoactive drugs such as cocaine, alcohol, and heroine. The combination of increased sympathetic tone and local vasospasm and prolonged compression of the orbit were most likely responsible for orbital infarction⁽¹¹⁾.

The presented patient had extensive left common carotid occlusion with orbital infarction syndrome. He did not have significant cardiovascular risk factors except the history of smoking and nephrotic syndrome. The nephrotic syndrome has been recognized as a risk factor for stroke in the young, which was associated with hypercoagulable state⁽¹²⁾. Many coagulation abnormalities have been described in nephrotic syndrome. These include increased levels of factors V and VIII, increased fibrinogen levels, decreased plasminogen levels, deficiencies of antithrombin III/protein S, increased or decreased protein C concentration, thrombocytosis, and enhanced platelet agreeability, as with the nephrotic syndrome in general⁽¹³⁾. Thus, the urine analysis and blood chemistry (urine microprotein 24 hour,

albuminuria, serum albumin, and cholesterol) were necessary to exclude the young active nephrotic syndrome patient who presents with stroke.

However, in the presented patient, the evidence of active nephrotic syndrome and hypercoagulable state during admission were normal. Mild elevation of homocysteine (30 mg/dL normal range 3-12 mg/dL), cholesterol, and triglyceride can not explain the extensive thrombosis of the left common carotid artery in this case. Although, the laboratory investigations from a previous hospital were significant for hypoalbuminemia, hypertriglyceridemia, and hypercholesterolemia, unfortunately, the data of urine analysis at that time were lacking. However, he had bilateral leg edema during hospitalization in the prior hospital. This may reflect the possibility that he had active nephrotic syndrome before pulse methylprednisolone therapy.

Evidences from several studies and case reports established the course and resolution of hypercoagulable state after remission of nephrotic syndrome⁽¹⁴⁻¹⁶⁾. Yorgin et al⁽¹⁴⁾ reported the mean duration of pulse methylprednisolone therapy until remission was 23.4 ± 29.9 days (median 12 days) in pediatric patients. There was no data on resolution after steroid therapy or report in adults. Nevertheless, the authors might postulate that the active nephrotic syndrome could be subsided after the administration of pulse methylprednisolone and high dose oral steroid. Thus, the authors could not find the evidence of active nephrotic syndrome and hypercoagulable state in the presented patient during admission at Siriraj Hospital.

A literature review showed 13 cases reports of orbital infarction syndrome that are summarized in detail (Table 1) including two cases of giant cell arteritis, five cases of sickle cell disease with orbital cellulitis and vasculitis, one case of SLE, one case of cocaine, heroine intranasal use, and six cases of post operative intracranial aneurysm.

Conclusion

In summary, the objective of the presented report was to present a patient with underlying disease, active nephrotic syndrome, who developed total left common carotid occlusion and isolated orbital infarction syndrome. Thus, the presented case emphasizes this syndrome and must be suspected in the patient who has acute blindness, ophthalmoplegia, orbital pain, enlarged pupil, and particularly absent carotid pulse. Extensive investigations for the etiology of thrombosis must be done, especially hypercoagulable state in nephrotic syndrome patient.

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กลุ่มอาการ orbital infarction เหตุอุดตันหลอดเลือดแดงคาโรติด ในผู้ป่วย nephrotic syndrome

ทัตดาว วิโรจน์อุไรเรือง, นิพนธ์ พวงวรินทร์

กลุ่มอาการ orbital infarction หมายถึง ภาวะขาดเลือดของโครงสร้างต่างๆ ที่อยู่ในกระบอกตา ได้แก่ กล้ามเนื้อ กลอกลูกตา, เส้นประสาทสมองคู่ที่ 2 และจอประสาทตา สาเหตุของภาวะนี้ส่วนใหญ่เกิดจากการอุดตันของหลอดเลือดแดงคาโรติด ส่วนสาเหตุอื่น ๆ ได้แก่ การอักเสบของหลอดเลือด, การหดตัวของหลอดเลือดแดงและการกดทับต่อการไหลเวียนของหลอดเลือด ในอดีตไม่เคยมีรายงานว่าเกิดภาวะนี้ในผู้ป่วย nephrotic syndrome คณะผู้รายงานจึงรายงานผู้ป่วยชายไทย อายุ 42 ปี ที่มีอาการขาบวม ตรวจปัสสาวะพบโปรตีน ได้รับการวินิจฉัยว่าเป็น nephrotic syndrome ต่อมามีอาการหนังตาซ้ายตก ตามัวลง ปวดศีรษะ มองเห็นภาพซ้อนในแนวราบ กลอกตาซ้ายไม่ได้ทุกทิศทาง ผู้ป่วยได้รับการรักษาด้วย pulse methylprednisolone ทางหลอดเลือดดำนาน 3 วัน ขาบวมลดลง แต่อาการทางตาคงเดิม ผลการตรวจทางห้องปฏิบัติการไม่พบ hypercoagulable state ตรวจ magnetic resonance imaging, magnetic resonance angiography พบมีการอุดตันของหลอดเลือดแดงคาโรติดด้านซ้าย ตั้งแต่ระดับฐานกะโหลกศีรษะ จนถึงระดับ intracavernous part ตรวจ cerebral angiography พบการอุดตันของหลอดเลือดแดง common carotid ด้านซ้าย การตรวจเพิ่มเติมไม่พบสาเหตุการอุดตันของหลอดเลือดแดงคาโรติดหลังให้การรักษาด้วยยาต้านการแข็งตัวของเลือดอาการผู้ป่วยค่อย ๆ ดีขึ้นตามลำดับและไม่เกิดอาการซ้ำ สาเหตุของการเกิดการอุดตันหลอดเลือดแดงคาโรติดคือ ภาวะเลือดแข็งตัวง่ายจาก nephrotic syndrome