**INTRODUCTION**

Although Intra Ocular Pressure (IOP) remains a significant factor in glaucoma disease, many cases of glaucoma occur in the absence of high pressure readings during exams. In some cases, vascular factors appear to be particularly important and there is building evidence that systemic vascular dysregulation plays a major role in Normal Tension Glaucoma (NTG)\(^1\)\(^-\)^\(^4\). Subclavian steal syndrome is a vascular entity that can potentially decrease perfusion to the optic nerve head, making it more susceptible to damage from intra-ocular pressure, in presence of normal intraocular pressures\(^5\)^\(^-\)^\(^12\). The following case report describes a patient who developed subclavian steal syndrome and optic nerve head hypoperfusion.
A 74-years-old white female presented herself for a routine visual evaluation. She has had medical history of hypertension, increased cholesterol, type 2 diabetes mellitus for 5 years and peripheral arterial occlusive disease diagnosed 3 years ago (intermittent claudication of low members). She denied any symptoms of headache, pain or diplopia. There was no history of amaurosis fugax or transient ischemic attacks. She complained about occasional dizziness during mild exertion. She was medicated with simvastatin 20mg id, metformine 1000mg bid, clopidogrel id, enalapril 10mg id and lansoprazol 30mg id.

Her past ocular history revealed a left eye traumatic injury occurred during in her childhood (2-years-old), which resulted in an amblyopic eye. We had no prior registries in our clinic from this patient.

At our exam, the best corrected visual acuities (VA) were 80/100 in the right eye (OD) and 10/100 in the left eye (OS). Pupils were equal, round and reactive to light, without any relative afferent defect. Motility examination showed no limitation, with full ductions and versions presented, without diplopia.

Slit lamp microscopy revealed a clear cornea OD and a 5 mm diameter central corneal opacification OS, there was no evidence of iris neovascularization and the anterior chamber was clear on both eyes (OU). Examination upon pharmacological dilation revealed a bilateral mild nuclear lens sclerosis OU, macula and peripheral retina were healthy in both eyes without evidences of diabetic retinopathy. The optic nerves had a cup-to-disc ratio of 0.60 OD and 0.50 OS, a vertical elongation was detected OU and a superior notch was identified in the right optic nerve (Fig. 1 & 2).

Intra Ocular Pressures by Goldmann applanation tonometry measured 16mm Hg OU. Central corneal thickness was 522 µm OD and 506 µm OS, measured by ultrasonic pachymetry.

At this point, we had a patient with a suspected optic discs and a history with vascular risk factors presented.

The patient was instructed to relay her symptoms of dizziness to her primary care physician and to return for an Optical Coherence Tomography – Heidelberg Spectralis® (OCT) and a threshold visual field – 101 OCTOPUS® (both performed 2 weeks later).
The OCT revealed a generalized nerve fiber layer loss in OD with a supertemporal nerve fiber layer thinner than normal and, in OS, a slight decrease on the average nerve fiber layer thickness was noticed (Fig. 3). The visual field in the left eye was not reliable, because of its amblyopic feature. There were no substantial visual field alterations in the right eye (MD 3.2 / LV 6.7) (Fig. 4a).

She was sent for a carotid and vertebral artery color Doppler ultrasound, which she performed 4 months later. She came back 6 months after her first appointment bearing the prescribed tests. She complained about increased dizziness “when carrying bags from the supermarket”, she also mentioned that she didn’t contact previously her primary care physician, because she related it with her intermittent claudication and as result, didn’t give importance to that. She claimed that she had occasional left arm numbness on exertion. Doppler evaluation revealed normal flow velocities in the common carotid and internal carotid artery with no evidence of stenosis. However, a retrograde blood flow with high resistance patterns was shown in the left vertebral artery, suggesting left subclavian steal syndrome. The flow in the contralateral vertebral artery was higher (VS = 1.80 m/s; VD = 0.30 m/s).

Another ophthalmologic observation was made and she maintained the VA of 80/100 OD and 10/100 OS. Gonioscopy revealed a moderately open angle (grade III of Shaffer). The optic nerve maintained the same characteristic that was previously observed, with an IOP OD 14mmHg OS 15mmHg. The remaining ophthalmic examination was similar. Blood pressure was 157/90 (right arm) and 131/81 (left arm).

We requested a new visual field exam (Fig 4b) and an Ophthalmic Doppler to evaluate ocular hemodynamics (performed 1 month later). The visual field (good reliability), showed a possible loss of peripheral vision demonstrating delineation of a supero-inferior accuate scotoma (MD 4.6 / LV 20.5).
Fig. 4 – a) 1st visual field. b) 2nd visual field performed 6 months later. c) Visual field performed before stent intervention (11 months later).

The Ophthalmic Doppler (Fig. 5), showed an elevated Resistance Index (RI) in both orbits, especially at the microcirculation level, the Peak Systolic velocity (PS) of the right ophthalmic artery was 39.3 cm/s, End Diastolic velocity (ED) 6.8 cm/s, on the left side PS 42.3 cm/s and ED 7.6 cm/s.

Fig. 5 – Ophthalmic Doppler of the right and left ophthalmic artery (before stent intervention).

We referred this patient to vascular specialist and a CT-Angiography (Fig. 6) was performed, confirming the diagnosis of subclavian steal syndrome and revealing the left subclavian proximal stenosis. She was monitored regularly with regard to neurological signs and symptoms. Vascular Clinics proposed her for endovascular treatment (primary stenting of the subclavian artery). We did a third visual field before surgery (Fig 4c), that confirmed progression in the visual field defects, with a superior and inferior arcuate scotoma with visual fields defects detected closer to fixation (MD 8.3 / LV 57).
Subclavian Steal Syndrome and optic nerve damage

Fig. 6 – CT-Angiography showing the left subclavian proximal stenosis (arrow).

After vascular intervention, the patient did a new Carotid Doppler and Ophthalmic Doppler (Fig. 7) that showed restoration of the blood flow. On the right side the ophthalmic artery showed a PS 54.6 cm/s and ED 61.6 cm/s. On the left side, was detected PS 69.6 cm/s and ED 10.3 cm/s.

Fig. 7 – Ophthalmic Doppler of the right and left ophthalmic artery (after stent intervention).

A Visual Field exam was performed 3 months after the surgery (Fig. 8) that showed a relative improvement in the visual fields (MD 4.7 / LV 47.0) with a partial recuperation of the scotoma.
This patient had left subclavian steal syndrome which appears to have caused enough shunting of blood from the right carotid system to the left vertebral-basilar system (and subsequently the left subclavian artery) to decrease ocular perfusion on the right optic nerve head, making it more susceptible to glaucomatous damage, even at a lower IOP. IOPs after surgery were 15mmHg OU and the optic nerves maintained similar characteristics as previously described.
Subclavian Steal Syndrome (SSP) refers to subclavian artery steno-occlusive disease proximal to the origin of the vertebral artery and is associated with reversal flow in the vertebral artery. Anatomically, there is an occlusion of the subclavian artery just before the origin of the vertebral artery. This clinical entity is associated with neurological symptoms of vertebrobasilar insufficiency that occur during or following exercise of the ipsilateral arm. Symptoms of dizziness or vertigo occur in more than half of the patients, and syncope and dysarthria have been noticed in 18% and 12.5%, respectively. Since most patients do not seek medical advice unless symptoms manifest, the prevalence of subclavian artery occlusive disease and subclavian steal syndrome is unknown.

The most common cause of proximal subclavian artery occlusive lesions is arteriosclerosis. Some of the risk factors are cigarette smoking, hypercholesterolemia, type 2 Diabetes Mellitus, hypertension, and hyperhomocysteinemia. SSP occurs more often on the left side. When the arm is exercised, the blood vessels dilate to enhance perfusion to the ischemic muscle, thus lowering the resistance in the outflow vessels. The increased demand for blood by the left arm, results in the shunting of blood into the left subclavian artery. Blood crosses the basilar artery from the contralateral intracranial vertebral artery and flows retrograde down the ipsilateral vertebral artery towards the left arm (Fig. 9). This bypasses the stenosis in the left subclavian artery. When arm exercise ceases, the resistance in the outflow vessels of the arm increases, thereby reducing retrograde blood flow in the vertebral artery.

**DISCUSSION**

Subclavian Steal Syndrome and optic nerve damage

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Fig. 9 – Schematic of the path of the blood as it flows to supply the left subclavian artery distal to its occlusion.

If the blood flow demand in the arm increases, more arterial flow is siphoned from the cerebral circulation, satisfying increased oxygen demand through the exercising muscles of the upper extremity. This causes partial ischemia of...
the brain stem and posterior cerebral cortex and symptoms could be manifested 14,15. Indirectly, because of anastomoses between the carotid system and vertebrobasilar system at the circle of Willis, the remainder of the cerebral cortex may be affected during times of heightened activity (Fig. 9 and 10). Numerous symptoms are associated with posterior circulation cerebral ischemia. Visual symptoms secondary to vestibular dysfunction and/or nystagmus include a sensation of objects moving or the inability to focus as well as monocular or binocular visual loss. Diplopia occurs in 19% of the cases. The most frequent neurologic symptom is dizziness or vertigo, usually described as a sensation of lightheadedness, rocking, swaying, or tilting 15,18. On our examination, there was a blood pressure difference between the arms, usually this difference is at least 20mmHg lower on the involved side in SSP. The pulse is usually weak and the arms and feet may feel cool. Diagnosis is possible through non-invasive testing. SSP most commonly is diagnosed incidentally during carotid and vertebral artery color Doppler US, discovering abnormalities of blood flow direction in the vertebral artery. Angiography remains the definitive diagnostic test for confirming this condition 19. Although transient ischemic attacks are common, brain stem infarcts are rare. In general, most vascular surgeons do not perform surgical treatment, unless symptoms related to either cerebral or ipsilateral ischaemia are present. No medical therapy is known to effectively treat subclavian steal syndrome. However, if the cause of subclavian steal syndrome is atherosclerotic stenosis or occlusion of the proximal subclavian artery, patients should be treated with lifelong antiplatelet therapy to reduce the risk of associated myocardial infarction, stroke, and other vascular causes of death.

Ocular

Although glaucoma is a progressive degenerative disease, the etiology of this disease is not completely understood, it is quite probable that a combination of factors – mechanical, vascular, and possibly spontaneous nerve fiber atrophy – are involved. Vascular disease could be an underlying factor in determining patients with normal tension glaucoma 1, 3, 6. In this case there was an identified vascular factor disease causing lack of blood supply in the optic nerve, causing suffering of the ganglion nerve cells (probably worst after left arm exercise). An animal study consisting in clamping the left subclavian artery was performed by Reivich et al. 20. They found that there was 41% decrease of total cerebral blood flow. When flow was reversed in the left vertebral artery, there was an increase in flow through both carotid and right vertebral arteries that tried to partly compensate the loss of blood flow down the left vertebral artery. The increase in carotid artery flow occurring when the flow in the vertebrobasilar system is reduced, suggested that the carotid arteries probably contribute to the posterior cerebral circulation through the circle of Willis 15,16,17 (Fig. 10). This shunts blood away from the anterior cerebral and possibly the ocular circulations. It has been demonstrated that when the vertebral arteries were occluded, blood derived from the carotid arteries flowed into the posterior cerebral and basilar arteries 215,17. This may serve to decrease flow toward the ophthalmic artery, establishing hypopoefusion to the optic nerve.
head. Many studies suggested that abnormalities in nerve head circulation can contribute to the onset of low tension glaucoma. Hypoperfusion, will lead to a more susceptibility optic disc damages in normal values of IOP. The ciliary body will also decrease aqueous production, decreasing even more the IOP.

In 1997, C. Haskes reported a patient with subclavian steal syndrome (caused by an arteriosclerotic plaque in the left subclavian artery) and contralateral normal tension glaucoma; the patient was treated with warfarin and dorzolamide 2% ophthalmic solution. Several visual fields were performed, before and after the therapy, and revealed defect stabilization after the latter. In our case, the insertion of the subclavian stent restored the vascular flood back near physiologic condition, and as result we had a significant improvement in the visual fields.

The patient had visual fields with good reliability that showed a glaucomatous progression (Fig. 4). It appears that over time, enough blood was shunted away to compensate left subclavian / vertebrobasilar insufficiency, causing hypoperfusion of the optic nerve head. With the institution of the subclavian stent, restoring the normal arterial flow to the optic nerve, an improvement was noticed. In the last visual field performed (after stent intervention), we can notice that some areas recovered visual function (Fig. 8). So, one hypothesis is that the nerve fiber layers of those areas were less time exposed to ischemia, and consequently had time to recover and did not suffer cellular death after vascular intervention.

So far, IOP and visual fields remain stable. The patient recovered from his neurological symptoms (dizziness). She is being monitored regularly taking into account neurological signs.

The precise role of vascular factors in normal tension glaucoma is not entirely clear, but many believe it represents at least a partial explanation of...
the problem in some patients. Currently, more trials in this area are needed to study the effect of ocular blood flow on glaucoma prognosis. Although IOP control is the principal goal in glaucoma therapy, if such studies show a protective effect against Glaucoma, they will open a new era in glaucoma management.

★ CONCLUSION ★

The Subclavian Steal Syndrome is a vascular disorder that redirects cerebral blood flow to the subclavian artery affected by obstruction, causing a general reduction in blood flow to territories supplied by the carotid and vertebrobasilar systems. Hypoperfusion to the optic nerve and ciliary body can potentially create normal tension glaucoma. Increasing evidences are showing that vascular factors leading to ischemia, may have a fundamental role in the disease initiation or progression. It is important to recognize the Subclavian Steal Syndrome and its effects on ocular and systemic level, in order to make an early intervention, referral and an adequate follow-up of the disease.