Ocular Ischemic Syndrome Associated with Primary Hyperparathyroidism

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Authors’ contributions

This work was carried out in collaboration between all authors. Author ZA designed the case study, conducted diagnostic procedure and wrote the first draft of the manuscript. Authors LM and SS are conducted a diagnostic procedures and managed the literature searches. Authors VJ and AR are conducted diagnosis and treatment. All authors read and approved the final manuscript.

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ABSTRACT

Aim: To present a case of bilateral ocular ischemic syndrome associated with severe carotid artery occlusive disease and to discuss any possible etiological factors, including parathyroid adenoma.

Case Presentation: We report a rare and unusual case of bilateral ocular ischemic syndrome, secondary to internal carotid artery atherosclerosis, occurring as a result of primary hyperparathyroidism.

Discussion: A significant decrease in the visual acuity may be an early sign of PH. Considering calcium homeostasis in the eye is useful in establishing the right diagnosis of PH.

Conclusion: To our knowledge, this is the first report of bilateral ocular ischemic syndrome associated with primary hyperparathyroidism.

Keywords: Atherosclerosis; ocular ischemic syndrome; swollen optic disc; visual loss.
ABBREVIATIONS

OIS : Ocular Ischemic Syndrome
PH : Primary Hyperparathyroidism
MIBI scintigraphy : 99mTc-methoxyisobutylisonitrile parathyroid scintigraphy

1. INTRODUCTION

Ocular ischemic syndrome (OIS) is a rare condition, which is caused by ocular hypoperfusion. The most common etiology of OIS is severe unilateral or bilateral atherosclerotic disease of the internal carotid artery or marked stenosis at the bifurcation of the common carotid artery. Ocular signs and symptoms may be the first manifestations of carotid artery disease. OIS was originally described by Hedges, in 1963 and was initially called venous stasis retinopathy. In the same year, Kearnst and Hollenhorst reported ocular symptoms and signs in association with advanced carotid artery stenosis [1]. The term, ocular ischemic syndrome, was coined so as to sum up all ocular symptoms and signs that may accompany carotid artery occlusive disease. Common ocular findings may include advanced unilateral cataract, anterior segment inflammation, asymptomatic anterior chamber reaction, macular edema, dilated but non-tortuous retinal veins, mid-peripheral dot and blot hemorrhages, cotton wool spots, hard exudates and neovascularization of the disc and retina [2]. Disorders of the endocrine system can be a cause of secondary hypertension, the most common being the benign primary hyperaldosteronism, pheochromocytoma and Cushing’s disease [3]. Primary hyperparathyroidism (PH) is an endocrine disorder that affects any of the four parathyroid glands to release an excessive amount of parathyroid hormone; leading to the development of parathyroid adenoma. Increased parathyroid hormone results in increased calcium levels in blood and urine. Hypercalcemia, due to PH has also been associated with atherosclerotic disease and high blood pressure. However, altered functional properties of the vascular wall, which are generally believed to precede atherosclerosis, tend to be associated with PH [4]. Secondary hypertension is associated with PH in 10%-70% of the patients [5]. Simultaneous bilateral ocular involvement is even less common and has been reported in mere 22% of all OIS cases. According to our knowledge, PH has not been described as a cause of OIS. We single out a rare case of a 63 year-old woman with bilateral OIS and parathyroid adenoma.

2. CASE PRESENTATION

A 63 year-old female complained of decreased visual acuity and a foreign body sensation in both her eyes. Decreased visual acuity coupled with periorbital and ocular pain, had began three days prior to the examination. Systemic history revealed extremely high blood pressure treated as primary essential hypertension with multiple episodes of renal colic. On admission, blood pressure was 240/160 mmHg. The best corrected visual acuity in her right eye was 6/60 and in her left eye, 6/36. The intraocular pressure was 18 and 16 mmHg in the right and left eye respectively. Slit lamp examination revealed a mild, bilateral cortical cataract and no evidence of iris neovascularization. Dilated fundus examination of the right eye revealed accentuated retinal arteries and dilated retinal veins (Fig. 1a). Fundus examination of the left eye revealed branch retinal artery occlusion with Hollenhorst plaque and the resulting areas of the retinal hypoperfusion (Fig. 1b). Hemorrhages are located in mid-periphery while retinal arteriovenous communications are presented proximal to the areas of the avascular retina. Fundus autofluorescence demonstrates numerous, small, well-circumscribed areas of hyperautofluorescence in the sensory retina (Figs. 2a, 2b). OCT reveals bilateral optic disc swelling and thinning of the surrounding nerve fiber layer (Fig. 3). There is a bilateral decrease in total thickness and volume of the macula (Fig. 3b). Standard Automated Perimetry, SITA 24.2 protocols, demonstrates arcuate scotoma in the right eye and central scotoma in the left eye. Fluorescein angiography reveals multiple bilateral occlusions of the peripheral arterial branches and numerous arterial collaterals but there is no sign of choroidal neovascularization. The Color Doppler ultrasonography of the ophthalmic artery and the central retinal artery revealed a bilateral decrease in perfusion pressure. A scan and B-scan ultrasonography revealed dense echoes compatible with calcium deposits and orbital shadowing (Sclerochoroidal calcification) (Fig. 4a). Thorough laboratory workup indicates the following: increased serum PTH 420 pg/mL; increased serum calcium 13.2 mg/dL and decreased serum phosphorus 1.2 mg/dL. Computed tomography of the head
demonstrates diffuse calcifications of the brain tissue and multiple old lacunar ischemic lesions. MRI angiography revealed an atherosclerotic plaque in the left internal carotid artery (ACI) with carotid artery stenosis above the plaque. Doppler ultrasound of the neck confirmed significant carotid artery stenosis, as well as an eroded plaque in the left ACI (Fig. 4b). Doppler ultrasound examination of the abdomen and extremities was conducted but no significant stenosis was present. In cooperation with an endocrinologist, the following was confirmed: existence of bilateral parathyroid gland adenoma (Fig. 5) and diagnosis of PH after performing 99mTc-methoxyisobutylisonitrile parathyroid scintigraphy (MIBI scintigraphy). The patient was referred to the Endocrinology Clinic where multiple endocrine neoplasia was ruled out. It was concluded that surgical removal of the parathyroid gland was necessary. After surgery, histopathological examination confirmed diagnosis of parathyroid adenoma.

3. DISCUSSION

The OIS encompasses the ocular signs and symptoms that result from chronic vascular insufficiency. At the time of presentation of OIS, patients may be already diagnosed with some systemic disease. Amaurosis fugax, Hollenhorst plaques, and venous stasis retinopathy demonstrate moderate predictive values in identifying carotid artery occlusive disease [6,7]. A 5-year mortality rate of 40% in patients who have ocular ischemic syndrome reflects the severity of their systemic vascular disease. The main cause of death in these patients is ischemic heart disease, with stroke being the second most common cause of death [8]. Early diagnosis of OIS is important because a significant improvement or the cure of the condition will be achieved in most cases through surgical procedures [9]. In clinical studies, association between PTH and vascular stiffness or abnormal endothelial function demonstrates that PH is associated with clinical structural changes in the carotid vasculature and functional changes that reflect increased vascular stiffness. Increased carotid intima-media thickness is an early, clinical predictor of systemic atherosclerosis as well as coronary and cerebrovascular accidents [10-11]. Intima-media thickness was recently found to be markedly increased in patients with PH and high blood calcium level [12]. The main effects of PTH are to increase the concentration of plasma calcium by increasing the release of calcium and phosphate from bone matrix, increasing calcium reabsorption by the kidney, and increasing renal production of 1,25-dihydroxyvitamin D-3, which increases intestinal absorption of calcium. Thus, overproduction of PTH results in elevated levels of plasma calcium. The ocular symptoms of PH are due to the hypercalcemia itself and are not specific to hyperparathyroidism. In our case we trust that very high value of PTH (420 pg/mL, normal range 10 to 55 pg/ml) has a direct influence on atherogenesis via vascular remodeling and vascular calcification in the carotid artery. Our hypothesis is that not only PH but also high PTH may promote arteriosclerosis and thereby the risk of OIS, which may partly be explained by a direct relation of PTH to carotid calcifications in previously, published works [13]. Effect of PTH on the development of atherosclerosis which is supported by an in vitro study that demonstrated a proatherogenic effect of PTH on vascular smooth muscle cells [14]. Besides the bones and the kidneys, PTH affects other organs, and PTH-receptor mRNA has been found in such different locations such as the brain, adrenal gland, bladder, ileum, liver, lung, skeletal and vascular smooth muscle cells [15]. PTH stimulates the vascular smooth muscle cells by binding to the PTH/PTH related Peptide receptor and so increasing the intracellular cAMP-levels while reducing the influx of calcium [16]. This could be correct explanation for the vasodilating properties of PTH found in vitro as well as in vivo [17]. The most commonly encountered systemic diseases are hypertension, diabetes, ischemic heart disease, stroke, and peripheral vascular disease. To a lesser extent, patients manifest OIS as a result of giant cell arteritis. The differential diagnosis includes diabetic retinopathy, moderately advanced central retinal vein occlusion, hyperviscosity syndrome, and autoimmune uveitis. Ophthalmic changes accompanying PH can be very severe and, as in our case, have limited therapeutic options. A significant decrease in visual acuity may be an early sign of PH. Considering calcium homeostasis in the eye is useful in establishing the right diagnosis of PH. The spectrum of ocular changes can be a part of the masquerade syndrome, which makes differential diagnosis extremely important [18]. Long-term follow up studies of PH patients are concluded that the early surgically treatment of parathyroid glands was a very important factor in treating systemic and ocular manifestations of the disease [19,20].
Fig. 1a. Photo fundus of the right eye reveals narrowed retinal arteries and dilated retinal veins

Fig. 1b. Photo fundus of the left eye reveals a branch retinal artery occlusion with Hollenhorst plaque and hemorrhages in the mid-periphery

Figs. 2a and 2b. Fundus autofluorescence demonstrates numerous, small, well-circumscribed areas of hyperautofluorescence in the sensory retina

Fig. 3a. Cross-sectional OCT image showing swollen optic disc in the both eyes
Fig. 3b. OCT reveals a bilateral decrease in total thickness and volume of the macula. The arrows point to intraretinal calcium deposits.

Fig. 4a. B-scan ultrasonography reveals dense echoes compatible with calcium and orbital shadowing (Sclerochoroidal calcification).

Fig. 4b. Doppler ultrasound of the neck confirmed significant stenosis of carotid arteries. Arrow points to eroded plaque in the left ACI.

Fig. 5. MIBI scintigraphy confirmed the existence of active, bilateral, parathyroid gland adenoma.

4. CONCLUSION

For the first time, it was demonstrated through this particular case, that the bilateral OIS is caused by the atherosclerotic disease of the internal carotid artery, associated with PH. OIS should be treated not only by an ophthalmologist but by a multidisciplinary team.

CONSENT

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

ETHICAL APPROVAL

The cases study was approved by the local ethics committee according to the principles of
good clinical practice and with the ethical principles of the Declaration of Helsinki.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES


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