Nonarteritic Anterior Ischemic Optic Neuropathy in a Young Male Patient Taking Sildenafil Citrate

Sildenafil Sitrat Alan Genç Erkek Bir Hastada Nonarteritik Anterior İskemik Optik Nöropati*

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ABSTRACT

Sildenafil (Viagra), Phosphodiesterase 5 (PDE-5) selective inhibitor and partial phosphodiesterase 6 (PDE-6) inhibitor is frequently prescribed for treatment of erectile dysfunction (ED).[1] Instances of nonarteritic ischemic optic neuropathy (NAION) and permanent vision loss following ingestion of PDE-5 selective inhibitor have been reported.[2-4]

Sildenafil has been approved for the treatment of ED since 1998, and more than 150 million prescriptions have been written for more than 27 million men worldwide, many of whom are older, vasculopathic, and at risk for NAION.[5] A few cases of NAION following PDE-5 selective inhibitor intake have been reported with no vasculopathy risk.[5]

Our case was a 35 year old male patient who has been taking this medicine for three years without prescription. The only identifiable risk factor was small optic cup/optic disc ratio. The patient was evaluated clinically by angiography and optic coherence tomography.

Key Words: Sildenafil, nonarteritic anterior ischemic optic neuropathy, small optic cup/optic disc.

ÖZ

Fosfodiesteraz 5 (PDE-5) selektif inhibitörü ve parsiyel fosfodiesteraz 6 (PDE-6) inhibitörü olan Sildenafil (Viagra), erektil disfonksiyonun (ED) tedavisi için sıkça reçete edilmektedir.[1] PDE-5 selektif inhibitör alımını takiben gelişen kalıcı vizyon kaybı ve nonarteritik anterior iskemik optik nöropati (NAAİON) örnekleri daha önceleri rapor edilmiştir.[2-4] Sildenafil 1998'de erektil disfonksiyon tedavisi için onayını almış ve tüm dünyada 27 milyondan fazla erkeğe 150 milyondan fazla reçete edilmiştir. Bu hastaların çoğunluğu NAAİON için risk faktörleri taşıyan yaşlı ve vaskülopatik kişilerdir.[5] Bir kaç olgu sunumunda PDE-5 selektif inhibitör alımını takiben NAAİON gelişen, vaskülopatik risk faktörleri olmayan erkek hastalar yayınlanmıştır. Bu hastalarda tanımlanabilir tek risk faktörünün küçük optik kap/optik disk oranı olduğu gösterilmiştir.[5] Bizim olgumuz ise, üç yıldır reçetesiz bu ilacı kullanmakta olan 35 yaşında erkek bir hastaydı. Tek tanımlanabilir risk faktörü ise küçük optik kap/optik disk oranıydı. Hasta optik koherens tomografi ve anjiografi ile klinik olarak değerlendirildi.

Anahtar Kelimeler: Sildenafil, nonarteritik anterior iskemik optik nöropati, küçük optik kap/optik disk.

INTRODUCTION

PDE-5 inhibitors cause smooth-muscle relaxation in the cavernosal arteries, allowing penile vasodilation and erection in response to sexual stimuli.[6] PDE-5 inhibitors, particularly sildenafil citrate, cause minor visual changes (e.g., increased perception of light, blurred vision and distorted blue-green colour perception) which are transient, dose-related and likely due to cross-inhibition of PDE-6 in photoreceptor outer segments in the retina.[7] Although NAION is the most common acute optic neuropathy in people older than 50 years, it is actually a rare event in the general population, with only between 1500 and 6000 cases reported in the US each year.[8-9] It is characterised by sudden, painless, acute onset often on awakening, rapid progression, unilateral diminished visual acuity, visual field loss, relative afferent pupillary defect or optic disc edema, multiple flame shaped hemorrhages which may be irreversible.[10] Contralateral eye has an increased risk of vision loss.[11]

In this case report, a 35 years old male patient with NAION who has been taking sildenafil citrate without prescription for three years is presented.

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CASE REPORT

The patient was a 35 year old man who admitted to our clinic with a complaint of visual floaters like snow flakes in his right eye. He has been taken 50 mg. Sildenafil Citrate for about 50 times during the last three years, and he took one tablet just 20 hours before his complaint started. The drug was used without prescription. He had no history of systemic disease such as hypertension, hypercholesterolemia, diabetes, cardiovascular diseases, stroke, nocturnal hypotension, sleep apne and smoking. He did not describe any previous ocular complaint.

Best corrected visual acuities (BCVA) were 10/10 in both eyes. Examination of anterior segment was unremarkable in both eyes. There was an afferent pupillary defect in the right eye. There was orthophoria with normal extraocular muscle movements. Applanation Goldmann applanation tonometry disclosed intraocular pressure of 17 mmHg OD and 15 mmHg OS. In the right eye, color vision was defective using Ischiara color plates.

Fundus examination of the right eye revealed papiledema with peripapillary nerve fiber layer hemorrhage (Figure 1a). Fundus examination of the left eye showed a remarkable crowded disc (Figure 1b). Fundus fluorescein angiography of the right eye revealed, in the early phase, blockade because of peripapillary hemorrhage and in the late phase, increased hyperfluorescence inferior to the optic disc (Figure 2a). Fundus fluorescein angiography of the left eye was normal.

Spectral-domain optic coherence tomography (RTVue Model-RT100 Version 2.0 Optovue Inc. Fremont, CA) of the right eye revealed increased peripapillary thickness (RNFL), (Figure 2b). Peripapillary thickness (RNFL) of the left eye was normal.

On the 4 months follow up, he had a scotoma in the temporal visual field, although his complaints were minimal. He has not taken the drug since his complaint started. BCVA were 10/10 in both eyes. In the right eye, defective color vision and relative afferent pupillary defect were still present.

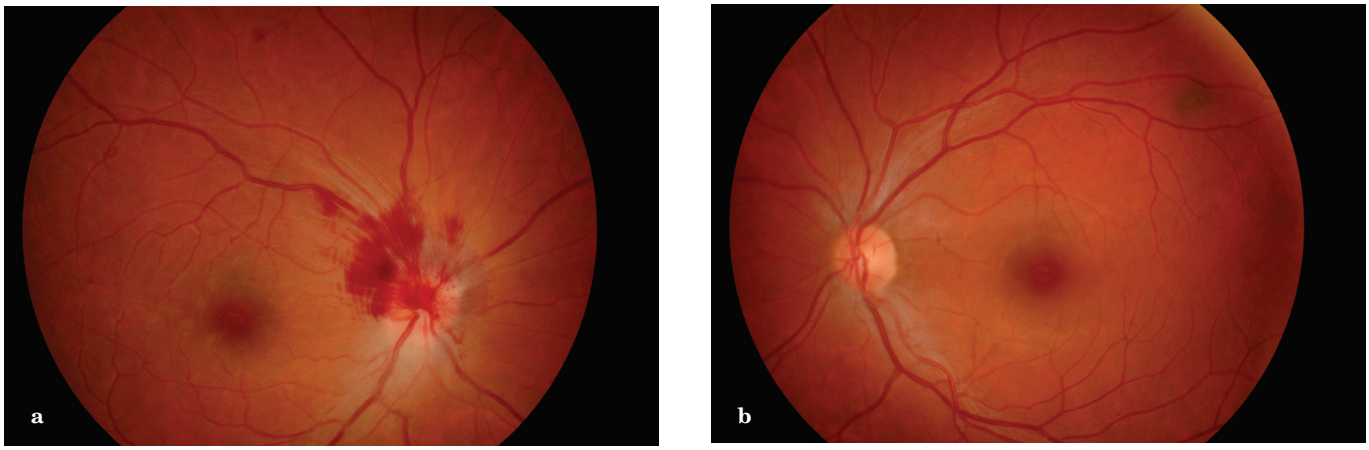

Figure 1a,b: *Fundus examination of the right eye revealed papilledema with peripapillary nerve fiber layer hemorrhage (a). Fundus examination of the left eye showed a remarkable crowded disc (b).*

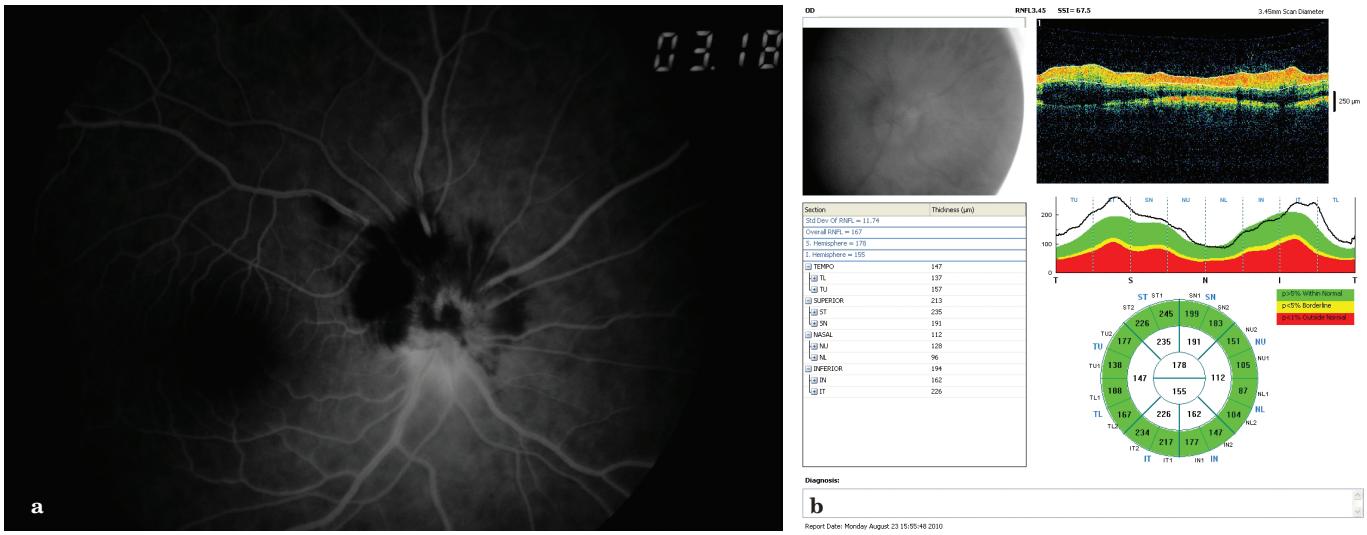

Figure 2a,b: *Fundus flourescein angiography of the right eye revealed blockade because of peripapillary hemorrhage and increased hyperfluorescence inferior of optic disc (a). Optic coherence tomography of the right eye revealed increased peripapillary thickness (RNFL) (b).*

Figure 3a,b: *After 4 months, fundus examination of the right eye: papilledema and peripapillary nerve fiber layer hemorrhage disappeared but optic disc was pale and crowded. (a).After 4 months, peripapillary thickness of the right eye showed significant thinning. (b).*

On fundus examination of the right eye revealed papilledema and peripapillary nerve fiber layer hemorrhage had disappeared but optic disc was pale and crowded (Figure 3a). Peripapillary thickness of the right eye showed significant thinning (Figure 3b).

The patient was advised to avoid taking this drug again because of its serious adverse effects and the increased risk of complications for his fellow eye.

This was an unusual case because the patient was young and he was using sildenafil citrate without prescription and the only identifiable risk factor was small optic cup/optic disc ratio for NAION.

DISCUSSION

Although a definitive cause has not been determined, NAION is thought to occur following an idiopathic ischemic event involving the short posterior ciliary arteries that supply blood to the most anterior part of the optic nerve.[12] Structural factors have also been implicated in the pathogenesis of NAION. It is believed that optic discs with small physiologic cups are more common in patients with NAION.[12,13] Crowding of the nerve fibers through a small scleral canal may make these optic nerves more susceptible to damage from ischemia. Burde[14] labeled the typical disc seen in NAION as a “disc at risk”, which he characterized as one having a small physiologic cup, elevation of the disc margins by a thick nerve fiber layer, anomalies of blood vessel branching, and the appearance of a crowded and small optic nerve head.

In addition to a crowded disc, other established risk factors for NAION include ages elder than 50 years and white race (an estimated 95% of cases occur in the latter group).[15]

Hypertension and diabetes also predispose to NAION development.[15] Other factors that have been hypothesised to associate with NAION include high cholesterol, arteriosclerosis, stroke, cardiac and intraocular surgery, tobacco use, nocturnal hypotension, blood loss, glaucoma, elevated homocysteine and sleep apnea.[13] The association between NAION and hypertension, high cholesterol and diabetes is stronger in individuals younger than 50 years than in older persons.[13]

PDE-5 selective inhibitor therapy is noted in 19 % of the FDA reports of drug-associated ocular toxicities, which makes it the most commonly reported drug class associated with this toxicity.[16] Patients with vasculopathy who also take antihypertensive medications, including or PDE-5 selective inhibitors may be at increased risk for NAION due to nocturnal hypotension.

The role which sildenafil may play in causing injury to the optic nerve is not known. Sildenafil citrate is a selective phosphodiesterase 5 inhibitor, and its mechanism of action works through the nitric oxide-cyclic GMP pathway. Nitric oxide has been implicated as a possible toxic agent to the optic nerve and to retinal ganglion cells, and has been implicated in the pathogenesis of glaucoma, a more common form of optic neuropathy than NAION. Inhibition of nitric oxide synthetase in an animal model for glaucoma rescued retinal ganglion cells from damage[17] and has been suggested as a means of neuroprotection for the optic nerve. Sildenafil may alter the perfusion of the optic nerve head by way of its influence over the level of nitric oxide. Nitric oxide is a potent vasodilator and its physiologically regulates

blood pressure. This compound may cause vasodilation of blood vessels on the optic nerve head and influence optic nerve perfusion.

Sildenafil citrate may cause episodes of hypotension and was temporally related to the onset of symptoms in this patient. Physicians should counsel patients with crowded optic discs and a history of nonarteritic anterior ischemic optic neuropathy in one eye that the use of sildenafil citrate might increase the risk of ischemic optic neuropathy in the fellow eye.

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