ROSENBERG SCHOOL of OPTOMETRY

Optometric Clinical Practice

Volume 4 | Issue 1

2022

Medication-Induced Oculomotor Dysfunction: a report of two cases

Eric Lee OD
Memphis VA, ericmleeod@hotmail.com

Recommended Citation

Lee E. Medication-Induced Oculomotor Dysfunction: a report of two cases. *Optometric Clinical Practice*. 2022; 4(1):17. doi: 10.37685/uiwlibraries.2575-7717.4.1.1027. https://doi.org/10.37685/uiwlibraries.2575-7717.4.1.1027

Medication-Induced Oculomotor Dysfunction: a report of two cases

Abstract

Background: Consideration of current medications and their interactions as a source of new onset oculomotor dysfunction is imperative for providing good eye care. Medication etiology should be particularly suspected when the symptoms begin with the initiation of a new medication and resolved with discontinuation of the same medication.

Case Reports: Presented are two cases demonstrating that it is prudent to be aware of medications capable of inducing oculomotor dysfunction. Each case reveals instances of acute oculomotor dysfunction after the initiation of a central nervous system affecting medication. Case 1 details a partial pupil sparing third nerve palsy after initiating the anti-anxiety drug, buspirone. Case 2 accounts the addition of zolpidem (Ambien), a sedative, and the subsequent new onset nystagmus and hypertropia.

Conclusion: In each case, no organic etiology was found, and the oculomotor dysfunction resolved following discontinuation of the recently added CNS affecting medication. Specific drug interactions are also considered as contributing factors to the oculomotor dysfunction in both cases.

Keywords

buspirone, nystagmus, oculomotor dysfunction, third nerve palsy, zolpidem (Ambien)

Background

New onset diplopia and nystagmus are sure to grab the attention of patients and providers alike. Havoc is wreaked upon the patient's visual status and the provider realizes the etiology may be sinister and challenging to elucidate. Context is king when determining the urgency of the case and what steps are needed to uncover the cause of the oculomotor dysfunction. Patient medical history must be thoroughly investigated, including cardiovascular disease (i.e. diabetes, hypertension, aneurysms and cerebral vascular accidents), primary and metastatic cancer, thyroid disease, infections, neuropathies (i.e. Multiple Sclerosis and Myasthenia Gravis) and inflammatory disease (i.e. giant cell arteritis)[1,2,3,4]. Relevant patient ocular history may include recent ocular trauma (i.e. blow-out fracture), past strabismus surgery or an established need for prismatic spectacle correction[1,2,3]. The clinician must consider simultaneously occurring associated factors, such as headache, eyelid ptosis, pupil dysfunction, optic neuropathy and other neurological signs (i.e. unilateral weakness or numbness, slurred speech, dizziness, nausea and altered mental status) as clues to organic etiologies[1,2,3]. Additionally, as demonstrated in the presented cases, side effects of current medications and/or medication interactions should be considered when presented with a case of new onset oculomotor dysfunction, especially when the onset of symptoms coincides with the initiation of a new drug [4,5,6].

CASE 1

A 65-year-old black male presented with a chief complaint of a constant inability to open his left eye with a sudden onset three days prior. No injury, pain, headache, double vision, nor blurry vision of the right eye were reported. He stated compliance with all prescribed medications and denied illicit drug use. Patient medical history was positive for insulin dependent diabetes (7 years duration), hypertension, hyperlipidemia, stroke, and anxiety. Patient ocular history was essentially non-contributory, being negative for past ocular surgeries, major injuries and ocular pathology. The patient had a positive history of cigarette smoking (discontinued 1 year previously) and recreational drug use (cocaine and marijuana, both discontinued multiple years earlier). The patient was unsure of his last blood glucose level, but his last HbA1c was 6.3% a month prior. Blood pressure measured 180/100 mmHg at his primary care provider's exam three weeks before presenting for this vision examination. The primary care provider's plan for addressing the high blood pressure was to continue the hydralazine and change the lisinopril to lisinopril/hydrochlorothiazide. Also, of note, the primary care provider added buspirone to address the patient's increased anxiety.

The corrected distance acuities were 20/20- and 20/25+ in the right and left eye (upon manually lifting the left upper eyelid) respectively. These acuities were stable compared to his last eye exam one month prior. There was a complete ptosis of the left upper eye lid. Confrontation visual fields were normal for each eye, and no pupillary defect was observed. The patient did, however, have restricted ocular movement to superior gaze of the left eye.

The patient's clinic picture at this visit was consistent with a painless, left, incomplete, isolated, pupil sparing, superior division ocular motor (CNIII) nerve palsy. In the context of vascular disease history, no reported headache, and no pupil involvement, a one-week follow-up visit with no additional ancillary testing is often appropriate. The exception to this general follow-up period is a superior division CNIII palsy, as this specific presentation is often the result of a space-occupying lesion[3]. Therefore, even though no pupil abnormalities were evident at this initial encounter, a head CT scan was ordered. Compliance with all medications was stressed, and the patient was instructed to contact the clinic with any new or worsening of symptoms. The examination findings were shared with the primary care provider with the suggestion that the patient discontinue his buspirone since the symptoms corresponded to the initiation of this drug.

The patient returned 11 days later having discontinued the buspirone, with no change in symptoms or signs except that the left pupil now measured 1.5 mm larger than the right pupil. Involvement of the left pupil was concerning; nevertheless, the head CT results revealed no compressive lesions nor evidence of ischemia (Figure 1). Again, the patient was instructed on medication compliance and to contact the clinic with worsening of symptoms. Six weeks later the patient returned to clinic with both resolution of his left upper eyelid ptosis and restoration of superior gaze of the left eye. Mild pupil asymmetry remained.

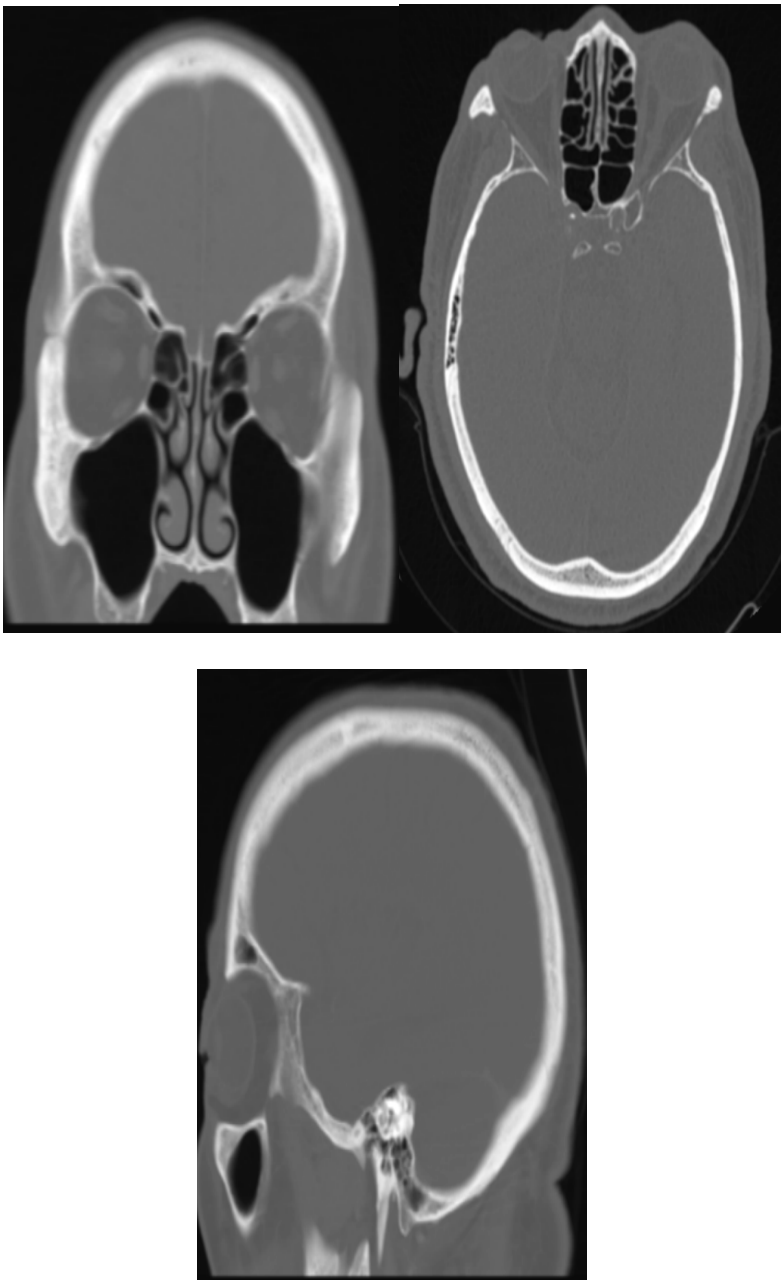

Figure 1 Case 1 Head CT. Coronal, Transverse and Sagittal, respectively. Note no lesions of the left superior orbit nor the cavernous sinus.

Discussion: Case 1

Medications affecting central nervous system activity, like buspirone, have been reported to cause diplopia (Tables 1 and 2)[5]. Given the correlation of initiating buspirone and the onset of a superior division ocular motor nerve palsy, followed

by its resolution after discontinuing the buspirone, attributing the cause of the transient neuropathy to buspirone use is reasonable. Furthermore, ischemia is the most common cause of a CNIII palsy[3]. Buspirone can increase the blood pressure lowering effects of blood pressure medications[7]. Since the patient was already taking hydralazine (a vasodilator) and his lisinopril (an ACE inhibitor) was changed to lisinopril-hydrochlorothiazide (a diuretic), the addition of buspirone may have caused a rapid drop in blood pressure, resulting in ischemia as a contributing causative factor of the partial third nerve palsy.[7]

Case 2

A 62-year-old white male presented to the emergency room complaining of constant binocular diplopia, with associated diffuse headache, beginning earlier that morning. The patient denied any other neurological symptoms or recent injury. The patient's medical history consisted of hypertension, hyperlipidemia, and generalized anxiety disorder. His blood pressure was measured as 170/93 mmHg in the ER. An in-patient head CT did not reveal evidence of cerebral vascular accident nor a space occupying lesion (Figure 2). Neurology, consulted from the ER, decided to admit the patient for further investigation of a stroke based on his risk factors. An in-patient neurology examination revealed the following findings: 20/25 corrected vision OD-OS, right abduction deficit, bilateral direction changing horizontal and rotary nystagmus in primary and lateral gazes with a vertical nystagmus in down gaze and no reported null point were evident. At this point, neurology was still concerned about a cerebral vascular accident (CVA) as the etiology of the CN VI palsy. Therefore, daily Aspirin 325mg was prescribed, and a brain MRI and head-neck MRA were ordered. Both the brain MRI and head-neck MRA were negative for CVA and any compressive lesion (Figure 3, 4).

This individual was an established patient at the optometry clinic. So, three days after he was discharged from the hospital, the patient presented to the optometry clinic, as a self-referral, with recalcitrant symptoms of nystagmus and binocular double vision. The patient's last vision examination was seven months prior, which reveal no ocular motility abnormalities. He stated compliance with the following medications: amlodipine, aspirin, atorvastatin, hydroxyzine, melatonin (natural hormone important for maintaining the biological clock; used off-label to treat insomnia)[7], mirtazapine, and propranolol. The patient believed his double vision coincided with the initiation of zolpidem (Ambien) to treat his insomnia. Zolpidem was not included in his active medication list, nor was zolpidem mentioned in the ER/neurology note. Visual acuities were 20/20 OD-OS, confrontation visual fields were full OD-OS, no pupil abnormalities were noted OU, and extraocular motility testing revealed bilateral constant right jerk horizontal and rotational nystagmus

that was worse in right and downward gaze, and a constant right hypertropia (vertical diplopia was neutralized and single vision was reported with 22 prism diopters of base-down prism OD in a trial frame). Intra-ocular pressures were normal OU, biomicroscopy of the anterior segment and dilated fundus evaluation were unremarkable OU (including no evident optic neuropathy), and H.R.R. color vision was normal OD-OS. Static threshold visual fields revealed no evidence of neurological defects OD-OS (Figure 5).

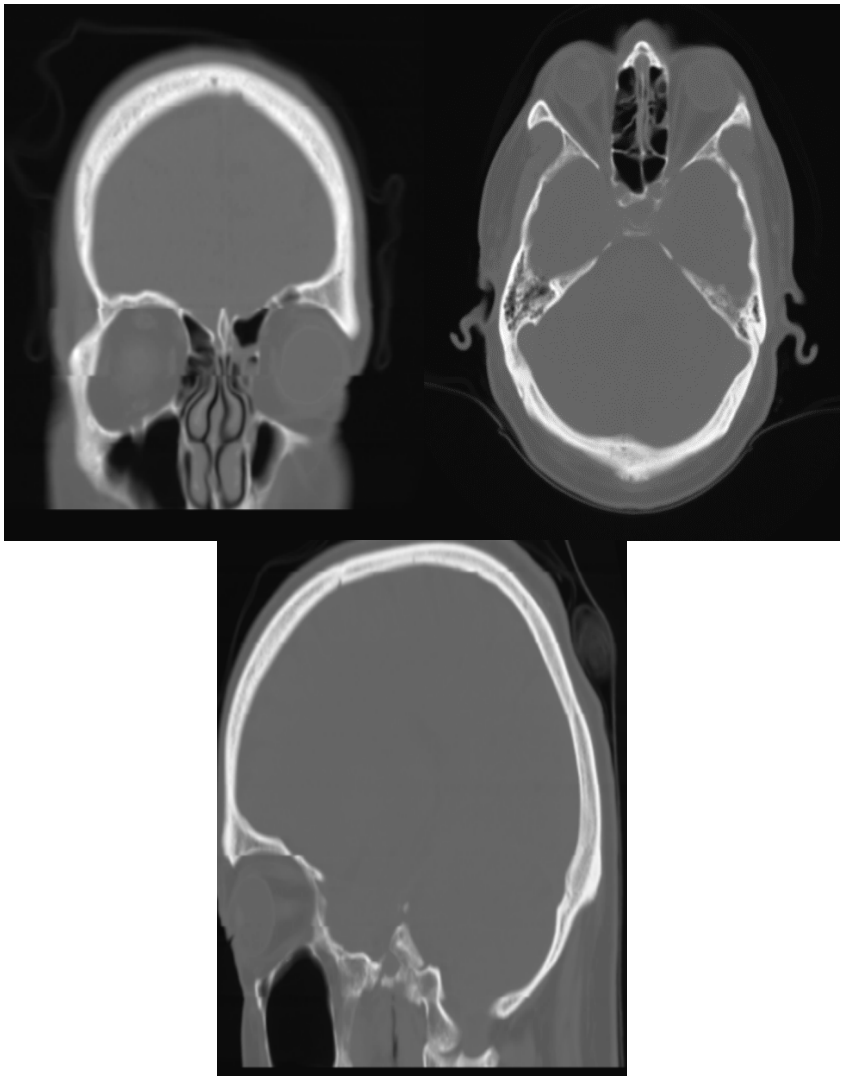

Figure 2 Case 2 Head CT; Coronal, Transverse and Sagittal, respectively. Note no lesions of right lateral orbit nor cavernous sinus.

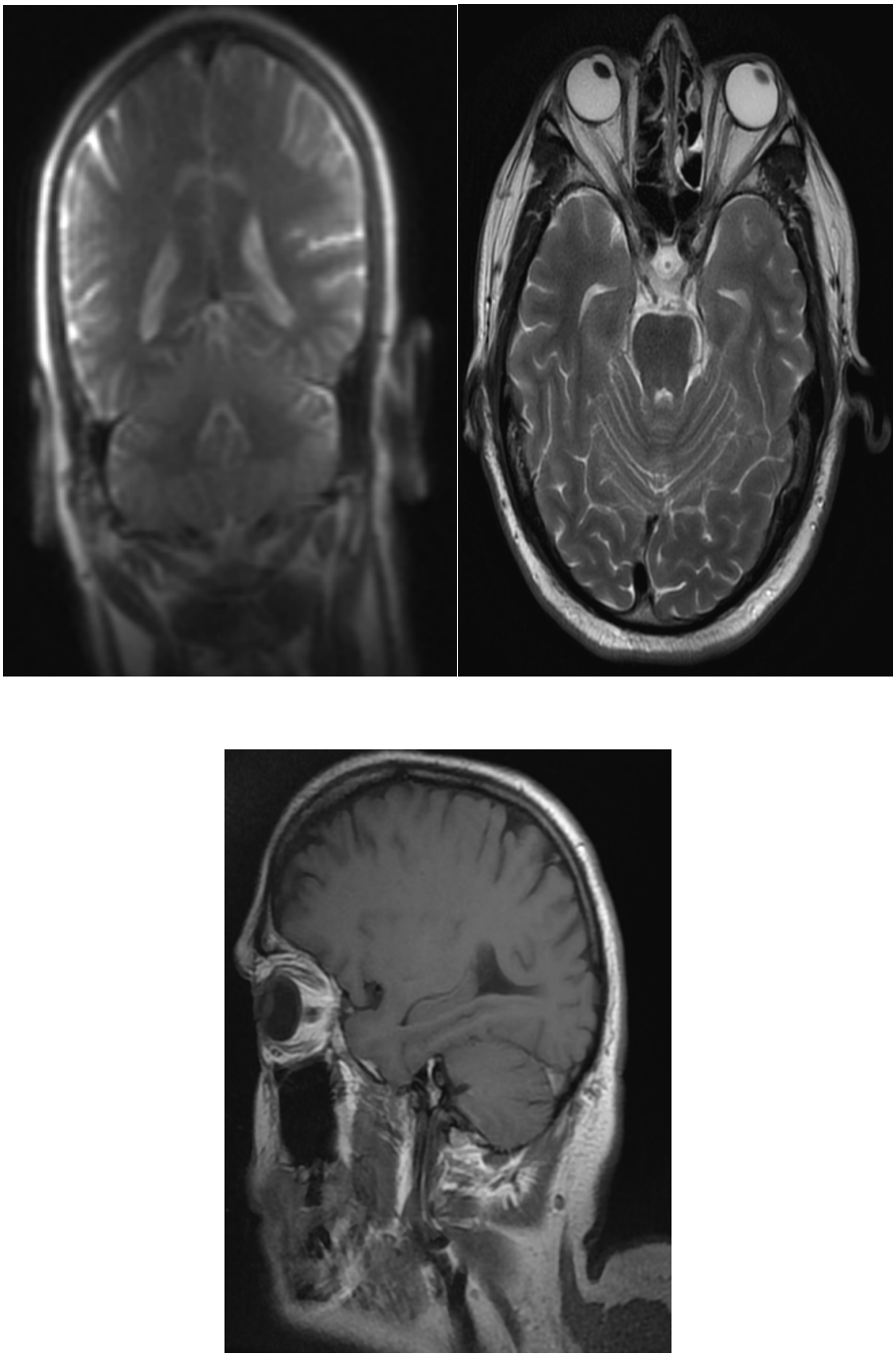

Figure 3 Case 2 Brain MRI; Coronal, Transverse and Sagittal, respectively. Note, absence of lesions of the right lateral orbit nor cavernous sinus.

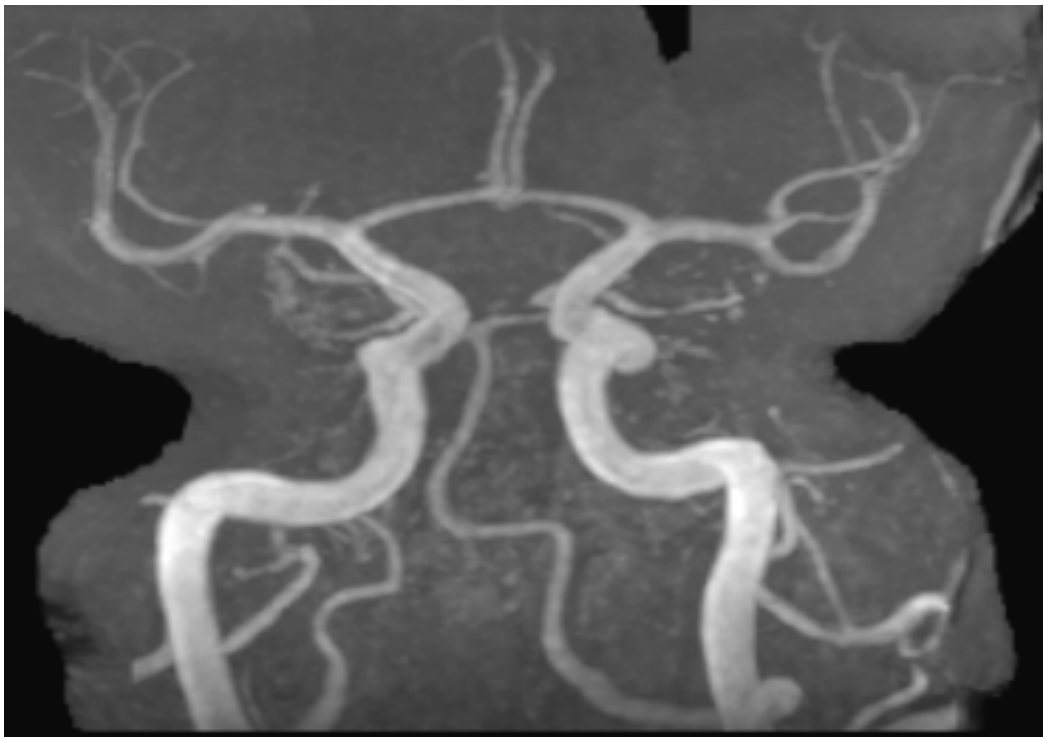

Figure 4 Case 2 Head-neck MRA. Note no lesions of the cavernous sinus nor circle of Willis.

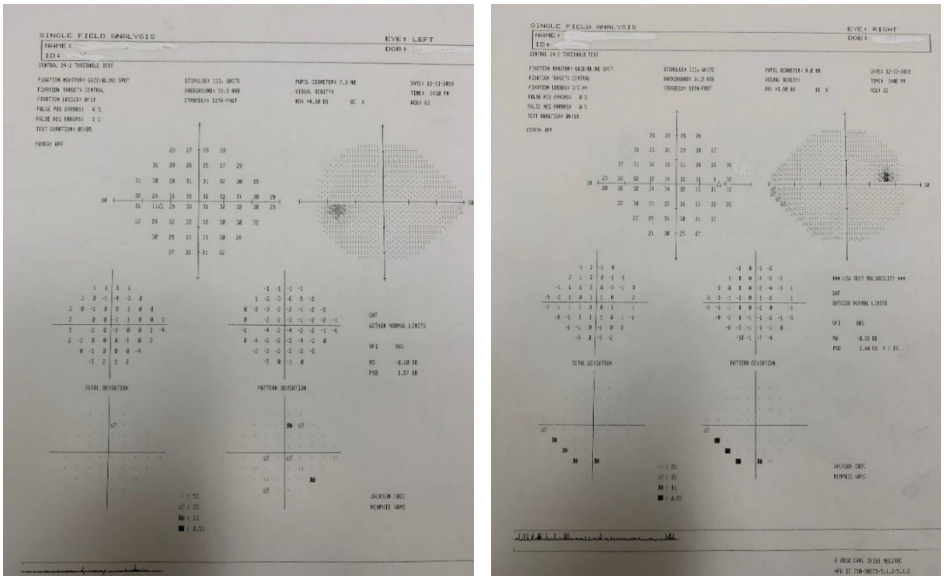

Figure 5 Case 2 visual fields; left and right, respectively.

Since the ocular alignment differed from the neurology assessment to this vision exam, Myasthenia Gravis was a possible diagnosis. However, the patient was adamant that his diplopia coincided with his initiating zolpidem. So, considering the lack of evidence suggesting a cerebral infarction or a space occupying lesion and with the absence of other neurological abnormalities (except for an associated headache), the patient was treated with 25 prism diopter base-down Fresnel prism to the right habitual spectacle lens. The neurologist was informed of the vision examination results and provided with a copy of the visual field results. Discontinuation of zolpidem was recommended. The patient was instructed to contact the clinic if changes to neurological symptoms, vision or ocular comfort occurred. Three weeks later, the patient returned for follow-up visit reporting compliance with all medications, including discontinuation of zolpidem. Corrected visual acuities measured 20/20 OD-OS, pupil testing remained unremarkable OD-OS, no restriction of extraocular motility was noted, and confrontation visual fields were still full OD-OS. While the bilateral nystagmus was still present (for which the patient was asymptomatic), the right hypertropia and double vision were resolved, such that the patient presented without the Fresnel prism on his spectacles.

Discussion: Case 2

Sedatives are one of the most common causes of nystagmus[3]. This patient was taking multiple medications that affect CNS activity (Tables 1, and 2). By excluding possible organic causes of the acute oculomotor dysfunction, it is reasonable to surmise this patient reached his tolerance limit for medications affecting the CNS activity.

DRUG CLASS	DRUG EXAMPLES
benzodiazepines	alprazolam (Xanax) clonazepam (KlonoPIN) diazepam (Valium) escitalopram (Lexapro) lorazepam (Ativan)
selective serotonin reuptake inhibitors	duloxetine (Cymbalta) paroxetine (Paxil) venlafaxine (Effexor) sertraline (Zoloft)
antidepressants	mirtazapine trazodone

DRUG CLASS	DRUG EXAMPLES
miscellaneous	buspirone/anti-anxiety gabapentin (Neurontin)/anti-epileptic hydroxyzine/antihistamine propranolol/beta-blocker

Table 1 Medications used to treat anxiety.[7]

DRUG CLASS	DRUG EXAMPLES
Antidepressants	amitriptyline
Antihistamines	diphenhydramine
Benzodiazepines	temazepam (Restoril)
Sedatives	eszopiclone (Lanesta), zolpidem (Ambien)

Table 2 Medications used to treat insomnia[7]. Notice the overlap with drugs used to treat anxiety.

Conclusion

Diplopia has been reported to occur following the initiation of central nervous system affecting drugs with the diplopia resolving once the new medication was discontinued[1,6]. Hence, obtaining an adequate patient medical and ocular history when confronted with new onset diplopia or nystagmus is imperative for good clinical care. As exhibited by the presented cases, the potential for drug side effects and interactions to be the etiology of a new onset oculomotor dysfunction may be suspected, particularly with medications that affect blood pressure and central nervous system functions (Tables 1 and 2).

References

1. Alves M, Miranda A, Narciso MR, Mieiro L, Fonseca T. Diplopia: a diagnostic challenge with common and rare etiologies. *Am J Case Rep*. 2015;16:220-223. doi: 10.12659/AJCR.893134
2. Bowling B. *Kanski's Clinical Ophthalmology: A Systematic Approach*. 8th ed. Elsevier; 2016:823-832.
3. Liu GT, Volpe NJ, Galetta SL. *Neuro-Ophthalmology: Diagnosis and Management*. 1st ed. W.B. Saunders Company; 2001.
4. Martin TJ, Corbett JJ. *Neuro-Ophthalmology. Krachmer JH, ed. The Requisites in Ophthalmology*. Mosby; 2000.

5. Bartlett JD, Jaanus SD. *Clinical Ocular Pharmacology*. 4th ed. Butterworth-Heinmann; 2001:918-938.
6. Mowla A, Ghanizadeh A, Ashkani H. Diplopia with citalopram: a case report. *J Clin Psychopharmacol*. 2005;25(6):623-624. doi: 10.1097/01.jcp.0000186900.41744.19
7. Drugs.com. https://www.drugs.com/