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Case report

Colored floaters as a manifestation of digoxin toxicity

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ABSTRACT

Purpose: Since its report in one patient more than 70 years ago, digitalis-induced colored muscae volitantes have not surfaced again in the literature. We report here a case of digoxin induced colored floaters.

Observations: An 89-year-old man on 0.25 mg digoxin daily developed visual hallucinations and colored floaters. He had floaters in the past but now they were in various colors including yellow, green, blue and red, though predominantly in yellow. These "weirdly" shaped little particles wiggled around as if in a viscous solution and casted shadows in his vision. He also saw geometric shapes, spirals, and cross hatch patterns of various colors that moved and undulated, especially on wallpaper. Ophthalmic examination revealed reduced visual acuity, poor color vision especially in his left eye, along with central depression on Amsler grid and Humphrey visual field in his left eye. Discontinuation of digoxin resulted in complete resolution of his visual symptoms. On subsequent ophthalmic examination, the patient's visual acuity, field testing and color vision improved and he had normal Amsler grid test results.

Conclusions and importance: Colored floaters may occur in patients taking cardiac glycosides but this association has not been explored. Unlike optical illusions and visual hallucinations, floaters are entoptic phenomena casting a physical shadow upon the retina and their coloring likely arise from retinal dysfunction. Colored floaters may be a more common visual phenomenon than realized.

1. Introduction

Since its isolation from the foxglove plant *Digitalis lanata* in the early 20th century, digoxin has been used for the same purposes as other cardiac glycosides to treat various heart conditions and is known to share similar visual disturbances to its pharmacologically related relatives.[1] Nearly 80% of patients receiving digoxin developed color vision deficiencies, even at therapeutic levels, though only some of the patients reported the color disturbances.[2] The best-known digoxin-induced ocular manifestations are yellow and green chromatopsias.[3] Additionally, patients may experience photopsias, snowy vision, visual hallucinations, bilateral central and paracentral scotomas and decreased visual acuity.[1,4] Patients can have abnormal electroretinograms which return to normal after stopping digoxin, suggesting the retina as the site of toxicity. Among the myriad visual symptoms induced by the cardiac glycosides family, there has only been one reported case of colored muscae volitantes, Latin for "flying flies." In 1944, Frank D. Carroll published in the *American Journal of Ophthalmology* the case of a physician patient whose floaters became colored, notably to red and green, following large doses of digitalis.[5] After a hiatus of more than 70 years, we report here the second case of cardiac glycosides induced colored floaters.

2. Case report

An 89-year-old man, with glaucoma, was referred for evaluation of headache, tired eyes with reading, floaters, which had turned into geometric patterns with a yellow tint for the past three months. He saw geometric patterns and spirals that were gray, white, green, blue, red, and yellow which happened on their own. They appeared constantly as if they were moving and undulating, especially on wallpaper. Sometimes he saw cross hatch patterns. There were concentric swirls with a fingerprint lasting minutes. He described little particles in "weird" shapes inside the eye that flitted around and casted shadows in his vision. They flew, wiggled, and floated around as if in a viscous solution. He had floaters in the past but now they were in "technicolor" including yellow, green, blue and red, though predominantly in yellow. He also complained of tiredness with reading, as though he were reading through a "light screen," and worsening headache at the top of his head and the left temple. The headache had been present for 10 years, can last hours, with a feeling of pressure at the top of his head, for which he takes Advil rarely or Tylenol once a week. He was a retired

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realtor with a history of transurethral resection of his prostate, atrial fibrillation for which he took digoxin 0.25 mg qd for twenty years, primary open-angle glaucoma (POAG) for 10 years on travoprost, 1 drop OU qd, and a cataract extraction only from the left eye. His other medications include rivaroxaban 15 mg qd, lisinopril 20 mg qd, atorvastatin 20 mg qd, mirabegron 50 mg qd, acetaminophen 325 mg prn, vitamins, and a probiotic.

On examination, his best corrected visual acuity was 20/25 OD and 20/40 OS. On AO-HRR color plates, he identified 3 of 6 test plates OD, and 2.5 of 3 controls, 0 of 6 test plates OS. His right pupil was 3 mm, his left was 4 mm, likely from post-surgical anisocoria. There was no dilation lag or relative afferent pupillary defect. In the left eye, he had some central depression on the Amsler grid along with central depression on Humphrey visual field. Sensation was intact in V1, V2, and V3, and the muscles of facial expression were intact. His palpebral fissures were 8 mm OU. There was injection of the conjunctiva medially in both eyes. His corneas were clear, and his chambers were quiet and deep. There was a posterior chamber intraocular lens on the left and nuclear sclerotic cataract on the right. Intraocular pressure (IOP) were 13 mm Hg OU. He was orthophoric at distance and near. Funduscopic examination revealed posterior vitreous detachment in both eyes. He had advanced glaucomatous cupping and peripapillary conus in both eyes. There was a disturbance of the retinal pigment epithelium with yellowing around the disc on the right and some splotchy pigmentation in the posterior pole on the left.

His visual symptoms raised concern for digoxin toxicity. He was advised to discontinue his digoxin in coordination with his internist. A serum digoxin level yielded a mildly supra-therapeutic concentration of 1.4 ng/ml (reference range 0.5–1.2 ng/ml). On the day following digoxin discontinuation, the patient reported “90% improvement” in his visual hallucinations and colored floaters.

Twelve days later, on his next office visit, the patient reported the complete resolution of his visual symptoms. In the week following digoxin discontinuation, he described a “miraculous recovery,” during which he had no visual disturbances, no colored floaters, and no headaches. However, his chronic headache recurred with labs notable for normal erythrocyte sedimentation rate and C-reactive protein. On examination, his visual acuity improved to 20/20 OD, 20/40 OS. He saw 3.5 of 6 test plates OD, and 2.5 of 3 controls, 0.5 of 6 test plates OS. Amsler grid testing was within normal limits OU. His IOP was elevated to 21 mm Hg OU. There was improvement in the visual fields of both eyes. His ophthalmic examination was otherwise unchanged. Neurologic consultant diagnosed him with tension headache.

On the following visit at five weeks from date of presentation, the patient denied any recurrence of his visual phenomena since his last visit. He continued to have the occasional floaters but they were no longer colored and had decreased in number and occurrence. The patient noted that his tension headaches were decreased in frequency and intensity and he attributed this “improvement” to digoxin discontinuation. His visual acuity improved to 20/20 OD and 20/25 OS. His IOP was 15 mm Hg OD but elevated at 26 mm Hg OS. His ophthalmic examination was otherwise unchanged. He was closely followed by his glaucoma specialist.

To confirm that the colored floaters were indeed digoxin-induced, the patient, in consultation with his internist, agreed to a two-week trial on digoxin 0.25 mg qd. However, this trial was aborted after three days. The patient called the office stating that his headaches exacerbated while on digoxin. He could not tolerate the headache so he stopped the digoxin.

3. Discussion

In 1944, Carroll described six patients with digitalis induced visual disturbances, including snowy vision, flashing and flickering lights, flowerlike figures, green and yellow vision, and colored floaters. Unlike the other digitalis induced visual symptoms, colored floaters had a physical basis within the eye itself. The colored floaters were described in one patient who was a physician. He had floaters in the past and after taking digitalis, his floating specks became colored, chiefly to red and green spots.[5] Despite these varied digitalis-induced symptoms, Carroll had negative findings on all six ophthalmic examinations. On visual hallucinations, Carroll postulated that digitalis impaired the central nervous system, stimulating the cerebrum to cause visual hallucinations and colored vision.

In recent decades, various forms of digitalis-induced optical illusions and visual hallucinations were described in case reports and series. In 1979, Volpe and Soave reported three patients with formed visual hallucinations of animals and household objects, as sole symptoms of digitalis intoxication.[6] In 1983, Clossom reported a case of an 84-year-old woman who saw blue, green, and yellow veils and pleasant visions of trees, pigs, and lamps.[7] These four patients were concomitantly on some form of diuretics, such as furosemide, hydrochlorothiazide, and triamterene. The diuretics contributed to intracellular depletion of potassium and predisposed the patients to neurotoxicity.[8] Lyon and Degraff suggested that the digitalis induced neurotoxicity occurred secondary to the membrane effect on intracellular potassium depletion in neurons.[8]

Various visual disturbances were known to occur at therapeutic and even sub-therapeutic doses of digitalis. Wolin reported a patient who had shimmering lights in the field of vision of both eyes that were worse when in sunlight and another patient who had generalized visual field depression in both eyes, both of whom had digoxin at therapeutic blood levels.[9] Butler et al. described six patients at therapeutic or sub-therapeutic levels of digitalis whose ocular symptoms included photopsias characterized by numerous points of light in the peripheral visual fields and exacerbated by external illumination such as upon awakening or outdoors in daylight.[3] The luminance dependence of digitalis-induced symptoms was consistent with digitalis's effect on retinal photoreceptors.[3,10–12]

Many clinical studies proposed Na-K-ATPase inhibition at the cellular level in the retina as the source for visual disturbances.[12–14] Retinal photoreceptor cells, glial Muller cells, and retinal pigment epithelial cells all contained digitalis-sensitive Na-K-ATPase isoforms whose inhibition would alter the electrochemical gradients and properties of retinal cells.[3,14,15] In normal people experimentally given standard doses of digitalis for two or four weeks, a reversible elevation of the dark adaptation threshold was found.[12] In addition, digitalis had a propensity to cone rather than rod impairment.[1,13]

Advanced age increased risk to digitalis induced adverse effects. Butler et al. suggested that the increased susceptibility to visual disturbances was conferred by age-related loss of photoreceptors and retinal pigment epithelial cells, decreased functional capacity of Na-K-ATPase pumps, and increased expression of digitalis-sensitive Na-K-ATPase isoforms.[3,16,17]

Since Carroll, colored floaters associated with cardiac glycosides ceased in the literature. Our case stands in contrast to other digoxin-induced visual disturbances in that floaters are entoptic phenomena. The debris inside the vitreous are made visible due to the physical shadows they cast upon the retina as they float inside the eye. Floaters are commonly age-related and secondary to natural changes in the vitreous. The patient's advanced age likely predisposed him to floaters and digoxin-induced visual disturbances.

The vitreous debris floating around in his eye casted shadows on his retina, contributing to local adaptation of his photoreceptors. As the floaters moved around, parts of the retina were subject to varying levels of light and darkness, and this patient perceived the floaters to be colored possibly due to the dysfunction of retinal photoreceptors. Similar to digitalis-induced photopsias that are worse early in the morning[3] or chromatopsias that increase in proportion to the intensity of illumination,[12] colored floaters may have resulted from the varying levels of light and shadows on dysfunctional retinal photoreceptors intoxicated by digoxin.

4. Conclusion

Digoxin-induced colored floaters may be overlooked amidst other visual disturbances. Colored floaters are rarely explored as a symptom of digoxin toxicity and may be a more common visual phenomenon in digitalized patients than realized.

Patient consent

Consent to publish the case report was not obtained. This report does not contain any personal information that could identify the patient.

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Conflicts of interest

The following authors have no financial disclosures: LS, LDS, JGO.

Authorship

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