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CASE REPORT

Bilateral multiple exudative retinal detachments and macular edema in a patient diagnosed with synthetic cannabinoid (Bonzai) intoxication

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Abstract
Purpose To report the first case of a patient with bilateral multiple exudative retinal detachments and macular edema after smoking Bonzai.
Methods A 17-year-old girl presented with a complaint of a sudden onset of reduced vision in both eyes. She was admitted to the emergency service 3 days ago with the symptoms of hallucination and convulsion and diagnosed with synthetic cannabinoid intoxication.
Results After consultation with an internal medicine specialist, intravenous fluid treatment was initiated. Laboratory findings resolved rapidly and recovery of fundus findings was achieved at 6 months of follow-up.
Conclusions Synthetic cannabinoid abuse has been increasing in young populations in recent years and has become an important health concern. It is important for health providers to be aware of ocular signs and symptoms of intoxication.

Keywords Bonzai · Exudative retinal detachment · Intoxication · Macular edema · Synthetic cannabinoids

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Introduction

The use of synthetic cannabinoids (SCs) has been increasing among teens and young adults and has become a critical phenomenon both worldwide and in Turkey. These synthetic drugs are known by different names in different countries such as 'K2,' 'Spice,' 'Aroma,' and 'Dream' and marketed as 'Bonzai' in Turkey [1]. Synthetic cannabinoids are the compounds which mimic the effects of cannabis and have various types of chemical structures. They exert their effects on cannabinoid receptors, CB1 and CB2. These receptors are mainly found in the central nervous system, multiple lymphoid organs, and immune cells and responsible for the psychotropic and adverse effects [2]. Clinical presentations following the use of SCs have included agitation, anxiety, emesis, hallucinations, psychosis, tachycardia, hypertension, myocardial infarction, acute kidney failure, convulsion, and also death [3, 4]. There are also some reports about the blurred vision following the use of these drugs; however, this is the first case of bilateral multiple exudative retinal detachments and macular edema in a patient who was admitted to the emergency service 3 days ago with the symptoms of hallucination and convulsion and diagnosed with synthetic cannabinoid intoxication.

Case report

A 17-year-old girl was admitted to the Ophthalmology Department of Bagcilar Training and Research Hospital, Istanbul, Turkey, with a complaint of a sudden onset of reduced vision in both eyes. Her medical history revealed that she was admitted to the emergency service 3 days ago with a complaint of headache, dizziness, hallucination, and convulsion soon after smoking 'Bonzai.' She also reported that she did not use any other drugs or medications and smoked 'Bonzai' for a few years.

At the initial evaluation, the best-corrected visual acuity (BCVA) was 3/10 on the right and 2/10 on the left eye. Slit-lamp examination findings were normal in both eyes. Fundus examination revealed bilateral multiple exudative retinal detachments and macular edema (Fig. 1). Fundus fluorescein angiography showed multiple hyperfluorescent dots around the optic disk and macula in the early phase and, with the pooling of fluid within the subretinal and intraretinal space, it showed multifocal placoid areas of hyperfluorescence during the late phase (Fig. 2). Spectral-domain optical coherence tomography (SD-OCT) showed bilateral macular thickening and macular edema with multiple cystic spaces, associated with neurosensorial retinal detachment (Fig. 3).

Review of the emergency records revealed that the patient's blood pressure was 195/100 mmHg at the time of arrival and laboratory test results including complete blood count and chemistries were normal. The patient did not undergo any intervention and was discharged after a short period of observation.

Based on the prior history, laboratory analysis was repeated. Serological tests were also performed in order to exclude the infectious disorders. The remarkable results were as follows: creatinine kinase (CK): 8515 U/I (normal 20–170 U/I), creatinine kinase MB (CK-MB): 65 U/I (normal < 25 U/I), and lactate dehydrogenase (LDH): 977 U/I (normal 120–130 U/I). After consultation with an internal medicine specialist, intravenous fluid treatment (% 5 dextrose/% 0.9 NaCl, 3 * 1, for 2 days) was initiated and laboratory findings resolved rapidly. For the ocular pathology, the patient was scheduled for follow-up without treatment.

The vision did not change within the first 3 days; however, thereafter, her vision started to improve and fundoscopy showed resolving retinal detachment with the absorption of retinal fluid (Fig. 4). Three weeks after, the BCVA was 5/10 in both eyes, and complete improvement in vision and recovery of SD-OCT findings were achieved at 6 months of follow-up (Fig. 5).

Discussion

Synthetic cannabinoids are much more potent than tetrahydrocannabinol (THC), which is the main active ingredient of natural cannabis (marijuana), and have a higher affinity than THC for the cannabinoid receptors [5]. The effect size, the incidence of adverse effects, and severity are higher than THC, which is why it causes more convulsions, anxiety, aggression, muscle rigidity, and confusion [3].

Although convulsions due to use of SCs have been described previously, it still appears to be exceptionally unusual. Although naturally occurring cannabinoids in cannabis such as cannabinol and cannabidiol have been shown in mouse models to be

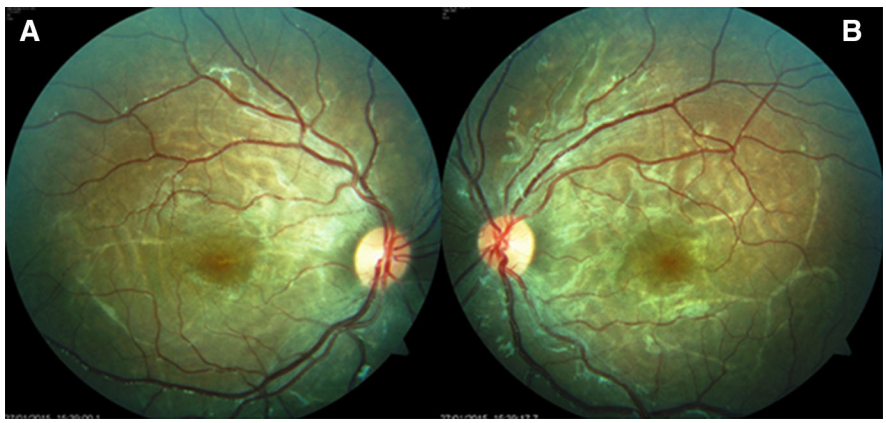

Fig. 1 Fundus images showing multiple exudative retinal detachments and macular edema in both right (**a**) and left (**b**) eyes

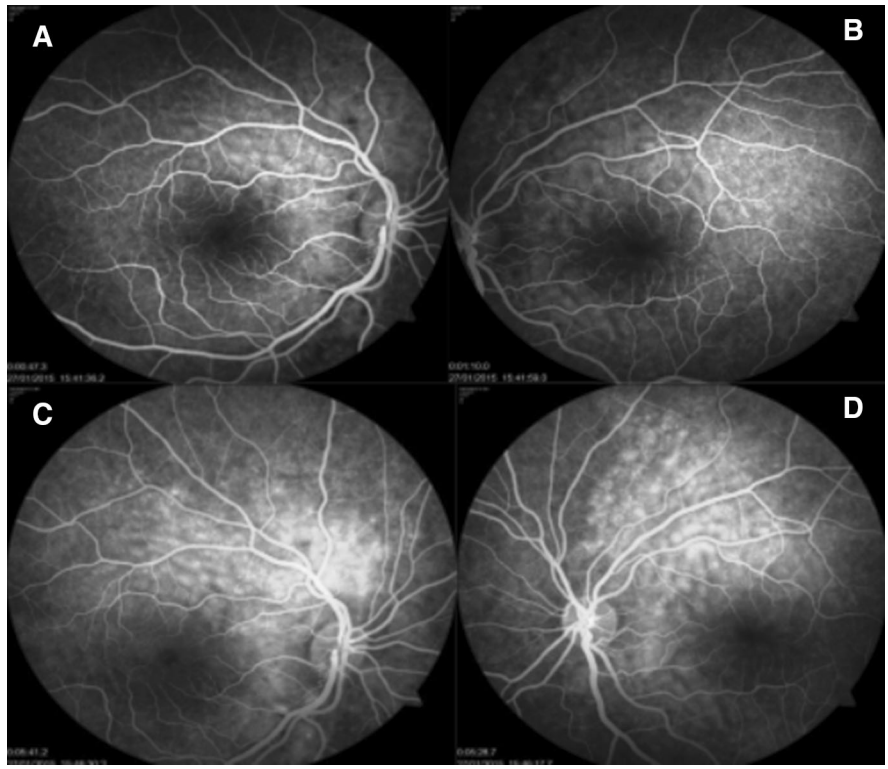

Fig. 2 Fundus fluorescein angiography showing multiple hyperfluorescent dots around the optic disk and macula in the early phase (**a** = right eye, 1.27 min, **b** = left eye, 1.42 min). With the pooling of fluid within the subretinal and intraretinal space, multifocal placoid areas of hyperfluorescence and cystoid macular edema became apparent during the late phase (**c** = right eye, 8.47 min, **d** = left eye, 8.58 min)

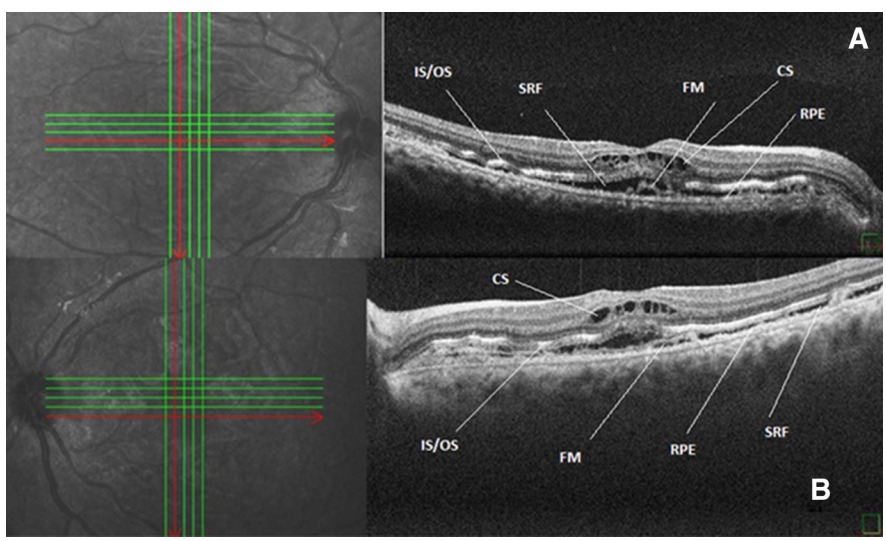

Fig. 3 SD-OCT images showing bilateral macular thickening and macular edema with multiple cystic spaces (CS) associated with a subretinal fluid (SRF) between the photoreceptor layer and the retinal pigment epithelium (RPE). RPE appears to be irregular and edematous. There are some inflammatory products such as fibrin membrane (FM) formed on the RPE in the subretinal fluid. The detached neuroretina composed of the photoreceptor inner segment/outer segment (IS/OS) complex and the outer limiting membrane was irregular and undulated resulting in hyperreflectivity in the parafoveal region (**a** = right eye, **b** = left eye)

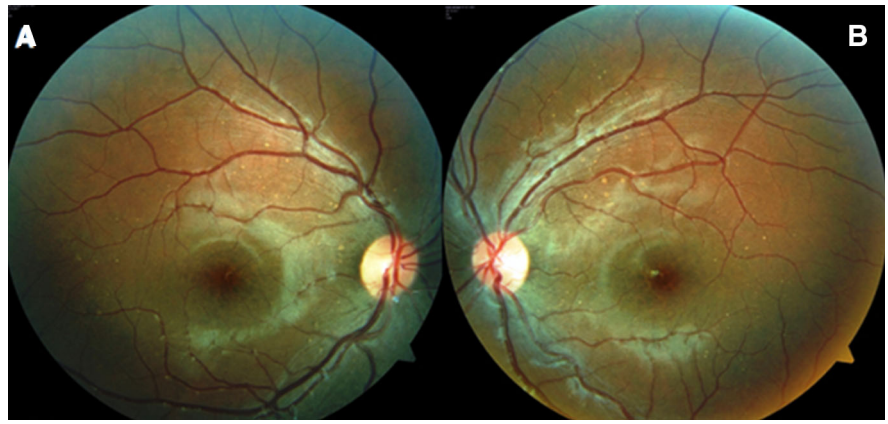

Fig. 4 Fundus images after 6 months showing an absence of retinal detachment and fully recovered retina (**a** = right eye, **b** = left eye)

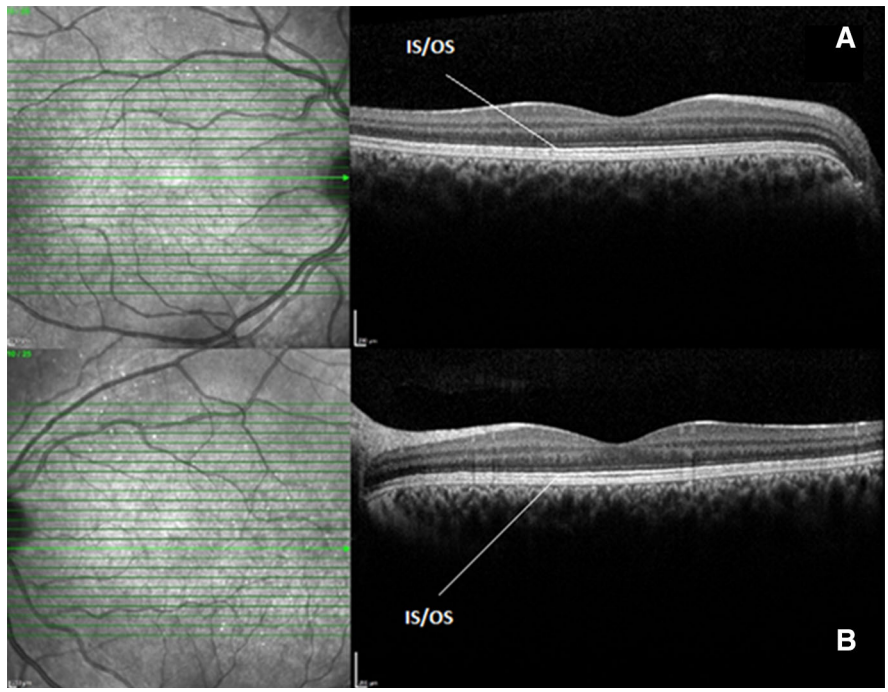

Fig. 5 SD-OCT demonstrating resolution of subretinal fluid and macular photoreceptor inner segment–outer segment (IS-OS) disruption with complete recovery of retinal anatomy in both eyes (**a** = right eye, **b** = left eye)

anticonvulsant, the absence of phytocannabinoids in synthetic cannabinoid products may result in an increased risk of seizures in users, as in our case [6].

There are very few studies in the literature reported the ocular adverse effects of SCs intoxication, and only the blurred vision, myosis, mydriasis, and nystagmus have been described in these reports [7, 8]. The cause of poor vision in our case was multiple exudative retinal detachments and macular edema. Although the reason for this pathology still remains unclear, we hypothesize that the increase in blood pressure may be the cause for fluid leakage to the intraretinal and subretinal space. It is well established that tachycardia and hypertension are the most common cardiovascular effects of SCs [9]. The vascular dysfunction in hypertension leads to the disruption of the blood–retinal barrier and leakage of plasma material causing fluid to accumulate in multiple layers of the retina. However, there were no hemorrhages and exudates in this case. The absence of vascular changes, hemorrhages, and exudates which can be seen in hypertensive retinopathy can be explained by the sudden interstitial fluid accumulation into the retinal layers.

In our patient, SD-OCT revealed a bilateral macular thickening and macular edema with multiple cystic spaces, associated with neurosensorial retinal detachment. The photoreceptor inner segment/outer segment (IS/OS) complex was irregular and undulated resulting in hyperreflectivity in the parafoveal region. Different irregularity detected on retinal pigment epithelium (RPE). There were some inflammatory products such as fibrin membrane formed on the RPE in the subretinal fluid. We hypothesize that this inflammation may be caused by sudden interstitial fluid accumulation that disrupts the RPE.

In addition, increased CK levels which are most probably due to rhabdomyolysis can be seen [10]; however, seizures activity associated with the muscle rigidity may be the cause for this increment. The increase in blood pressure and subsequent retinal pathologies may also appear as a chain of events after convulsion. Nevertheless, further investigations are needed for the actual cause of exudative retinal detachment and macular edema in SCs toxicity.

Regulation of blood pressure and correction of electrolyte imbalances can lead to resolution of the subretinal fluid in such cases; therefore, we decided to follow our patient after intravenous fluid treatment. Spontaneous absorption of the subretinal fluid and full recovery was achieved at 6 months of follow-up.

In conclusion, health providers should be aware of ocular side effects associated with SCs and, although the mechanism still remains to be elucidated, retinal pathologies should be kept in mind in patients with a complaint of blurred vision associated with synthetic cannabinoid intoxication.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent Informed consent was obtained from all individual participants included in the study.

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