



## Central serous chorioretinopathy associated with Adderall (dextroamphetamine-amphetamine) and topical steroid use

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### ABSTRACT

**Purpose:** To report a case of central serous chorioretinopathy (CSC) associated with Adderall (dextroamphetamine-amphetamine) and topical steroid use.

**Observations:** A 34-year-old man presented for evaluation of a “cloud” in his vision for three months. He was taking Adderall for attention deficit hyperactivity disorder and mometasone 0.1% topical cream for eczema. He was found to have subretinal fluid in the left eye consistent with CSC. The subretinal fluid persisted despite cessation of the steroid cream but resolved after cessation of the Adderall. The subretinal fluid returned when the patient restarted Adderall and again resolved after he stopped it for a second time.

**Conclusions:** Though we cannot prove causality, the course of events was suggestive of a direct relationship between Adderall use and CSC in this patient, with exogenous steroid as a possible modifying factor.

### 1. Introduction

Central serous chorioretinopathy (CSC) is a condition characterized by serous retinal detachment related to choroidal hyperpermeability and dysfunction of the retinal pigment epithelium.<sup>1</sup> Whereas multiple studies have found a correlation between steroids and CSC,<sup>1</sup> there are very few prior reports of CSC associated with the use of sympathomimetic agents.<sup>2–4</sup> We report a case of CSC in a patient taking the sympathomimetic drug Adderall (dextroamphetamine-amphetamine) and a topical steroid cream. The subretinal fluid persisted despite cessation of the steroid cream but resolved after discontinuation of the Adderall, and recurred when the Adderall was restarted.

### 2. Findings

A 34-year-old man presented for evaluation of a “dark cloud” in his left eye for three months. He had never had this problem before. Past medical history included attention deficit hyperactivity disorder (ADHD) for which he had been taking Adderall for the past ten years, currently at a dosage of 30 mg per day, and also eczema for which he had been using mometasone 0.1% topical cream for the past year. He was otherwise healthy and denied recent stress and “type A” personality

traits. Vision was 20/20 in the right eye and 20/30 in the left eye. Examination of the right eye showed a subtle small cluster of yellow deposits at the level of the retinal pigment epithelium in the macula, but was otherwise unremarkable (Fig. 1A). Examination of the left eye revealed a localized serous detachment in the macula (Fig. 2A). Optical coherence tomography (OCT) of the right eye showed choroidal thickening but no subretinal fluid (Fig. 1C), and the left eye showed choroidal thickening and subretinal fluid (Fig. 2C). He was diagnosed with central serous chorioretinopathy and advised to stop the mometasone steroid cream, which he did immediately. At three and four months follow up, however, he remained with persistent subretinal fluid (Fig. 2D).

At the four months follow up visit, he was advised to stop the Adderall, which he did promptly. He returned two months later (six months from his initial visit) and reported that his vision had started to improve within a few days of stopping the Adderall. Acuity was improved to 20/20 in the left eye and the subretinal fluid had resolved (Fig. 2E) and remained resolved at a subsequent visit one month later.

He returned two months later (nine months from his initial visit) with decreased vision in the left eye. Two months previously he had started atomoxetine as an alternative treatment for ADHD at 40 mg daily. He took the atomoxetine for two weeks but then stopped due to side effects of headache and nausea. He then restarted the Adderall at 40

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mg per day and after being on it for a month noticed again a dark cloud in his left eye. He denied any steroid use. Acuity was decreased to 20/25 in the left eye and there was recurrent subretinal fluid in the macula (Fig. 2F). He was advised to stop the Adderall. He returned three weeks later and reported again that his vision began to improve within a matter of days after stopping the Adderall. Acuity was 20/20 in the left eye and OCT showed resolved subretinal fluid (Fig. 2G).

### 3. Discussion

Adderall, which is used in the treatment of ADHD and narcolepsy, is a central nervous system stimulant that increases synaptic concentrations of norepinephrine, dopamine, and serotonin through multiple mechanisms.<sup>5</sup> It has been reported to be one of the most commonly prescribed agents for ADHD in the United States<sup>6</sup> and the most frequently abused prescription stimulant among college students.<sup>7</sup>

Prior reports of sympathomimetic agents associated with CSC are limited. Michael and colleagues reported four patients taking either pseudoephedrine, oxymetazoline, or the illicit substance methylenedioxymethamphetamine (MDMA)<sup>2</sup>; Hassan and colleagues reported one patient taking MDMA<sup>3</sup>; and Pierce and Lane reported three patients taking ephedra.<sup>4</sup> CSC has been reported in a patient concurrently taking spironolactone and Adderall, but in that particular case the Adderall use was not modified throughout the follow up period and the CSC resolved following spironolactone discontinuation, and returned after the patient took spironolactone again.<sup>8</sup>

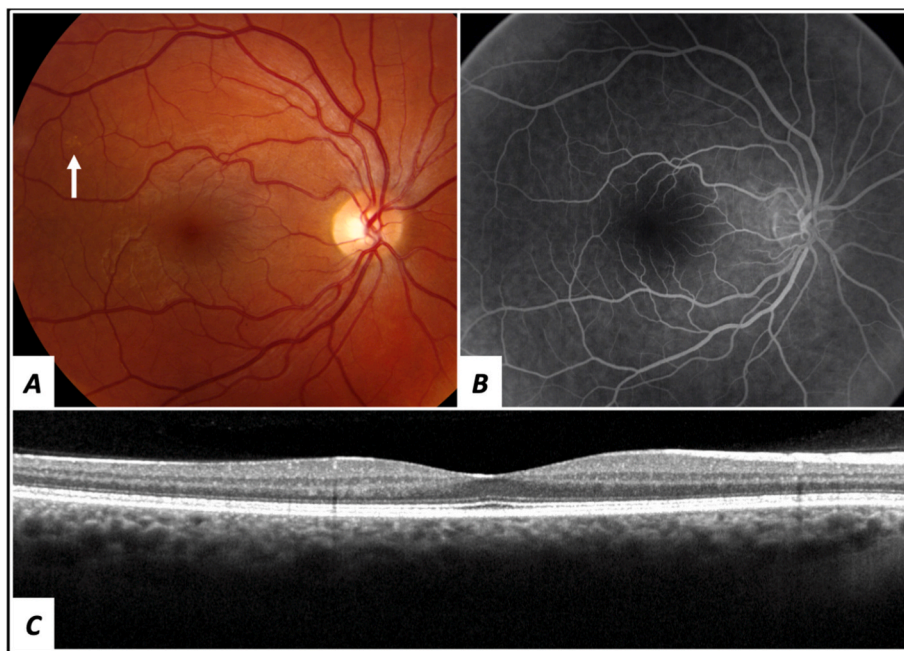
In the case reported here, the patient had been taking Adderall for a decade. He had started taking a steroid cream one year prior to the development of his eye symptoms, leading us to initially suspect the steroid was the primary culprit, but the subretinal fluid did not resolve when the steroid was stopped and the Adderall continued. When the Adderall was later stopped, however, he had resolution of his symptoms and the subretinal fluid. After he restarted the Adderall, furthermore, his symptoms returned and he was found to have recurrent subretinal fluid, which resolved rapidly after cessation of the drug for a second time. The patient took atomoxetine, a selective norepinephrine reuptake inhibitor used for the treatment of ADHD, for two weeks starting two months prior

to his second episode of CSC; the use of this drug did not correlate with the onset of his symptoms.

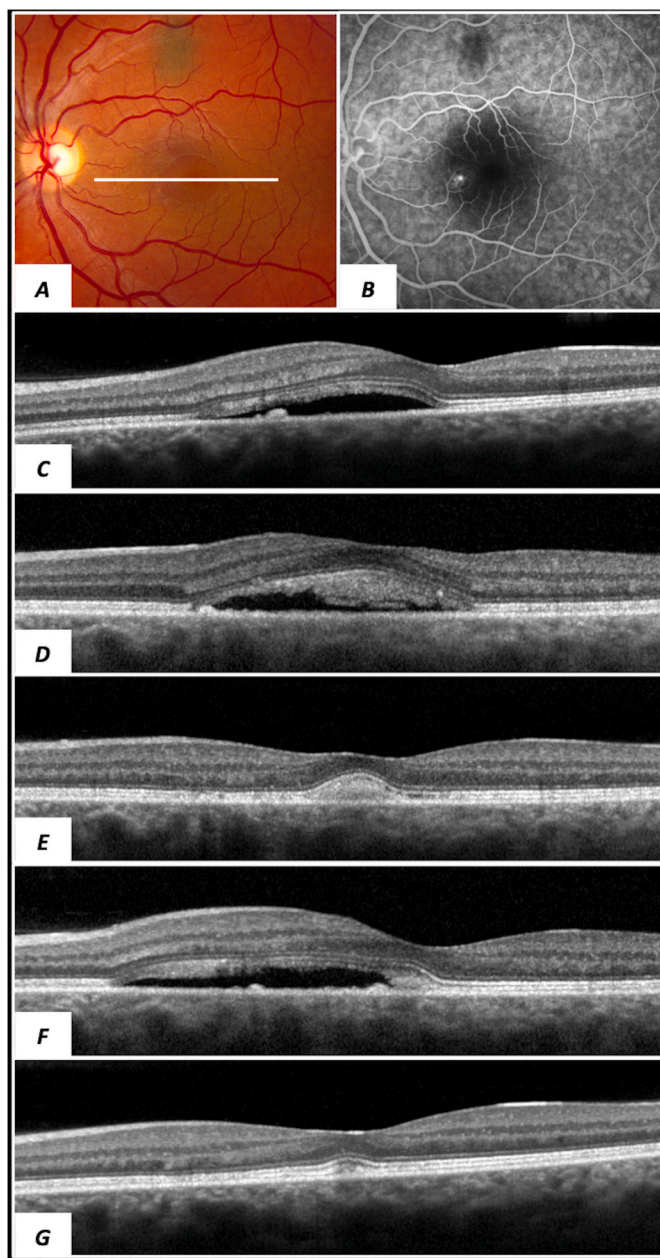
The exact pathogenesis of CSC remains elusive, and the potential relationship between Adderall and CSC in this case is unclear. Repeated intravenous administration of epinephrine has been shown to produce serous retinal detachments resembling CSC in monkey eyes.<sup>9</sup> A number of studies have found a correlation between exposure to exogenous corticosteroids or pathologic increases in endogenous cortisol (such as in Cushing disease) and CSC,<sup>1</sup> and amphetamine administration increases plasma concentrations of steroids in healthy subjects.<sup>10</sup> It has also been hypothesized that certain sympathomimetic drugs may contribute to CSC development via a direct effect on the retinal pigment epithelium.<sup>3,4</sup>

Evidence of autonomic nervous system dysfunction with a predominance of sympathetic activity, as measured by heart rate variability, has been found in patients with CSC.<sup>11,12</sup> Since choroidal blood flow is modulated by input from the autonomic nervous system, and alterations in choroidal circulation have been associated with CSC, this has led to the suggestion that autonomic dysfunction could be responsible for choroidal blood flow changes resulting in CSC.<sup>11,12</sup> Evidence of autonomic dysfunction with a predominance of sympathetic activity has also been found in patients with ADHD under treatment with amphetamines.<sup>13</sup>

Though we cannot rule out the possibility that the patient had prior episodes of CSC that went undetected, his presumed first episode developed after taking Adderall for a decade. Of note, he had started the steroid cream one year prior to presentation. A synergistic effect between steroids and catecholamines in CSC pathogenesis has been proposed.<sup>14</sup> Corticosteroids may influence the transcription of genes for  $\alpha$ - and  $\beta$ -adrenergic receptors.<sup>15,16</sup> It is possible that the introduction of exogenous steroid potentiated the effect of the Adderall. If the steroid cream increased his sensitivity to Adderall, the sensitivity continued for an extended period after cessation of the steroid, as he had a recurrent CSC episode after restarting the Adderall despite having been off the steroid for eight and half months.



**Fig. 1.** Imaging of the right eye. Color fundus photography (A) showed a subtle small cluster of yellow deposits at the level of the retinal pigment epithelium in the superotemporal macula (white arrow). Fluorescein angiography (B) was unremarkable. Optical coherence tomography (C) showed a thickened choroid. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)



**Fig. 2.** Imaging of the left eye. Color fundus photography (A) showed a serous detachment in the macula. There was a small, flat choroidal nevus in the superior macula. The horizontal white line represents the location of the optical coherence tomography (OCT) scans used in the figure. Fluorescein angiography (B) revealed a focal leak at the level of the retinal pigment epithelium (RPE). OCT scan at presentation (C) showed subretinal fluid and a focal RPE elevation. At this time, the patient was taking Adderall and using a steroid cream. He was advised to stop the steroid cream. Repeat OCT scan four months later (D) demonstrated persistent subretinal fluid despite having stopped the steroid cream. There was also some accumulated subretinal hyperreflective material. At this visit he was advised to stop the Adderall. Two months later (E) the subretinal fluid was resolved, with some residual subretinal hyperreflective material. Three months later (F) he returned with new subretinal fluid, having restarted the Adderall six weeks previously. He stopped the Adderall and then returned three weeks later (G) and the subretinal fluid had again resolved. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

#### 4. Conclusions

Though we cannot prove causality based on this single case, the course of events was suggestive of a direct relationship between Adderall use and CSC in this patient, with exogenous steroid as a possible modifying factor. Naranjo and colleagues developed a probability scale to assess for a causal relationship between the administration of a drug and a subsequent adverse clinical event.<sup>17</sup> Using this probability scale, we calculated a total score of 5 for the case reported here, assigning it to the “probable” adverse drug reaction category. Further study is needed.

#### Patient consent

The patient provided verbal consent to publish the case. This report does not contain any personal information that could lead to identification of the patient.

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#### Conflict of interest

None of the authors have a proprietary interest in the material presented in this study.

#### Other disclosures

None.

#### Authorship

The authors attest that they meet the current ICMJE criteria for authorship.

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