Charles Bonnet Syndrome

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INITIAL PRESENTATION

Chief Complaint: "I see people outside my home."

History of Present Illness: A 51-year-old female, legally blind due to a complicated ocular history including proliferative diabetic retinopathy OU, history of combined tractional-rhegmatogenous retinal detachment OU, and mixed mechanism glaucoma, reported to clinic for routine follow-up. Overall, her vision was stable since her last visit, however, she had noticed occasional "snow" in her vision. Upon further questioning, she also reported episodes of vivid visual hallucinations, including seeing people walking around outside whom she knew were not really there. These did not occur at specific times of day and varied in their duration.

Past Ocular History:

- OD:
  - Combined tractional-rhegmatogenous fovea splitting detachment, status post repair with vitrectomy, scleral buckle, laser, and silicone oil; subsequent oil removal
  - Cystoid macular edema
- OS:
  - Combined tractional-rhegmatogenous retinal detachment (macula-on) status post repair with vitrectomy, laser, silicone oil placement
  - Mixed mechanism glaucoma status post Ahmed seton
- OU:
  - Proliferative diabetic retinopathy
  - Mixed mechanism glaucoma
  - Fuchs' endothelial dystrophy
  - Pseudophakia

Past Medical History:

- Sleep apnea
- Diabetes
- Hypertension
- GERD
- Neuropathy
- Anxiety
- Smoker

Ocular Medications:

- Timolol OD

- Artificial tears PRN OU

Allergies: Sulfa, neomycin & polymyxin

Family History: No pertinent family history

Social History: Non-contributory

Review of Systems: A review of the neurological system was performed and was negative except for a history of neuropathy of the distal lower extremities. The ocular system was also reviewed, and the findings are described above in the history of present illness.

OCULAR EXAMINATION

Visual Acuity without correction:

- Right eye (OD): 20/250, no improvement with pinhole
- Left eye (OS): 20/600, no improvement with pinhole

Ocular Motility/Alignment: Motility full with normal alignment.

Intraocular Pressure (IOP):

- OD: 14
- OS: 12

External: Normal external exam

Slit lamp exam:

- Lids/lashes: Normal OU
- Conjunctiva/sclera: Clear and quiet OD, corneal patch graft and tube well covered OS
- Cornea: 3+ guttata with diffuse endothelial pigment OU, 1+ punctate epithelial erosions OU
- Anterior chamber: deep and quiet OU, superotemporal tube near cornea OS
- Iris: Patent peripheral iridectomy inferiorly, no transillumination defects, no iris neovascularization OU
- Lens: Posterior chamber intraocular lens with open capsule centrally OU

Dilated fundus examination (DFE):

- Vitreous: optically empty, no vitreous heme OU
- Disc: Pale, no active NVD, no disc heme OU
- Cup-to-disc ratio: difficult to estimate due to pallor OU

Additional testing: None

Differential Diagnosis:

Visual hallucinations can be due to:

- Charles Bonnet syndrome
- Psychiatric illness (e.g., schizophrenia)

    - Neurodegenerative disease (e.g., Lewy body dementia, Parkinson disease, Alzheimer disease, Creutzfeldt-Jakob disease)
- Delirium
- Seizure disorders
- Alcohol and drug use and/or withdrawal
- Metabolic encephalopathy
- Migraine
- Peduncular hallucinosis (e.g., secondary to thalamus or midbrain lesion)
- Anton's syndrome (i.e., visual anosognosia with confabulations)

DISCUSSION:

Introduction

This patient was diagnosed with Charles Bonnet Syndrome (CBS), a condition characterized by the occurrence of visual hallucinations in patients with diminished visual acuity, usually those with severe vision loss in both eyes. CBS is a diagnosis of exclusion that often goes unrecognized or is misdiagnosed [1 ,2]. While typically not disabling, CBS may cause significant distress to patients [3]. This article will review the etiology, epidemiology, pathophysiology, clinical characteristics, differential diagnosis, and treatment of this condition.

Etiology/epidemiology

Charles Bonnet Syndrome is relatively common, with an estimated prevalence of 10-40% in visually impaired patients [3-5]. The visual hallucinations in CBS have been described with conditions of visual loss affecting any part of the visual system, including the eye, optic nerve, and brain [2 ,6], and may occur in almost any acquired disorder of the visual system [1 ,2 ,7 ,8]. The most common conditions among patients with CBS include age-related macular degeneration, glaucoma, diabetic retinopathy, and stroke.

Hallucinations in CBS may manifest at the same time as acute vision loss or after a brief period of latency, ranging from hours to several weeks [9]. One cross-sectional analysis of patients with retinal disease found that 61.5% of those patients with CBS reported a duration of hallucinations of less than 1 year [2]. Despite the myriad of conditions contributing to CBS, the majority of patients had not previously reported their symptoms to their physician or family members prior to diagnosis, indicating that the condition may be more prevalent than is often thought, and highlighting the hesitancy that patients may have regarding sharing their symptoms, even with close relatives [1 ,2].

Visual hallucinations of CBS have been reported in patients of all ages [10]. However, CBS has not been reported in patients with congenital blindness [11]. Several studies have found advanced age to be a risk factor for development of CBS, with one study noting a significant association between development of hallucinations and age over 64 years [4 ,8 ,12]. The greater prevalence of CBS in older patients likely corresponds to the increasing prevalence of common conditions causing vision loss, such as age-related macular degeneration or advanced glaucoma [6]. Other risk factors which have been implicated in the development of CBS include visual acuity worse than 20/60, binocular disease, cognitive impairment, cerebrovascular disease, cortical atrophy, and social deprivation [4 ,12].

Pathophysiology

While the underlying pathophysiology of CBS is poorly understood, several theories have been proposed. The most widely discussed theory for hallucinations in CBS is that they represent "cortical release." This theory proposes that under normal, non-pathologic conditions, many irrelevant sensory inputs are actively censored in higher-order cortical functioning. However, with the loss of visual stimuli, the cortex no longer inhibits irrelevant afferent impulses, thus leading to the registering of previously-censored visual stimuli [13]. Previous studies have suggested that CBS patients experience this aberrant firing in the ventral occipital lobe around the fusiform gyrus (Brodmann area 37), which is responsible for object naming and visual object recognition. This theory is supported by studies in which patients were subjected to visual deprivation and subsequently developed increasingly complex visual hallucinations [7]. Furthermore, functional magnetic resonance imaging (fMRI) studies have demonstrated spontaneous activity in the ventral occipital lobe of CBS patients during active hallucinations [14]. A separate study showed hyperperfusion of the lateral temporal cortex, striatum and thalamus on computed tomography (CT) during the experience of complex visual hallucinations [15].

Clinical Characteristics

Visual hallucinations in the setting of CBS have a variety of manifestations. Some patients report simple images, such as lines, flashes of light, or patterns. Other patients may experience more complex visual hallucinations such as those of animals or people [2]. These images may be static or animated and may last seconds or several hours. Studies suggest that simple hallucinations (51%) are more common than complex hallucinations (21%), although there may be significant variation in complexity even within individual patients [8]. Hallucinations typically correspond with the laterality of visual loss, but may occur in one or both eyes, or in part of the visual field [16].

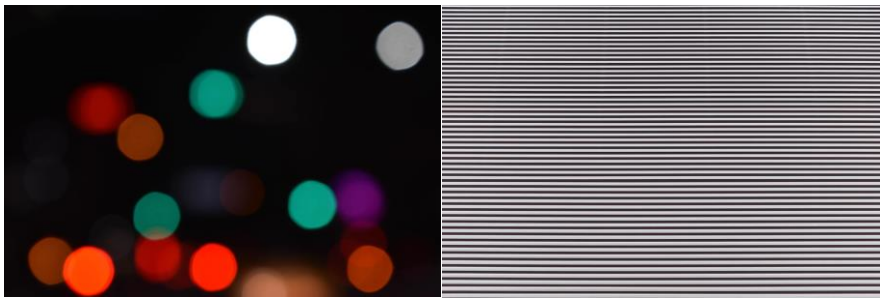

Figure 1 Colorful dots and lines, representing examples of simple hallucinations which may be experienced by patients with Charles Bonnet Syndrome. Photos by Anit Manoharan and Bernard Hermant (public domain).

One of the most important distinguishing features of visual hallucinations secondary to CBS is that the patient generally has insight into their condition and knows that the images are not real [1 ,2]. Another characteristic of hallucinations unique to CBS includes that they predominately occur when the eyes are open, and tend to resolve when a patient closes their eyes or looks away [6 ,17]. One study found that the hallucinations tend to be more prevalent in the setting of sensory deprivation, such as in low light situations, in social isolation, and general inactivity [6].

Patient Testimony

https://www.youtube.com/watch?v=Rerzmm41g_Y

Commented [DR1]: Here on the website we can embed this video; it's a patient testimonial

Diagnosis & Differential Diagnosis

Charles Bonnet Syndrome is largely a clinical diagnosis, and patients who experience visual hallucinations in the classic clinical context of low vision with good insight into their condition may not need diagnostic testing. However, patients with suspected visual hallucinations should undergo neurologic evaluation with screening for cognitive impairment, parkinsonism, or any other deficits if clinically appropriate. A careful review of medication lists for pharmacologic agents known to cause visual hallucinations, such as digoxin, sildenafil, or anticholinergics is also advised. Screening should also be done for drugs of abuse, particularly hallucinogens, with monitoring for withdrawal from substances like alcohol and benzodiazepines. Generally, CBS can be distinguished from other causes by a lack of other neurologic deficits and the presence of known ocular disease. In the case that a patient presents with symptoms suggestive of CBS, but without known eye disease, a full ophthalmologic exam should be performed [18].

Table 1 Differential Diagnosis of Charles Bonnet Syndrome

Etiology		Features of Visual Hallucinations
Psychiatric Illness		Generally accompanied by auditory hallucinations and may be frightening to the patient, who may lack insight into the condition.
Neurodegenerative Disease	Lewy Body Dementia	Hallucinations usually manifest early, prior to motor symptoms and occur throughout the entire visual field.
	Parkinson Disease	Hallucinations manifest late in disease, following the onset of motor symptoms.
	Alzheimer Disease	Hallucinations are uncommon, and usually reflect a superimposed delirium, medication side effect, or vision loss.
	Creutzfeldt-Jacob Disease	In the Heidenhain variant, patients experience poor vision and disturbed color sense in the setting of rapidly progressive dementia, myoclonus and a normal eye exam.
Delirium		Hallucinations may be frightening, and insight is generally limited.
Seizures		Hallucinations are simple, brief, and consistent (colored spots/flashing shapes).
Migraine Aura		Patients often see flickering, zig zagging lines starting centrally and progressing peripherally. Patients generally have good insight.
Alcohol/Drug Use		Hallucinations are often frightening and may result from intoxication or withdrawal.
Metabolic Encephalopathy		Presentation is similar to delirium.
Peduncular Hallucinosis		Related to thalamic and midbrain lesions, these hallucinations often occur in the dark and last minutes, with good insight.
Anton's Syndrome		Patients confabulate their vision, insisting they are capable of seeing despite evidence of cortical blindness.

CBS is under-recognized and underdiagnosed, and several groups have advocated for screening in order to identify affected patients. One simple approach recommends utilizing a combination of indirect and direct questioning in all patients with underlying vision loss. First, patients are asked non-leading, indirect questions:

- Indirect: “Apart from blurred vision, have you noticed anything unusual about your vision? Have you had any unusual visual experiences?”

If the patient is not forthcoming about a history of hallucinations, a more direct line of questioning can then be used [19].

- Direct: “It is well known that some people with blurred vision can sometimes see things that they know are not real. Have you experienced anything like this?”

Prognosis & Treatment

The prognosis of CBS varies widely depending upon the underlying cause of visual loss. In patients with chronic vision loss, hallucinations may persist for many years. For example, 75% of those with CBS in the context of macular disease experienced hallucinations for a period of at least 5 years [3]. However, in the case of reversible vision loss, as with cataracts, hallucinations often resolve once vision is corrected or improved [7]. Hallucinations may also cease over time in more progressive and permanent causes of vision loss, particularly in cases of acute cerebral injury [9].

No definitive treatment exists for the visual hallucinations associated with CBS, and the therapeutic approach to these patients relies primarily on providing reassurance and normalization, depending on the degree of patient distress. It is important for patients to understand that they are not alone, as there is a relatively high incidence of CBS among those with vision loss. Patients should also be reassured that these hallucinations are not a sign of psychiatric illness or dementia, as fear of being deemed “crazy” is a frequently-cited concern [1]. Beyond reassurance, there are behavioral interventions which may benefit select patients. For instance, temporary suppression of hallucinations may be achieved in patients who utilize rapid eye movement and blinking [20]. There is also anecdotal evidence to suggest that increased visual stimulation, arousal, and social interaction may help to suppress symptoms [21].

Medical management of CBS, particularly in those patients experiencing distress from their hallucinations, remains an area of controversy. Several case studies have reported symptomatic improvement following treatment with antipsychotic medications such as haloperidol, olanzapine and thiothixene, though results are largely mixed [22-25]. Certain anticonvulsive medications such as carbamazepine, clonazepam, gabapentin and valproate have also been found to be useful in case reports [26-29].

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