Evaluation of the Clinical Features, Management, and Prognoses of Patients With Charles Bonnet Syndrome

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Abstract: Charles Bonnet syndrome (CBS) is characterized by visual hallucinations with preservation of cognitive abilities. The hallucinations consist mostly of vivid (realistic) objects and tend to reoccur. Here, we evaluate the etiologies, symptoms, treatments, and prognoses of 13 CBS cases. All patients had visual hallucinations but were normal on cognitive and psychiatric assessments. Patient demographic and clinical characteristics, treatment options, and 3-month follow-up data were retrospectively reviewed. The possible causes of CBS and what the patients perceived during their hallucinations were recorded. Antipsychotic agents, such as risperidone and quetiapine, and anticonvulsants, such as levetiracetam, may be effective in some cases.

Key Words: Charles Bonnet syndrome, hallucinations, visual impairment

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Charles Bonnet syndrome (CBS) was first described by Charles Bonnet in the 1970s. Bonnet recognized that his grandfather (who had lost his sight after cataract surgery) retained normal cognitive skills but developed visual delusions (Jackson and Ferencz, 2009). Bonnet experienced a similar complaint toward the end of his life. In 1967, Morsier defined the clinical presentation as CBS (de Morsier, 1967), characterized by visual hallucinations with preservation of cognitive abilities. The hallucinations consist mostly of vivid (realistic) objects and tend to reoccur. Patients are aware that the images are not real, but they may be disturbing. The hallucinations may be logically coherent and may not be distinguished from real objects (Vukicevic and Fitzmaurice, 2008). Although CBS can be an early sign of dementia in the elderly, most patients are neurologically normal (Pliskin et al., 1996). A lesion anywhere in the visual pathway can trigger CBS, as (sometimes) can loss of central visual acuity (Vukicevic and Fitzmaurice, 2008). We, here, evaluated the etiologies, symptoms, treatments, and prognoses of 13 CBS cases.

METHODS

The study was conducted in Karatay University School of Medicine of Konya Medicana Hospital. Patients were diagnosed in the Elbistan State Hospital, the Baskent University Faculty of Medicine, the Aksaray Education and Research Hospital, and the University of KTO Karatay (where the authors work). This retrospective study was approved by the ethics committee of the University of KTO Karatay, where the study was performed (approval number 2018/018), and adhered to all relevant tenets of the Declaration of Helsinki. The medical records of patients with CBS diagnosed by two neurologists and one psychiatrist were reviewed. Patients with visual hallucinations but who were normal on cognitive and psychiatric evaluations and were aware that the images were not real were included. The exclusion criteria included patients a) who experienced visual hallucinations but were not aware that they were unreal, b) who were diagnosed with a pathology upon psychiatric examination, c) who reported nonvisual hallucinations, and d) who were cognitively impaired. Eight patients with nonvisual hallucinations, 19 with psychiatric disorders who were not aware of their hallucinations, and 1 patient lost to follow-up after diagnosis were excluded.

Procedure

The purpose and plan of the study were described to all patients and their first-degree relatives, and verbal and written consent were recorded. We evaluated 3 months of records and noted demographic and clinical characteristics. The possible causes of CBS and what patients perceived during their hallucinations were recorded. We also noted treatments and the 3-month prognoses.

RESULTS

The mean patient age was 73.76 ± 9.64 years; seven were women and six were men. Four of the patients were able to count fingers from a distance of less than 1 m, and the other nine from a distance of more than 1 m. The hallucinations were caused by ocular pathologies in eight patients and nonocular pathologies in five (Table 1). Two hallucinations were in the form of people, five in the form of animals, and six were nonliving things. Seven of the hallucinations were complex, but six were simple. Five patients experienced dynamic hallucinations, and the other eight fixed hallucinations. Six hallucinations were colored, and seven were in black and white. The duration of hallucinations was less than 1 month in two patients, 1 to 3 months in three, 3 to 6 months in four, and more than 6 months in four (Table 2).

All patients received oral medications including anticonvulsants, antidepressants, and antipsychotics. Four patients received risperidone, two levetiracetam, four quetiapine, two carbamazepine, and one escitalopram. At the 3-month follow-up, two of the four treated with risperidone had improved, but one had not. One patient who received risperidone was lost to follow-up. One patient who received levetiracetam entered remission, but the other did not. Two patients who received quetiapine entered remission, one did not, and the other was lost to follow-up. Neither patient treated with carbamazepine entered remission. The only patient who received escitalopram was lost to follow-up. The efficacies of medications assessed at the 3-month follow-up are listed in Table 3.

DISCUSSION

We examined the clinical and demographic characteristics and treatment outcomes of patients with CBS. CBS is a rare clinical syndrome characterized by visual hallucinations but with preservation of cognitive skills (Vukicevic and Fitzmaurice, 2008). Although the pathophysiology of CBS remains unclear, the condition is believed to reflect an increase in spontaneous neural activity with a concomitant reduction in cortical inhibition when visual pathways are interrupted. Increased pathological activity in the visual cortex may cause visual delusions by creating anatomical connections in the visual field (Santhouse et al., 2000). The hallucinations may be basic in nature (geometric forms, bright lights, and patterns) or may be complex (human faces, animals, bright objects, and vivid scenes). The hallucinations may be in

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TABLE 1. Demographic Characteristics of Patients, Visual Acuity, and Etiological Factors

	No. (%)
Sex	
Female	7 (53.80)
Male	6 (46.20)
Visual acuity	
<1 m counting fingers	4 (30.70)
>1 m counting fingers	9 (69.30)
Ocular causes	
Retinal detachment	1 (7.69)
Cataract operation	2 (15.38)
Diabetic retinopathy	1 (7.69)
Glaucoma	1 (7.69)
Macular degeneration	3 (23.0)
Nonocular causes	
Occipital infarct	4 (30.76)
Benign intracranial hypertension	1 (7.69)

TABLE 2. Features of Hallucinations

	No.
Type	
Human	2
Animal	5
Pattern	5
Lifeless entity	1
Active	5
Static	8
Colored	6
Black-white	7
Time	
<1 mo	2
1–3 mos	3
3–6 mos	3
6–12 mos	4

black and white or in color and may be fixed or dynamic (Gonzalez-Delgado et al., 2004). Some studies found that minor visual losses caused simple hallucinations, but severe losses complex hallucinations (Scott et al., 2001), that may be episodic, chronic, or cyclical in form, although generally persisting for less than 12 months. However, some rare cases report hallucinations of 2 years in duration (Nesher et al., 2001). All of our patients had either simple or complex hallucinations, in line with the literature, of duration less than 12 months. The most common cause of CBS is senile macular degeneration, but glaucoma and cataracts are other common causes (Ffytche et al., 1998). In addition, CBS may be attributable to nonocular pathologies such as a cerebrovascular accident, optic chiasma meningioma, mesial temporal and occipital lobectomy, or temporal arteritis (Lerario et al., 2013). Eight of our patients had ocular etiologies, the most common of which was macular degeneration. The most common nonocular cause was an occipital infarct. Although the most important risk factor for CBS development is advanced age, CBS has been noted in those of all ages, including childhood (Schwartz and Vahgei, 1998; Tan et al., 2004). No between-sex differences have been described (Cohen et al., 2003).

The clinical features of CBS remain rather vague. Importantly, although the CBS prevalence has been reported to be as high as 11%, patients may not complain because of concern that they will be judged to have a mental disorder; physicians must inform and question patients with suspected CBS (Batra et al., 1997). The reported CBS prevalence in the visually impaired varied widely among studies, from 0.4% to 12% (Kester, 2009; Plummer et al., 2007; Schadlu et al., 2009). One study evaluated 264 patients with retinal disease and found this "rare" syndrome in 17 (Nalcaci et al., 2016). Another study found that 72.8% of primary care physicians had seen patients experiencing visual hallucinations within the past year, but 54.7% knew little about CBS. Therefore, the syndrome may, in fact, be rather common (Gordon and Felfeli, 2018). Although various mechanisms may be in play, more work is needed.

The "deafferentation" theory maintains that reduced sensation and/or vision, as in those with phantom pain syndrome, stimulates intracerebral perception (Burke, 2002). The "perceptual release" theory suggests that a reduction in perception decreases suppression by higher cortical centers; perceptual pathways that are generally inhibited become liberated. In 1987, Rosenbaum noted spontaneous cell discharge from the visual association cortex attributable to a reduced afferent stimulus caused by blindness and termed the phenomenon the "irritable cortex." This theory was accepted by Schultz and Melzack in 1991, working in the context of sensory deprivation (Schultz and Melzack, 1993). The most effective CBS treatment is vision restoration (Ashwin and Tsaloumas, 2007). When the visual cortex is deprived of stimulation, the serotonin level falls significantly. Dopamine and acetylcholine (other neural transmitters) may also be involved in visual hallucinations. Few reports have sought to treat CBS medically, and follow-up durations have been short. Overall, the number of patients treated pharmacologically is small, and no consensus has emerged in terms of an optimal medical treatment. Psychotropic medications such as antidepressants, anxiolytics, antipsychotics, and anticonvulsants have been used to treat CBS hallucinations, with varying results. These agents include carbamazepine, valproate, gabapentin, melperone, ondansetron, mirtazapine, donepezil, venlafaxine, cisapride, and risperidone (Coletti Moja et al., 2005; Eperjesi and Akbarali, 2004; Jackson and Ferencz, 2009; Pang, 2016). We selected treatments after evaluating published case reports; we also considered any additional diseases. We found that antipsychotics such as risperidone and quetiapine, and the antiepileptic drug levetiracetam were effective in some cases. However, the etiology does not indicate which

TABLE 3. The Efficacy of Drugs at the 3-Month Follow-up

	n	Effective	Noneffective	Out of Follow-Up
Risperidone	4 (4 OP)	2 (2 OP)	1 (1 OP)	1 (1 OP)
Levetiracetam	2 (1 PP, 1 CP)	1 (1 CP)	1 (1 OP)	—
Quetiapine	4 (1 OP, 3 CP)	2 (1 CP) (1 OP)	1 (1 CP)	1 (1 CP)
Escitalopram	1 (1 OP)	—	—	1 (1 OP)
Carbamazepine	2 (1 OP, 1 CP)	—	2 (1 OP, 1 CP)	—

CP indicates cerebral pathology; OP, ocular pathology.

treatment may be optimal. Traditionally, antipsychotics were thought to reduce hallucinations by blocking the dopamine receptor (Pang, 2016). However, levetiracetam may be more effective. One of two patients who were treated experienced a reduction in symptoms; the CBS etiology in this case was an infarction. The improvement was remarkable, consistent with the literature. One case report described an 85-year-old woman with CBS and a history of hypertension, coronary artery disease, multi-infarct syndrome, and progressive bilateral peripheral vision loss caused by cataracts and glaucoma. Although valproic acid and carbamazepine were effective, levetiracetam was not (Segers, 2009). Another study observed that levetiracetam eliminated hallucinations in a patient with an infarction in the region of the left posterior cerebral artery (Gruter et al., 2016). Levetiracetam reduces neuronal excitability, affecting the GABAergic system by interacting with synaptic vesicle protein 2 that, in turn, controls the exocytosis of neurotransmitter-containing vesicles and modulates calcium homeostasis; calcium is an important second messenger involved in protein transcription and gene expression. Thereby, levetiracetam may modulate the activity of the ventral, extrastriate visual cortex (Deshpande and Delorenzo, 2014). Notably, we found that carbamazepine was ineffective in two patients with ocular disease and occipital infarctions. Serotonin reuptake inhibitors inhibit occipital lobe neurons involved in visual hallucinations (Pang, 2016). Although escitalopram was prescribed for one patient with depressive symptoms, he was lost to follow-up.

CONCLUSIONS

The pathophysiology and optimal treatment of visual hallucinations remain unclear. Psychiatric and neurological conditions, and toxic and metabolic causes of such hallucinations, should be excluded before a diagnosis of CBS. Some patients may avoid mentioning the problem because they fear that they will be diagnosed with a mental disorder. Therefore, the CBS frequency may be higher than reported. Partial responses to various treatments have been noted. The major limitations of our study are the short follow-up period and the use of only single oral medications. However, we performed detailed neuropsychiatric and ophthalmological examinations and imaging to seek structural abnormalities. In conclusion, elderly patients at risk should be screened for CBS and treated accordingly. Further large-scale studies are required.

DISCLOSURE

The authors declare no conflict of interest.

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