

Charles Bonnet syndrome in age-related macular degeneration – prevalence and clinical features in a Portuguese population

Síndrome de Charles Bonnet na degeneração macular relacionada à idade – prevalência e características clínicas numa população portuguesa

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ABSTRACT

Objective: Age-related macular degeneration (AMD) is the most prevalent cause of irreversible visual loss in the developed world. In late stages, it may lead to extremely low visual acuities, especially when associated with geographic atrophy or choroidal neovascularization. According to recent literature, Charles Bonnet syndrome (CBS) may be a rather common feature of late AMD.

Methods: One hundred patients with late-stage age-related macular degeneration were actively asked whether they had symptoms of Charles Bonnet syndrome. Those that answered positively underwent a comprehensive questionnaire about the details of the visual hallucinations.

Results: The following factors were significantly associated with Charles Bonnet syndrome: older age (+6.3 years; $p=0.003$), lower visual acuity in the better eye (Charles Bonnet Syndrome Group: 0.11; Non-Charles Bonnet Syndrome Group: 0.42; $p=0.005$) and female sex (Charles Bonnet Syndrome Group: 88%; Non-Charles Bonnet Syndrome Group: 43%; $p=0.02$). The visual hallucinations occurred mainly straight ahead ($n=5$), once per day ($n=4$), at no particular time ($n=6$), lasted some minutes ($n=5$), and disappeared after blinking ($n=3$) or looking away ($n=3$). The majority of patients lived alone ($n=7$), had not told anyone about the hallucinations ($n=6$), and associated the episodes with severe distress ($n=5$).

Conclusion: Charles Bonnet syndrome was fairly prevalent in this late-stage age-related macular degeneration population. Our sample shows the importance of directly asking subjects about Charles Bonnet syndrome since they are often reluctant to admit to having visual hallucinations. Reassurance about its benignity is crucial to improve their quality of life.

RESUMO

Objetivo: A doença macular ligada à idade (DMI) é a causa mais prevalente de perda visual irreversível nos países desenvolvidos. Em estádios avançados, esta doença pode levar a acuidades visuais extremamente baixas. De acordo com literatura recente, a Síndrome de Charles Bonnet (SCB) pode acontecer de forma relativamente comum na DMI tardia.

Métodos: Cem doentes com degeneração macular da idade avançada foram interrogados ativamente sobre terem sintomas da síndrome de Charles Bonnet. Os que responderam de forma positiva foram submetidos a um questionário oral detalhado sobre os pormenores das alucinações visuais.

Resultados: Os seguintes fatores foram significativamente associados à síndrome de Charles Bonnet: idade avançada (+6,3 anos; $p=0,003$), menor melhor acuidade visual corrigida no melhor olho (Grupo com Síndrome de Charles Bonnet: 0,11; Grupo sem Síndrome de Charles Bonnet: 0,42; $p=0,005$) e sexo feminino (Grupo com Síndrome de Charles Bonnet: 88%; Grupo sem Síndrome de Charles Bonnet: 43%; $p=0,02$). As alucinações visuais ocorriam principalmente em frente ($n=5$), uma vez por dia ($n=4$), em qualquer altura do dia ($n=6$), duravam alguns minutos ($n=5$) e desapareciam após pestanejo ($n=3$) ou desvio do olhar ($n=3$). A maioria dos doentes vivia sozinha ($n=7$), não tinha partilhado sua condição com ninguém ($n=6$) e associava os episódios a uma sensação angustiante ($n=5$).

Conclusão: A síndrome de Charles Bonnet teve prevalência relativamente alta nessa população de degeneração macular da idade. Nossa amostra sublinha a importância de questionar diretamente sobre a síndrome de Charles Bonnet, uma vez que os doentes se sentem muitas vezes relutantes em admitir alucinações visuais. A reafirmação da benignidade da situação é crucial para aumentar a qualidade de vida desses indivíduos.

INTRODUCTION

Age-related macular degeneration (AMD) is the most prevalent cause of irreversible visual loss in the developed world.⁽¹⁾ By 2040, it is expected to affect nearly 300 million people.⁽²⁾ Early AMD is defined by medium-sized drusen or retinal pigmentary changes in the macular region.⁽³⁾ It is often asymptomatic and accounts for most of the cases.⁽⁴⁾ It is characterized as neovascular in late stages if choroidal neovascularization is present or non-neovascular, generally associated with geographic atrophy.⁽⁵⁾ In this phase, AMD may be responsible for extremely low visual acuities, possibly leading to legal blindness. According to recent literature, Charles Bonnet syndrome (CBS) may be a common feature of late AMD (AREDS 4).⁽⁶⁾ An isolated case of this syndrome was first reported in 1769 by Charles Bonnet, but the term was only coined almost 200 years later by Georges de Morsier.^(7,8) This condition is conventionally characterized by complex visual hallucinations that recur in subjects with severe vision impairment due to ocular pathology who are otherwise psychiatrically and neurologically healthy.⁽⁹⁾ The content of the visual hallucinations varies but often consists of life-like images, such as faces, trees, or animals which are beyond the individual's control. These images may be related to a pleasant feeling and, in some cases, to distress and fear of an imminent mental disorder.⁽¹⁰⁾ Recognition of this condition in the clinical setting by directly asking about the appearance of visual hallucinations is crucial, as many individuals do not report it spontaneously.⁽¹¹⁾ Despite its innocuous nature, other possible neurologic causes should be ruled out, and a multidisciplinary approach with the neurology and the psychiatry departments may be helpful, especially in cases accompanied by another type of hallucinations, a low level of insight, or a possible intellectual deterioration.⁽¹²⁾ Different treatment options for CBS have been discussed, but clinician awareness and reassurance about its benignity remain the cornerstones of CBS management.^(11,13)

METHODS

One hundred consecutive patients with no history of psychiatric or neurological disease attending assessment consultations due to late-stage AMD (AREDS 4) were actively asked whether they had symptoms of CBS. The question asked was a Portuguese translation of the following question proposed by Holroyd et al.: "When people have trouble with their eyes, it frequently affects their vision. It may make it difficult to see things that are there, but sometimes people see things that are not there or see

things that other people don't see. Has this ever happened to you?".⁽¹⁴⁾ The following data was gathered: patients' demographics, including sex and age, medical and ophthalmic previous history, best corrected visual acuity (BCVA) in the decimal scale and type, and bilaterally of AMD analyzed through slit-lamp fundoscopy and optical coherence tomography.

Regarding BCVA, individuals were categorized into one of three groups according to BCVA in their best-seeing eye as follows: BCVA in the better eye $\geq 0,5$; BCVA in the better eye $< 0,5$ but $> 0,1$; BCVA in both eyes $\leq 0,1$.

Those that answered positively to the question underwent an oral comprehensive questionnaire about the details of the visual hallucinations. Exclusion criteria included reporting delusions or hallucinations in other sensory modalities, having no insight over the visual symptoms, and answering the question with simple hallucinations, such as floaters and flashing lights, as these were not considered symptoms of CBS. Individuals diagnosed with CBS were asked to describe their visual hallucinations concerning the content, location, color, movement, duration, frequency, onset, time of day of appearance, precipitating circumstances, and method of making images disappear. Patients were further inquired about how they felt during the hallucinations and whether any level of anxiety or distress accompanied them. In addition, they were asked if they had already discussed their condition with anyone. If yes, with whom, and if they lived alone (Table 1). At the end of the questionnaire, subjects were briefly instructed about the benign nature of their condition. A p-value of < 0.05 was considered significant.

Table 1. Oral questionnaire applied to patients who answered positively to the question "When people have trouble with their eyes, it frequently affects their vision. It may make it difficult to see things that are there, but sometimes people see things that really are not there or see things that other people don't see. Has this ever happened to you?"

Can you describe the images that you most often see?
Does the image have color or is it black and white?
Does the image ever move?
Does the image appear straight ahead or on the side of your vision? Can it appear anywhere?
Does the image occur only in the eye with poorer vision?
How frequently do you see these images?
How long does each episode last?
Do you do something for the images to disappear? If yes, what do you do?
Is there any situation that makes the image more likely to appear?
How do you feel when you see the images?
How long have you seen these images?
Has the frequency of hallucinations changed or remained the same since it started?
Have you ever talked to anyone about your hallucinations? If so, to whom?
Do you feel better now that you know that this condition does not mean you have a mental illness?

RESULTS

One hundred and four patients were initially eligible for the study, and four subjects were posteriorly excluded because of a history of psychiatric or neurological disease. One hundred individuals were asked the previously mentioned question. Eight patients out of 100 (8%) reported having visual hallucinations consistent with CBS and were therefore included in the CBS Group. The remaining 92 patients (92%) were ascribed to the Non-CBS Group. Many individuals complained of seeing floaters, shadows, and flashing lights and were not considered as having CBS.

The mean age in the non-CBS Group was 82 ± 6 years (range from 69 to 95), and 56,5% (n=52) of patients were men. In the CBS Group, the mean age was 88 ± 7 years (range from 74 to 94), and only one patient (12,5%) was male. In our sample, CBS was significantly more common in women ($p=0.02$) and older individuals ($p=0.003$), with a mean age difference of +6.3 years. The mean BCVA in the best-seeing eye was 0.42 in the Non-CBS Group, in which 29% of patients had a best-seeing eye with a BCVA $\leq 0,1$. In the CBS Group, BCVA in the best-seeing eye was much lower (on average 0.11), and this difference (-0.3) was statistically significant ($p=0.005$). In this group, more than half of patients (n=5; 62,5%) had a BCVA in the best-seeing eye $\leq 0,1$. Most patients in both groups had neovascular AMD in one or both eyes – 72% in the Non-CBS Group and 75% in the CBS Group. Fewer patients had a non-neovascular form of AMD – 16% in the Non-CBS Group and 25% in the CBS Group. Some patients in the Non-CBS Group (12%) had both forms, either in one eye or a different one in each eye. Bilaterality of AMD was more frequent in the CBS Group (87,5%) than in the Non-CBS Group (56,5%), but this difference was not statistically significant ($p=0.136$).

All patients considered to have CBS complained of complex, formed, and recurrent visual hallucinations with regular insight and no auditory hallucinations. The clinical features of the visual hallucinations are summarized in table 2. In three cases, the images resembled people; in two cases, geometric patterns; in two cases, plants or trees and in the remaining case, most often animals. In five patients, the visual hallucinations usually occurred straight ahead, and in two cases, they were more often presented peripherally. One patient said the location of the images varied.

In most cases, the hallucinations had color (n=6), and there were moving parts within the image, or the image itself was moving (n=5). No patient reported that

Table 2. Characteristics of the visual hallucinations

Characteristic	n (%)
Content	
People	3 (37.5)
Plants/trees	2 (25)
Geometric patterns	2 (25)
Animals	1 (12.5)
Location	
Straight ahead	5 (62.5)
Peripherally	2 (25)
Variable	1 (12.5)
Colour	
Yes	6 (75)
No	2 (25)
Movement	
Yes	5 (62.5)
No	3 (37.5)
Duration	
Seconds	3 (37.5)
Minutes	5 (62.5)
Frequency	
Daily	4 (50)
Weekly	3 (37.5)
Monthly	1 (12.5)
Time of occurrence	
Morning	1 (12.5)
Afternoon	0
Evening	1 (12.5)
Variable	6 (75)
Distress	
None	1 (12.5)
Some	2 (25)
Severe	5 (62.5)
General impression	
Pleasant	1 (12.5)
Unpleasant	6 (75)
Impartial	1 (12.5)
Method of disappearance	
Blinking	3 (37.5)
Looking away	3 (37.5)
Nothing	2 (25)
Lives alone	
Yes	7 (87.5)
No	1 (12.5)
Told someone	
Yes	2 (25)
No	6 (75)

the symptoms lasted more than some minutes, and three patients mentioned only a few seconds. The frequency of hallucinations was mainly once per day (n=4), but in some cases less often, such as weekly (n=3) or monthly in one case. Predominantly, symptoms occurred at no particular time of the day (n=6), but one patient referred to having hallucinations mainly in the morning and another most often in the evening. Individuals were also asked how they felt during the episodes, how they perceived their condition, and what they would typically do to make the images disappear. Only one patient reported a positive feeling associated with the hallucinations, and the

majority said they felt severe distress when they thought about their condition (n=5). Six patients made the images disappear by blinking (n=3) or looking away (n=3), but two said they had to wait until the images vanished by themselves. Most patients lived alone (n=7) and had not told anyone about the hallucinations before (n=6). The two patients who discussed their symptoms with someone else had chosen a family member. In two cases, the symptoms had disappeared over time in association with, according to the patients, visual improvement after cataract surgery. All patients were aware of the unreal nature of their hallucinations but were much relieved when instructed about the benign nature of their condition.

DISCUSSION

Our study aimed to analyze the prevalence and clinical features of CBS in a group of Portuguese patients with late-stage AMD and, consequently, raise awareness for this still underdiagnosed condition.

To our knowledge, this is the third Portuguese study approaching this topic.^(15,16) The prevalence of AMD has been rising fast over the last decades, and this disease seems to affect Europeans earlier and more often than Africans or Asians.⁽²⁾ Different studies have suggested a connection between late-stage AMD and CBS, which may imply that the prevalence of CBS will also rise.^(6,17-21) Visual hallucinations in late-stage AMD may therefore represent a substantial economic and social burden in the near future. According to a recent systematic review and meta-analysis, the overall prevalence of CBS was 15.8% in patients with AMD, but when considering consecutively enrolled patients, the value was around 7.2%.⁽⁶⁾ In our sample, we also consecutively enrolled patients, and the prevalence of CBS (8%) was similar to the latter. We believe that this method of recruiting patients is more representative of the population seen in clinical practice.

Unfortunately, some authors have suggested that the prevalence of CBS may be underestimated because patients may be reluctant to admit to having hallucinations for fear of being considered mentally ill.^(22,23) Singh et al.⁽²⁰⁾ referred that 36% of the patients had not told anyone about their symptoms before, and Nalcaci et al.⁽¹⁹⁾ found this number to be even higher – 53%. In our study, three-quarters of the individuals had not talked about their hallucinations before, highlighting the importance of directly inquiring patients about CBS. Furthermore, some studies have demonstrated that living alone or feeling lonely places individuals at the most risk of developing CBS.^(14,24,25)

Charles Bonnet syndrome most often affects individuals between 75 and 85 years of age which is probably associated with the most common occurrence of visual loss in this age group.^(10,26,27) In our sample, the mean age was 88 years, and the CBS Group was significantly older than the Non-CBS Group. This is consistent with the literature.^(17,28) Our findings also support that CBS is more common in females, as 88% of the patients in the CBS Group were women. This result is also compatible with some recently published studies,^(19,20) although others have demonstrated no difference between the sexes.^(14,28)

Many works have studied the characteristics of visual hallucinations in visually impaired patients, and there has been some controversy regarding defining criteria for CBS. It is generally accepted that visual hallucinations must be complex, recurrent, accompanied by regular insight, and occur in neurologically and mentally healthy individuals.⁽¹⁰⁾ That is why we did not consider one-time hallucinations and simple hallucinations, such as floaters and flashing lights, as symptoms of CBS and also why we excluded patients with a history of psychiatric or neurological disease.

Study limitations

This study has some limitations and deficiencies. Due to the small number of CBS cases, we could not analyze other risk factors for CBS. As more subjects are studied, we may be able to determine if there is any predilection for this syndrome among patients with AMD and, therefore, possibly avoid patients' distress and anxiety caused by this condition.

CONCLUSION

Charles Bonnet syndrome was fairly prevalent in our late-stage age-related macular degeneration population. Older age, lower best corrected visual acuity in the better eye, and female sex were the most significantly associated factors with the development of Charles Bonnet syndrome. Our work suggests that the classic Charles Bonnet syndrome hallucination associated with age-related macular degeneration may resemble the image of a person, with movement and color, occurring straight ahead, once per day, at no particular time of the day, lasting for some minutes and possibly disappearing after blinking or looking away. Our sample also shows that many patients who experience Charles Bonnet syndrome live alone and associate the episodes with severe distress. Despite the innocuous nature of Charles Bonnet syndrome, other possible neurologic causes should be ruled out, and a

multidisciplinary approach with the neurology department may be helpful in some instances. Our sample shows the importance of directly asking subjects about Charles Bonnet syndrome since they are often reluctant to admit to having visual hallucinations. Reassurance about its benignity is crucial to improve the quality of life of these patients.

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