CHARLES BONNET SYNDROME: NEUROBIOLOGICAL INSIGHTS

HARPREET S. DUGGAL & JOSEPH N. PIERRI

ABSTRACT

A case of Charles Bonnet syndrome in an elderly patient with occipital lobe lesion is described. Authors have highlighted the complex interplay of various neurobiologicat factors such as cortical blindness, structural brain lesion and epileptiform brain activity in the pathophysiology of this syndrome. The impact on the clinical presentation of brain changes on aging and those following cortical blindness and peripheral visual loss is also discussed.

Key words: Charles Bonnet syndrome, neurobiology, aging, structural lesion

Charles Bonnet Syndrome (CBS) is characterized by vivid, complex and recurrent visual hallucinations associated with eye pathology in cognitively intact persons. Though mostly associated with peripheral causes of visual impairment, it is reported to occur with visual system lesions at any level (Gold & Rabins, 1989; Fernandez et al., 1997). While one of the putative mechanisms of complex visual hallucinations in CBS is an abnormal release of central processing phenomenon, the level of this release is not clear (Manford & Andermann, 1998). This article describes CBS in an 81-year-old woman who had an occipital lobe calcification consequent to central nervous system (CNS) infection and discusses possible pathophysiological mechanisms.

CASE REPORT

Patient, FA, is an 81-year-old right-handed female who had been treated for bacterial meningitis at the age of 36 years. During the illness, she had been in coma for 9 months. On recovery, she had some sensorineural hearing loss, weakness in her left leg and visual impairment. Though she was completely blind immediately following her illness, her vision gradually returned, but only to the extent of recognizing colour, shape, and movement at a close distance. Fifteen years after recovering from meningitis, she developed complex partial seizures characterized by episodes of staring and automatisms with secondary generalization followed by post-ictal lethargy. These were treated with phenytoin (300 mg/day), which was discontinued when she remained seizure free for the next ten years. Between the ages of approximately 61 to 75 years, no change was noticed in the patient's mental status.

From the age of 75 years onwards, FA's vision progressively deteriorated so that she could now perceive only movement at a distance of one foot and diffuse light-dark discrimination. This progressive diminution in vision was accompanied by sudden onset of complex and vivid visual hallucinations, which were more intense for the initial two months of the start of this second phase.
of visual impairment, but plateaued after her visual acuity became static. FA's hallucinations involved seeing small children (4-5 years of age) dressed in colourful clothes, men and women dressed in formal attire, people going up and down on elevator, and trees and other plants. These hallucinations occurred in the centre of her field of vision and lasted for hours at a stretch. They disappeared when FA closed her eyes and FA responded to them in a pleasant manner, even though she had some insight into the fact that she was hallucinating. During the hallucinations, no automatisms or postictal phenomena were noted and the content of the hallucinations was not related to past memories. Her neurological examination at that time was unremarkable other than weakness in her left leg, bilateral sensorineural hearing loss and reduced visual acuity (perception of light and movement in both eyes). Examination of fundi revealed bilateral optic atrophy secondary to her meningitis. No deficits in cognition were evident.

FA's clinical presentation met commonly used clinical criteria for Charles Bonnet syndrome (Gold & Rabins, 1989). A CT scan of the brain done at that time (approximately three months after the onset of hallucinations) revealed a circumscribed area of calcification measuring 2.1 x 1.6 cm in the left occipital lobe, occupying the entire primary visual cortex, including the occipital pole. This lesion was accompanied by encephalomalacia in the left occipital horn of the lateral ventricle with ex-vacuo dilatation. These findings most likely reflected the sequelae of possible meningitis/brain abscess that the patient had almost 40 years ago. Her EEG showed spike and slow wave complex at a single site in left temporal leads. In view of these findings, she was restarted on phenytoin. However, she never returned for follow-up and also discontinued the phenytoin. Meanwhile, her visual hallucinations continued unchanged and did not interfere with her activities of daily living.

Interestingly, FA returned five years after her initial consultation with a sudden one-day worsening of these hallucinations to the extent that she was preoccupied with them. She started talking with these images and pointing towards them, but did not display any ictal or post-ictal phenomena. A repeat brain CT scan showed no changes compared to previous scans other than volume loss associated with aging. Her visual acuity was unchanged, but her EEG showed more frequent temporal spikes compared to her last EEG. However, there were no features typical of her previous complex partial seizures. The patient was again started on phenytoin and her visual hallucinations decreased, but did not disappear entirely.

**DISCUSSION**

This case presents a complex interplay of factors that could have lead to visual hallucinations such as a decrease in visual acuity, aging, temporal lobe epilepsy, and a structural brain lesion. Decreased visual acuity and aging have been associated with CBS (Teunisse et al., 1995), but the peculiarity of this case was the appearance of visual hallucinations many years after the beginning of the visual impairment following meningitis. CBS in our patient occurred only with advanced age and the further deterioration in vision. Thus, advanced age may be a critical factor for the appearance of visual hallucinations of CBS. This may be partly explained by the observation that visual hallucinations have been reported to occur in elderly people even without visual impairment (Arya, 1995). Indeed, aging has been regarded as the 'cerebral factor' contributing to CBS by way of associated microvascular changes (Unni et al., 1996). However, evidence supporting advanced age, as the sole cause for hallucinations in CBS is not substantial and forces us to consider other explanations.

Temporal lobe epilepsy has been associated with complex visual hallucinations (Manford & Andermann, 1998) and patients have been known to respond to anticonvulsants (Bhatia et al., 1992). Our patient too had evidence to support epileptiform activity in her left temporal lobe. These seizure discharges may have contributed to the worsening of the hallucinations.
CHARLES BONNET SYNDROME: NEUROBIOLOGICAL INSIGHTS

during her most recent consultation as corroborated by the more abnormal EEG. However, these discharges could not entirely explain her clinical picture, as initially, when she actually had clinical seizures, these were not accompanied by visual hallucinations. Later when she developed visual hallucinations, there was not enough clinical evidence to suggest simultaneous complex partial seizures such as accompanying automatisms or post-ictal phenomena. Moreover, her hallucinations were continuous, non-fragmentary, not related to past memories and they lacked an affective component, which is not typical of visual hallucinations associated with temporal lobe epilepsy (Manford & Andermann, 1998). This leaves us to explore the final putative mechanism for visual hallucinations in CBS, namely the presence of a structural brain lesion.

Presence of lesions of occipital lobe have been previously reported in patients with CBS, but most of these cases are of cerebrovascular disease and neoplasms, and they usually are associated with visual hallucinations restricted to the hemianopic field which was not the case with this patient (Lance, 1976; Kolmel, 1985; Kishi et al., 1998; Kishi et al., 2000). A visual hallucination which always appears in the entire visual field rather than hemifield usually suggests stimulation of extra-striate areas (Kolmel, 1985). The circumscribed calcification encompassing most of the primary visual cortex in this patient provides an opportunity to consider this type of lesion as a possible factor contributing to the generation of visual hallucinations in CBS.

Brain calcification as a result of CNS infection, as in our patient, is known to develop over many years and can act as a focus for epileptiform discharges. Thus, the calcification in the striate cortex of our patient may have triggered the initial episodes of complex partial seizures, and later, with aging, the seizure activity could have spread to the neighbouring posterior parietal or temporal association areas, possibly due to a loss of inhibitory neurotransmission, as gamma-aminobutyric acid (GABA), the inhibitory neurotransmitter, is known to decrease in aging brains (Grachev & Apkarian, 2001). Taken together with the observation that pathological excitation of aforementioned areas, especially in the elderly, is documented to result in complex visual hallucinations (Manford & Andermann, 1998; Adachi et al., 2000), we can speculate that with advancing age, a lesion in the striate cortex might become a pathological excitatory focus for the brain regions responsible for complex visual hallucinations.

An alternative way in which this calcified lesion may have contributed to complex visual hallucinations is by way of "release phenomenon" (Gold & Rabins, 1989). Evidence suggests that visual hallucinations associated with lesions of occipital cortex may be caused by the release of visual association cortex because of loss of input from the primary visual cortex (Manford & Andermann, 1998). In addition, the presence of peripheral visual loss by way of optic atrophy could have further altered input to visual association areas through modulation of GABA in the primary visual cortex (Hendry & Jones, 1986). This possibility of complex visual hallucinations developing as a result of a "release" of visual association areas is also supported by the observation that in patients with cortical blindness, there is enhanced responsiveness of extra-visual areas, including increased activation of parietal cortex (Rausch et al., 2000).

To conclude, visual hallucinations of CBS may be the end result of multiple neurobiological aetiological factors such as brain changes occurring with aging, decreased visual acuity, subclinical seizure activity and structural brain changes, the latter two more applicable to patients with a demonstrable brain pathology. Of significant clinical importance is the observation that despite the presence of a demonstrable brain lesion and an abnormal EEG, age may independently demonstrate a threshold effect modulating the appearance of visual hallucinations of CBS possibly through changes at a cellular level.

REFERENCES

Adachi, N., Watanabe, T., Matsuda, H. & Onuma, T. (2000) Hyperperfusion in the lateral
temporal cortex, the striatum and the thalamus during complex visual hallucinations: SPECT findings in patients with Charles Bonnet syndrome. Psychiatry and Clinical Neurosciences, 54, 157-162.

Arya, D.K. (1985) Charles Bonnet syndrome. British Journal of Psychiatry, 167, 114-115.

Bhatia, M.S., Khastigir, U. & Malik, S.C. (1992) Charles Bonnet syndrome. British Journal of Psychiatry, 161, 409-410.

Fernandez, A., Lichtshein, G. & Vieweg, W.V.R. (1997) The Charles Bonnet syndrome: a review. Journal of Nervous and Mental Disease, 185, 195-200.

Gold, K. & Rabins, P.V. (1989) Isolated visual hallucinations and the Charles Bonnet syndrome: a review of the literature and presentation of six cases. Comprehensive Psychiatry, 30, 90-98.

Grachev, I.G. & Apkarian, A.V. (2001) Chemical network of the living human brain: evidence of reorganization with aging. Cognitive Brain Research, 11, 185-197.

Hendry, S.H. & Jones, E.G. (1986) Reduction in number of immunostained GABAergic neurones in deprived-eye dominance columns of monkey area 17. Nature 320, 750-753.

Kishi, T., Ishino, H. & Naganuma, R. (1998) Insight into phosphenes: a case with occipital lobe damage. General Hospital Psychiatry, 20, 260-261.

Kishi, T., Uegaki, J., Kitani, M., Fujimoto, A. & Naganuma, R. (2000) The usefulness of in Charles Bonnet syndrome: a case report with occipital lobe involvement. General Hospital Psychiatry, 22, 132-135.

Kolmel, H.W. (1985) Complex visual hallucinations in the hemianopic field. Journal of Neurology Neurosurgery and Psychiatry, 48, 29-38.

Lance, J.W. (1976) Simple formed hallucinations confined to the area of a specific visual field defect. Brain, 99, 719-734.

Manford, M. & Andermann, F. (1998) Complex visual hallucinations: clinical and neurobiological insights. Brain, 121, 1819-1840.

Rausch, M., Widdig, W., Eysel, U.T., Penner, I.K. & Tegenthoff, M. (2000) Enhanced responsiveness of human extravisual areas to photic stimulation in patients with severely reduced vision. Experimental Brain Research, 135, 34-50.

Teunisse, R.J., Cruysberg, J.R.M., Verbeek, A. & Zitman, F.G. (1995) The Charles Bonnet syndrome: a large prospective study in the Netherlands. British Journal of Psychiatry, 166, 254-257.

Unni, K.E.S., Venugopal, M., Gupta, S., Sudha Rani, R. & Patro, D.K. (1996) Management of Charles Bonnet syndrome in the elderly. Indian Journal of Psychiatry, 38, 265-268.