Of UFOs and other thoughts

P McCrory

I was recently whiling away a few joyful hours in transit in yet another anonymous airport on the way to another conference. After contemplating why in American airports it is physically impossible to get any sort of food that is capable of sustaining a healthy life, I felt the need to search for something to read. At a news stand, I found a copy of the Worst Case Survival Handbook (by Joshua Piven and David Borgenicht, Hardie Grant Books) to re-read. I was of course immediately taken by the instructions on how to foil an alien abduction. Some of you may think this is somewhat farfetched however I draw your attention to a recent survey that suggested 4 million Americans have been the victims of such events. Forearmed with that knowledge and with one eye looking for flying saucers, I was entranced.

Boxing

Cavum septi pellucidi—a reason to ban boxers?

P McCrory

There is no evidence that a cavum septum pellucidum correlates with neuropsychological or clinical abnormality.

INCIDENCE OF CAVUM SEPTI PELLUCIDI

The two leaves of the septum are separated in utero up to the 36 week stage of gestation.22 As the fetus approaches term, the persistence of the cavum decreases, so that only about one third of term infants maintain the fetal state.23 There is no clear information on the persistence of the cavum septum pellucidi in the general population at any time after the neonatal period.22,23 Corsellis et al24 reported an incidence of 3% in 500 adult brains from a psychiatric hospital population; however, Schwidde,25 in an unselected series of 1032 autopsies, found a cavum septum pellucidum in 20%, and Van Wagenen and Aird26 reported an incidence of 60% in their study of 30 adults. Imaging studies (discussed below) variously report cavum septum pellucidum incidence ranging between 0.7% and 37% (table 1).

NEUROPATHOLOGICAL STUDIES

Relatively few detailed studies of neuropathological changes in ex-boxers have been performed.24,26–28 There have been a number of individual case reports with varying amounts of clinical and pathological information provided.24,26 In only one of these case reports was a cavum septum pellucidum noted.24 Payne studied six boxers, all of which had a cavum septum (with fenestrations noted in three).24 He assumed that the septal abnormalities were a secondary consequence of the enlarging ventricles. The largest of the studies, by Corsellis et al,29 examined 15 ex-boxers (12 professional) whose brains had been collected in a pathology department brain bank and their boxing and social history sought retrospectively. These boxers had fought in the period 1900–1940; eight were national or world champions in their weight division. One of the striking features was their extraordinarily high exposure to boxing. The number of bouts fought ranged from 400 to 700+, with many also fighting in fairground boxing booths (up to 30–40 fights per day over a number of years). In this study, Corsellis et al detailed a number of neuropathological features that have become the sine qua non of chronic traumatic encephalopathy. These included:

1. abnormalities of the septum pellucidi;
2. cerebellar and other scarring of the brain;
3. substantia nigral degeneration;
4. regional occurrence of neurofibrillary tangles (these have been subsequently shown to be ubiquinated tangles that have tau immunoreactivity21,30).

With regard to the septal abnormalities, a cavum was noted in 12/13 brains (two brains having an intraventricular haemorrhage that made determination of primary septal abnormalities impossible). The maximum coronal width ranged from 1 to 8 mm (mean 5.2 mm). In 11/13 cases, the cavum showed pronounced fenestration, and in most only a “few thin tags” remained. The cavum in boxers was described as having a characteristic appearance with not only fenestration but with detachment of the fornix from the undersurface of the corpus callosum, with the two flattened fornical bodies splaying out horizontally over the dorsal surface of the thalamus. The body of the corpus callosum was often thinned as well.

Corsellis et al also speculated on the mechanism of cavum formation. Payne24 had suggested that passive ventricular enlargement stretches the leaves of the septum apart. Mawdsley and Ferguson31 invoked the concept of repeated sudden rises in intraventricular pressure leading to rupture of the septal leaves. Corsellis et al felt that, because the dorsal attachment of the septum is relatively thin and fragile, repeated head blows strain the dorsal septal attachment because of the repeated movements of the corpus callosum on the tethered fornix. He felt that once this process has been initiated, then ventricular enlargement stretches the septum and the fenestrations enlarge.

RADIOLOGICAL STUDIES

Pneumoencephalographic evidence

The presence of a cavum septum pellucidi was first noted by Spillane32 who described five retired professional boxers who developed a chronic neurological problem in later life. He described in detail the clinical and pneumoencephalographic findings in these boxers and noted incidentally the presence of a cavum septum pellucidum in two of the boxers. Interestingly all of the boxers had a high exposure, with none having less than 200 bouts. One of the boxers had also gone on to fight in fairground boxing booths, having 30–40 fights per day for several years.

This work was expanded by Mawdsley and Ferguson33 and Isherwood et al34 who analysed pneumoencephalographic changes in 16 boxers. Of the 12 boxers with evidence of cortical atrophy, eight had a cavum septum pellucidum. Unfortunately little clinical information or boxing exposure was reported which would have enabled more detailed analysis. Finke et al35 reported an incidence

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Table 1: Incidence of cavum septi pellucidi (CSP) in various studies

<table>
<thead>
<tr>
<th>Type of evidence</th>
<th>CSP incidence (%)</th>
<th>Reference</th>
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<td>Neuroradiology</td>
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<td>3 4 7</td>
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<td></td>
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<td>49 49</td>
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19th century. In the modern era, the association of a cavum septum pellucidi and boxers was first incidentally noted by Spillane.32,33

The septum pellucidi rostrally forms the medial wall of the bodies of the lateral ventricles. The posterior margin is the fornix and the rostral and superior limits are formed by the corpus callosum. The septum consists of two leaves of glial tissue with both white and grey matter components, connected by the medial forebrain bundle to the hippocampus and through the fornix to the limbic system. In coronal section, the two leaves are usually fused or contiguous in adults. If they remain separated, then the closed space between them anteriorly is known as a cavum septum pellucidum, and posteriorly to the fornix as a cavum vergae. Such cavum will communicate with the ventricular system only when their leaves are ruptured or fenestrated and it is therefore inappropriate to use the term “fifth” and “sixth” ventricles for these structures. In addition, the cava have a different embryonic development from the ventricular system and are not lined by ependymal cells. The role of the septum is relatively thin and fragile, repeated head blows strain the dorsal septal attachment because of the repeated movements of the corpus callosum on the tethered fornix. He felt that once this process has been initiated, then ventricular enlargement stretches the septum and the fenestrations enlarge.

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cavum septum pellucidum of up to 37% from pneumoencephalographic studies.

**Computed tomography (CT) evidence**

Harvey and Davis described a young boxer with chronic traumatic encephalopathy having had only 100 fights (25 as a professional). CT scanning showed ventricular enlargement which was confirmed by pneumoencephalography. A cavum septum pellucidum was also noted. There have also been a number of case series of active and/or retired boxers with a variety of minor radiological findings reported. In the study by Ross et al of 38 ex-boxers, 70% of the CT scans were normal. There was no correlation between the number of bouts or the number of knockouts with the radiological findings. It has also been questioned whether the abnormal CT scan findings noted in the older boxers were a manifestation of the normal ageing process rather than changes caused by boxing. A similar finding was noted in a study of amateur boxers in which neuropsychological function before and after a fight showed no significant differences. CT scans were performed one week after the fight; however, the results were not discussed in the paper.

“Boxers with a cavum septum pellucidum were more likely to have cerebral atrophy”

The largest study of CT scans in boxers is that of Jordan et al, who reported the findings in 388 active professional boxers. CT was normal in 93% and showed “borderline” atrophy in 6%. Boxers with a cavum septum pellucidum (14%) were more likely to have cerebral atrophy.

Bogdanoff et al reported the presence of a cavum septum pellucidum as a manifestation of chronic traumatic encephalopathy; however, this study has severe methodological problems. In their study of 1914 consecutive patients, only five had been boxers. Three of these boxers had been referred for cerebral imaging for investigation of a chronic neurological condition.

A contrary finding was noted by MacPherson and Teasdale. In 1000 consecutive patients seen at a neurosurgical trauma centre, they identified a cavum septum pellucidum in 5.5% of subjects. They concluded that the presence of an isolated cavum septum pellucidum almost certainly represents a persistent congenital anomaly of no clinical significance, and, apart from regular observation, this finding alone should not affect a boxer’s career.

**Magnetic resonance imaging (MRI) evidence**

One of the earliest studies using MRI in boxers was by Cabanis et al. They examined 12 active and 40 retired boxers (13 amateur, 39 professional). A cavum septum pellucidum was noted in two boxers only. Cerebral atrophy was noted in eight, and the mamillary bodies and optic chiasm was described as small in 30. No correlative clinical data were presented, and, given that this was in the early days of MRI using a 0.15 T scanner with 9 mm slices, technical limitations are likely to limit any conclusions that may be drawn from their findings.

“No clear relation between boxing exposure and radiological findings was noted”

Levin et al and Jordan and Zimmerman each studied nine amateur boxers and found no abnormal MRI findings. Jordan and Zimmerman subsequently examined 21 active boxers (16 professional) and one retired professional boxer. Most of both the CT and MRI studies were normal; however, the authors emphasised the superiority of MRI over CT as an imaging modality and its usefulness in delineating equivocal CT abnormalities. No clear relation between boxing exposure and radiological findings was noted.

A Swedish study comparing 22 experienced amateur boxers (mean number of bouts 54) with age matched soccer playing and athletic controls was performed. No significant difference was observed between the groups. Only two boxers had a cavum septum pellucidum, as did one footballer and three track athletes.

Other prospective studies such as those by Holzgrafe et al and Butler et al did not find any specific MRI abnormalities related to boxing. Another finding reported in autopsy studies of retired boxers was superficial siderosis of the cerebellum. Although this should be detectable using MRI, no case reports exist in which this condition has been noted.

To date radiological imaging has been unsuccessful in finding any systematic evidence of brain injury in boxers. Early anecdotal reports have not been validated using newer technologies. Clearly there are considerable differences in MRI techniques, patient positioning, slice thickness, and magnet strength, all of which may influence the findings.

One of the abnormalities that has been reported to be of significance in earlier neuropathological studies is a cavum septum pellucidum. The finding of this abnormality varies between 0.7% and 37% using various radiological techniques; however, this finding does not correlate with either clinical or neuro-psychological deficits nor with boxing exposure (table 1).

**Magnetic resonance spectroscopy**

Magnetic resonance spectroscopy has been reported in ex-boxers with parkinsonism showing a reduction of N-acetylaspartate in the lentiform nucleus and is thought to indicate neuronal loss. One of three boxers studied in this fashion has a cavum septum pellucidum. The specificity of this technique is not known at this time.

**Radionuclide studies**

A study reported cerebral blood flow measurements in a small cohort of amateur and professional boxers. The professional boxers were reported to have significant reductions in cerebral blood flow over the cortex, particularly in the parietal and temporal lobes. Another study of cerebral blood flow using HMPAO SPECT was performed in 42 amateur boxers from the armed services. There was no correlation between SPECT abnormalities and neuropsychological test performance or number of bouts fought. The relation of cavum septi pellucidi to the putative cerebral blood flow abnormalities was not discussed in either study.

**CHANGES IN CAVUM SEPTUM PELLUCIDUM ON SERIAL IMAGING**

An early study examining the change in size of ventricles was performed using pneumoencephalography. In this study, two patients with cavum septum pellucidum were noted, and more importantly the size and structure of the cavum varied from day to day. About one third of patients undergoing pneumoencephalography were noted to have “bulges” in the septum pellucidum toward the ventricles between examinations including one patient in whom this change was noted over five minutes. This suggests that the septum, with or without a cavum septum pellucidum, is not a rigidly fixed structure and may vary between examinations.

Only one study has been published of the findings of serial CT scanning in active boxers. In this study, 45 professional boxers in New York State had serial CT scans with a mean duration between scans of 31 months. Six (13%) showed evidence of “progressive brain injury”, with three displaying progressive cortical atrophy (one with bilateral parieto-occipital encephalomalacia), and
three developing a cavum septum pellucidum on the repeat scans. The progressive CT changes were associated with losing more than 10 fights. No report of changes in previously documented cavi were noted.

CONCLUSIONS

The presence of a cavum septum pellucidum is a common and usually incidental finding on neuroimaging or neuropathological studies. In limited autopsy studies of boxers with extreme boxing exposure—for example, 400–900 bouts—a number of abnormalities have been noted that form part of a constellation of the pathological changes of dementia pugilistica. One of these features is a fenestrated cavum septum pellucidum. Despite this pathological evidence, imaging studies using pneumoecephalography, CT, and MRI have failed to show consistent imaging abnormalities that correlate with this clinical state. Newer imaging modalities using high field MRI, diffusion tensor imaging, and measures of cortical atrophy may hold promise in the future if applied prospectively to this population.

SUMMARY

● The actual incidence of a cavum septum pellucidum in the adult population is not known but varies between 0.7% and 60% depending on the study cited.

● The presence of an isolated cavum septum pellucidum is unlikely to be of clinical importance and should not preclude a boxer from taking part in his or her sport. There is no evidence that a cavum septum pellucidum necessarily correlates with neuropsychological or clinical abnormalities or boxing exposure.

● The cavum septum pellucidum abnormality noted in the neuropathological studies as being suggestive of dementia pugilistica is fenestrated as well as being associated with fornical abnormalities. A cavum septum pellucidum with intact walls is not a diagnostic finding of this condition.

● Very limited published evidence suggests that a cavum septum pellucidum may vary in morphology between examinations; however, the new development or serial enlargement of a cavum septum pellucidum on neuroimaging studies suggest the early development of dementia pugilistica particularly if associated with other evidence of boxing related neurotrauma. Insufficient prospective studies have been published to confirm this finding.

● There is no compelling evidence at this time that routine MRI (or other) neuroimaging will detect early evidence of chronic damage in boxers. Prospective studies are required to answer this question using more sophisticated imaging protocols.


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REFERENCES


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REFERENCE