

NEUROPSYCHIATRIC MANIFESTATIONS OF COLLOID CYSTS: A REVIEW OF THE LITERATURE

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SUMMARY

Colloid cysts account for approximately 2% of primary brain tumours and the majority of cases are identified in the fourth and fifth decade. They are small, gelatinous neoplasms lined by a single layer of mucin-secreting columnar epithelium that are thought to arise from errors in folding of the primitive neuroepithelium. They develop in the rostral aspect of the third ventricle in the foramen of Monro in 99% of cases and despite their benign histology carry a poor prognosis, with a mortality greater than 10% in symptomatic cases.

The location of colloid cysts within the ventricular system results in obstruction of the foramen of Monro as the cyst grows, disrupting the circulation of cerebrospinal fluid (CSF) and causing hydrocephalus. This is the mechanism behind the most common presenting symptoms of postural headache, nausea and vomiting - a clinical picture synonymous with hydrocephalus and intracranial pathology.

In addition to these classical neurological symptoms, there is a high prevalence of psychiatric symptoms in the patient population, with symptoms ranging from anterograde amnesia to gustatory hallucination. These symptoms can occur with or without the presence of hydrocephalus, and are thought to be secondary to compression of connecting pathways between the mesocortices and subcortical limbic regions. These symptoms have been shown to be comparative in frequency to the classical symptoms, yet are rarely the reason for referral to a neurological or neurosurgical service for investigation.

Key words: colloid cyst - psychosis

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INTRODUCTION

The colloid cyst was first described by Wallmann in 1858 in a patient presenting with gait ataxia and incontinence (Wallmann 1858). It was 64 years later that William Dandy performed the first successful surgical resection of such a lesion, located in the 3rd ventricle (Dandy 1922).

Since these early cases, there has been great development in our understanding of the pathophysiology of colloid cysts.

In keeping with the findings of Dandy and Wallmann, colloid cysts are now understood to be primary brain tumours that arise in the ventricular system. In the vast majority of cases (99%) they develop at the dorsal aspect of the foramen of Monro, presenting in the 4th and 5th decades of life. This position within the ventricular system means the cysts are liable to compress the foramen of Monro and disrupt the normal circulation of cerebrospinal fluid (CSF) as they enlarge, causing hydrocephalus. In addition to this mechanism, colloid cysts may also directly compress periventricular structures resulting in a separate set of neurological sequelae, with psychiatric symptoms dominating.

The symptoms of hydrocephalus are well recognised by physicians as being synonymous with intracranial pathology, and invariably result in prompt referral to neuroimaging services. By contrast, psychiatric symptoms are not specific to one type of pathology and investigation and treatment are thus more likely to take a protracted course, with referral to psychiatric services commonly taking place prior to a full diagnostic work-up for organic causes of the symptoms. Colloid cysts carry a poor prognosis once symptomatic (de Witt Hamer 2002) and as such prompt diagnosis, facilitated by a clear understanding of their histology, neuroanatomy and variety of clinical presentation is crucial.

ANATOMY

Ventricular system

The ventricular system of the brain consists of four ventricles (paired lateral, a third and a fourth), which produce cerebrospinal fluid (CSF), connected by foramina. The lateral ventricles connect to the midline third ventricle via the foramina of Monro, with fluid passing from the third to the fourth via the aqueduct of Sylvius. From here fluid passes into the subarachnoid space via

the midline foramen of Luschka and the paired foramina of Magendie. The vast majority of colloid cysts develop just posterior to the foramen of Monro.

Histology

Colloid cysts consist of various components. An outer fibrous capsule lies over an inner epithelium, which is most often a layer of ciliated epithelium and mucin-producing goblet cells. This results in the cyst containing a mucoid substance, which stains positive for mucicarmen. This is the main constituent of the cyst and its volume will be the mainly determined by the amount of mucoid material present. This goes some way to explaining the variability in the size of colloids cysts, which can be between 2 and 50 millimetres in diameter. The fact that they are rarely seen in children indicates that they must enlarge with time (Gontier 2000). The origin of colloid cysts continues to be uncertain. Hypotheses include diencephalic ependymoma, and invagination of the neuroepithelium of the ventricles (Javed 2014).

PRESENTATION AS EXPLAINED BY NEUROANATOMY

Colloid cysts with associated hydrocephalus

As colloid cysts enlarge they may partially obstruct the foramen of Monro, causing obstructive hydrocephalus and dilatation of the lateral ventricles. This will result in the classical symptoms of hydrocephalus, most commonly headache with postural component, nausea, vomiting and decreased conscious level. In addition to these classical symptoms, there are several reported cases of hydrocephalus secondary to colloid cysts which have presented chiefly with psychiatric symptoms, for example progressive dementia, that have resolved on removal of the colloid cyst (Jones 1993, Lobosky 1984).

The psychiatric symptoms caused by dilatation of the lateral ventricles can be explained by their adjacent structures. The lateral ventricles lie in the cerebrum and can be divided into a central portion and 3 horns (frontal, temporal and occipital):

- The central portion is located in the parietal lobe, with its roof formed by the corpus callosum and the anterior body of the fornix forming part of its floor.
- The occipital horn is located within the occipital lobe.
- The frontal horn is bound inferiorly and laterally by the head of the caudate nucleus, with the corpus callosum forming its roof and anterior border.
- The temporal horn is located within the temporal lobe and its medial wall and its floor are formed by the hippocampus and its associated structures.

Of these structures, compression of the hippocampal formation and fornix by the dilated lateral ventricles may explain the development of progressive dementia. These medial temporal lobe structures are particularly important in the encoding of new memory, especially episodic (the recollection of personally experienced

events). For example, the widely studied patient Henry Molaison suffered severe anterograde amnesia after a bilateral medial temporal lobe resection in 1953 that included the hippocampal formation and most of the amygdaloid complex and entorhinal cortex (Smith 2007). A review of 147 cases of patients with damage to the hippocampus and fornix has also shown that this can lead to impaired anterograde semantic memory (memory for facts) and a variable temporal gradient of retrograde amnesia (Spiers 2001).

Colloid cysts without associated hydrocephalus

There have been cases of patients presenting with psychiatric symptoms caused by colloid cysts without evidence of hydrocephalus. Lobosky et al and Javed & Dutta presented cases of patients presenting with symptoms including hypomania, paranoid delusions, memory loss and anxiety attacks (with tachycardia, tachypnoea and diaphoresis) that improved after operative removal of the colloid cyst (See table 1). Lobosky et al suggested that these symptoms could be caused by direct pressure on the structures surrounding the third ventricle. This theory is supported by cases of patients with colloid cysts who develop complex neuropsychiatric symptoms as a consequence of damage to structures surrounding them during surgery (Hodges 1991, Aggleton 2000, Brand 2004, Poreh 2006, Tsivilis 2008 - see table 2)

The third ventricle lies in the diencephalon and the structures that surround it are the medial thalamus and hypothalamus laterally, the fornix and corpus callosum superiorly and the infundibulum inferiorly, which attaches mammillary bodies to the upper end of the mid-brain. These structures are important components of the putative limbic system, an interconnected network of cortical and subcortical areas involved in visceral and autonomic processes. Cortical structures including the hippocampal formation and cingulate gyrus are connected by pathways (fimbria-fornices and mammillary bodies) to subcortical regions such amygdala, nucleus accumbens, hypothalamus and anterior thalamic nucleus.

In terms of the symptoms experienced by patients, the hypomania and delusions could be linked to dysfunction of both the nucleus accumbens, which forms part of the dopaminergic pathway associated with pleasurable stimuli and delusions and hallucinations (Olds 1954, Pankow 2012), and the amygdala, which plays a key role defining a stimulus and how to respond appropriately (Pessoa 2010). Specific lesions of the connections involving the mammillary bodies and mamillo-thalamic tract have been shown in monkeys to produce the same amnesic pattern as medial temporal lobe damage (Graff-Radford 1990). Finally Damasio has shown that lesions affecting the periventricular and cortical limbic areas can cause emotional disturbances (Damasio 1983). Damage to the hypothalamus could result in anxiety attacks with physiological abnormalities as it provides connections to the anterior and posterior pituitary gland, the autonomic nervous system and the reticular formation (Figure 1).

Table 1. A summary of case reports where neuropsychiatric symptoms are the main presenting feature of a colloid cyst

Study	Presentation	Findings	Outcome
Radley-Smith EJ. 1955 - case series	1. 42 year old male with Progressive deterioration of intellect; laziness, apathy, dementia & incontinence.	Dilated lateral ventricles, 3 rd ventricle cyst with obstruction of foramen of Monro	Died four days following removal
	2. 60 year old male with laziness, somnolence & incontinence.	Dilated lateral ventricles, colloid cyst blocking the foramen of Monro	Rapid deterioration and death prior to surgery
Lobosky JM. 1984 - case series	1. 64 year old female with progressive memory defects, confabulation & anterograde amnesia	Dilated lateral ventricles, 2cm colloid cyst.	Improvement of all symptoms after removal
	2. 33 year old male with 8 year history of anxiety attacks consisting of agitation, chest pain, diaphoresis, tachycardia, tachypnoea and sense of doom.	2cm colloid cyst in the anterior 3 rd ventricle. No hydrocephalus.	Resolution of anxiety
	3. 28 year old female with 2 year history of worsening amnesia paranoia, depression and social withdrawal.	2cm colloid cyst in the 3 rd ventricle. No hydrocephalus	Resolution following removal until relapse 12 months later
Winer RI. 1985	67 year old female with 1-year history of confusion and anterograde amnesia	Colloid cyst of the third ventricle. No hydrocephalus.	No procedure offered.
Upadhyaya AK. 1988	42 year old female with erotomanic and persecutory delusions, delusions of reference, depression and guilt	Colloid cyst of anterior 3 rd ventricle with lateral ventricle dilatation	Resolution of symptoms post-removal (with the aid of pharmacotherapy)
Faris AA & Terrence CF. 1989	46 year old male with olfactory and gustatory hallucinations	3 rd ventricular colloid cysts without hydrocephalus	Resolution following stereotactic aspiration
Jones AM. 1993	42 year old female with labile mood, restlessness, insomnia, poor concentration and self-neglect	3 rd ventricle colloid cyst with minimal hydrocephalus	Complete resolution following removal
Ferrera PC & Kass LE. 1997	65-year old with 1-year history of anterograde amnesia	3 rd ventricular colloid cyst	Resolution but hemiparesis post surgery
O'Neill of Tyrone A & Fernandez JM. 2000	29 year old female with multiple episodes of dissociative states.	Colloid cyst obstructing the foramen of Monro causing lateral ventricle dilatation	Resolution following V-P shunting
Lajara-Nanson WA. 2000	48 year old male with personality change, mood disturbance, sexual disinhibition and paranoid ideation.	3 rd ventricular colloid cyst without hydrocephalus	Resolution of sexual disinhibition only
Grabsu, BL & Alberico AM. 2011	41 year old male with anterograde amnesia, personality change and paroxysmal headache.	Colloid cyst obstructing foramen of Monro causing dilated lateral ventricles	Resolution of symptoms following microsurgical resection
Bhatia MS et al. 2013	24 year old female with recurrent mania	Colloid cyst obstructing foramen of Monro causing dilated lateral ventricles	Complete resolution of symptoms six months post operatively
Champeaux C & Grivas A. 2015	46 year old female with confusion and visual loss post-seizure	Colloid cyst obstructing foramen of Monro causing dilated lateral ventricles	Symptoms remained post-excision



Figure 1. Diagrammatic representation of colloid cysts with (left) and without (right) associated hydrocephalus

Table 2. A summary of studies showing the neuropsychiatric effects of colloid cyst removal

Study	Procedure Details	Outcome
Hodges JR & Carpenter K. 1991	Two patients underwent transcallosal-transventricular removal of 3 rd ventricular colloid cysts.	Isolated anterograde amnesia following damage to the fornical columns.
Aggleton JP et al. 2000	Three patients who underwent resection of colloid cysts via right frontal, transcallosal and left transfrontal approaches respectively	These patients developed anterograde amnesia. MRI evaluation showed fornix damage in these patients.
Brand M et al. 2004	Microsurgery via right frontal transventricular approach	Depression and executive dysfunction
Poreh A et al. 2006	Removal of colloid cyst via right frontal transcortical approach	Retrograde and anterograde amnesia with bilateral fornix lesions
Tsivilis et al. 2008	Study of 38 individuals following cyst removal.	Study showed significant correlation between mammillary body and fornix volume and episodic memory recall. There was no correlation with recognition memory.

INVESTIGATION AND MANAGEMENT

Colloid cysts can be visualised using Computerised Tomography (CT) and Magnetic Resonance (MR) imaging. The cysts have a characteristic appearance as circular well-demarcated lesions, most frequently located in the third ventricle. Cyst density varies from hypo to hyperdense on both CT and MR images, with MRI demonstrating areas of heterogeneity within an individual cyst. The heterogeneous appearance was originally postulated as due to paramagnetic ion concentration but this has subsequently shown to not be the cause. The radiological density of the cyst is related to cholesterol content of cyst fluid and is clinically relevant as iso/hypodense cysts are associated with successful needle aspiration (Maeder 1990). The more viscous hyperdense

cysts are difficult to drain and often require further neurosurgical intervention (Kondziolka 1991).

Treatment of colloid cysts further depends on both size of the lesion and the symptoms experienced by the patient. Smaller cysts, usually those less than 1cm, can be monitored with imaging whilst intervention is reserved for patients with sizeable symptomatic cysts. Surgical management includes stereotactic aspiration and either endoscopic or microsurgical resection.

Microsurgical resection, involving a craniotomy, can be carried out using a transcortical or transcallosal approach, with each route having its own disadvantages. Endoscopic intervention negates the need for craniotomy and instead uses a burr-hole to gain access. Bimanual dissection can be achieved with a dual port endoscopic technique (Bergsneider 2007). Several

groups have sought to compare outcomes between endoscopic and microsurgical intervention (Sheikh 2014). Of note, mortality and neurological outcomes do not differ significantly between the two treatment groups. Morbidity, including infection rate, need for VP shunt, haematoma and infarction is higher in the craniotomy group, whilst recurrence rate is significantly lower. Currently there is no agreed consensus over which technique to use as first-line (Horn 2007).

CONCLUSION

Large retrospective studies of 3rd ventricular neoplasms have shown psychiatric symptoms to be comparable in frequency to the classical symptoms of an intracranial mass. This review has highlighted the key neuroanatomical structures involved in this symptomatology, both in the presence and absence of hydrocephalus.

Psychiatric symptoms remain an uncommon reason for referral to neurosurgical or neurological services in this patient group. Given the high frequency of psychiatric symptoms and the poor prognosis of symptomatic colloid cysts, it is vital that clinicians have an in depth and up-to-date knowledge of the organic causes of psychiatric disturbance if we are to optimise outcomes for these patients.

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References

1. Aggleton JP, McMackin D, Carpenter K, et al: *Differential Cognitive Effects of Colloid Cysts in the Third Ventricle That Spare or Compromise the Fornix. Brain: a Journal of Neurology* 2000; 123:800-815. doi:10.1093/brain/123.4.800.
2. Bergsneider M. *Complete microsurgical resection of colloid cysts with a dual-port endoscopic technique. Neurosurgery* 2007; 60(Suppl 1):33-42,42-43. doi:10.1227/01.NEU.0000249227.82365.36.
3. Bhatia MS, Srivastava S, Jhanjee A, Oberoi A: *Colloid cyst presenting as recurrent mania. J Neuropsychiatry Clin Neurosci* 2013; 25:E01-E02. doi:10.1176/appi.neuropsych.11110352.
4. Brand M, Kalbe E, Kracht LW, et al: *Organic and psychogenic factors leading to executive dysfunctions in a patient suffering from surgery of a colloid cyst of the Foramen of Monro. Neurocase* 2004; 10:420-425. doi:10.1080/13554790490894002
5. Champeaux C, Grivas A. *Teaching NeuroImages: Cortical blindness following acute obstructive hydrocephalus by a colloid cyst. Neurology* 2015; 84:e41-e42. doi:10.1212/WNL.0000000000001229.
6. Dandy WE: *Diagnosis, localization and removal of tumours of the third ventricle. Bull Johns Hopkins Hosp* 1922; 33:188–9.
7. Damasio AR, Van Hoesen GW: *Emotional disturbances associated with focal lesions of the limbic frontal lobe. in: K.M. Heilman, P. Satz (Eds.) Neuropsychology of Human Emotion. Guilford Press, New York, 1983; 85–110.*
8. de Witt Hamer PC, Versteegen MJT, De Haan RJ, et al: *High risk of acute deterioration in patients harboring symptomatic colloid cysts of the third ventricle. J Neurosurg* 2002; 96:1041-1045. doi:10.3171/jns.2002.96.6.1041
9. Faris AA, Terrence CF: *Limbic System Symptomatology Associated with Colloid Cyst of the Third Ventricle. Journal of neurology* 1989; 236:60-61. doi:10.1007/BF00314222
10. Ferrera PC, Kass LE: *Third ventricle colloid cyst. Am J Emerg Med* 1997; 15:145-147. doi:10.1016/S0735-6757(97)90086-3
11. Gontier MF: *Pathological anatomy of tumors of the third ventricle. Neurochirurgie.* 2000; 46:257-267. doi:MDOI-NCHIR-06-2000-46-3-00283770-101019-ART15 [pii]
12. Graff-Radford NR, Tranel D, Van Hoesen GW, Brandt JP: *Diencephalic Amnesia. Brain: a Journal of Neurology* 1990; 113:1-25. doi:10.1093/brain/113.1.1
13. Grasu BL Alberico AM: *Colloid cyst: a case report. W V Med J* 2015; 107:18-19. <http://www.ncbi.nlm.nih.gov/pubmed/22034805>. Accessed June 21, 2015
14. Hodges JR, Carpenter K: *Anterograde Amnesia with Fornix Damage Following Removal of IIIrd Ventricle Colloid Cyst. Journal of neurology, neurosurgery, and psychiatry* 1991; 54:633-638. doi:10.1136/jnnp.54.7.633
15. Horn EM, Feiz-Erfan I, Bristol RE, et al: *Treatment options for third ventricular colloid cysts: Comparison of open microsurgical versus endoscopic resection. Neurosurgery* 2007; 60:613-618. doi:10.1227/01.NEU.0000255409.61398.EA
16. Javed Q, Dutta A: *Third Ventricular colloid cyst and organic hypomania. Prog Neurol Psychiatry* 2014; 18. doi:10.1002/pnp.355
17. Jones AM: *Psychiatric presentation of a third ventricular colloid cyst in a mentally handicapped woman. Br J Psychiatry* 1993; 163: 677-678. doi:10.1192/bjp.163.5.677.
18. Kondziolka D, Lunsford LD: *Stereotactic management of colloid cysts: factors predicting success. J Neurosurg* 1991; 75:45-51. doi:10.3171/jns.1991.75.1.0045.
19. Lajara-Nanson WA: *Neuropsychiatric Manifestations of a Third Ventricular Colloid Cyst. The West Virginia medical journal* 2015; 96:512-513. <http://www.ncbi.nlm.nih.gov/pubmed/10986924>. Accessed June 21, 2015
20. Lobosky JM, Vangilder JC, Damasio AR: *Behavioural Manifestations of Third Ventricular Colloid Cysts. Journal of neurology, neurosurgery, and psychiatry* 1984; 47:1075-1080. doi:10.1136/jnnp.50.9.1244-a
21. Maeder PP, Holtås SL, Basibüyük LN, Salford LG, Tapper UA, Brun A: *Colloid cysts of the third ventricle: correlation of MR and CT findings with histology and chemical analysis. AJNR Am J Neuroradiol* 1990; 11:575-581.
22. Olds J, Milner P: *Positive reinforcement produced by electrical stimulation of septal area and other regions of rat brain. J Comp Physiol Psychol* 1954; 47:419-427. doi:10.1037/h0058775.
23. O'Neill of Tyrone A, Fernandez JM: *Dissociative Disorder Associated with a Colloid Cyst of the Third Ventricle: Organic or Psychogenic Amnesia? Psychotherapy and psychosomatics* 69:108-109. doi:12374.
24. Pankow A, Knobel A, Voss M, Heinz A: *Neurobiological correlates of delusion: Beyond the salience attribution*

- hypothesis. *Neuropsychobiology* 2012; 66:33-43. doi:10.1159/000337132
25. Pessoa L: Emotion and cognition and the amygdala: from “what is it?” to “what’s to be done?”. *Neuropsychologia* 2010; 48:3416-3429. doi:10.1016/j.neuropsychologia.2010.06.038
26. Poreh A, Winocur G, Moscovitch M, et al: Anterograde and retrograde amnesia in a person with bilateral fornix lesions following removal of a colloid cyst. *Neuropsychologia* 2006; 44:2241-2248. doi:10.1016/j.neuropsychologia.2006.05.020
27. Radley-Smith EJ: Colloid cyst of the third ventricle. *Proc R Soc Med* 1955; 48:602-603.
28. Sheikh AB, Mendelson ZS, Liu JK: Endoscopic versus microsurgical resection of colloid cysts: a systematic review and meta-analysis of 1,278 patients. *World Neurosurg* 2014; 82:1187-1197. doi:10.1016/j.wneu.2014.06.024
29. Smith E & Kosslyn S: *Cognitive Psychology: Mind and Brain*. New Jersey: Prentice Hall. pp. 21. 194-199.
30. Spiers HJ, Maguire EA, Burgess N: Hippocampal amnesia. *Neurocase* 2001; 7:357-382. doi:10.1076/neur.7.5.357.16245
31. Tsivilis D, Vann SD, Denby C, et al: A disproportionate role for the fornix and mammillary bodies in recall versus recognition memory. *Nat Neurosci* 2008; 11:834-842. doi:10.1038/nn.2149
32. Upadhyaya AK, Sud PD: Psychiatric presentation of third ventricular colloid cyst. A case report. *Br J Psychiatry* 1988; 152:567-569. doi:10.1192/bjp.152.4.567
33. Wallmann H: Eincolloidcysteimdrillen Hirnventrikel und ein Lipomim plexus Choroides. *Virchows Arch Pathol Anat* 1858; 14:385–8.
34. Winer RI: Behavioral manifestations of third ventricular colloid cysts. *J Neurol Neurosurg Psychiatry* 1985; 48:847.

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