Natural history of asymptomatic colloid cysts of the third ventricle

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Object. To determine the natural history of colloid cysts of the third ventricle in patients in whom the cysts were incidentally discovered, the authors retrospectively reviewed cases observed during the modern neuroimaging era (1974–1998).

Methods. During this 25-year interval, 162 patients with colloid cysts were examined and cared for at our center. Sixty-eight patients (42%) were thought to be asymptomatic with regard to their colloid cyst and observation with serial neuroimaging was recommended. The mean patient age was 57 years at the time of diagnosis (range 7–88 years) and the mean cyst size was 8 mm (range 4–18 mm). Computerized tomography scanning revealed a hyperdense cyst in 49 (84%) of 58 patients. Three patients were excluded from the study because they died of unrelated causes within 6 months of scanning and seven patients were lost to follow-up review. Clinical follow-up evaluation was available at a mean of 79 months (range 7–268 months) in the remaining 58 patients. The numbers of patients who participated in follow-up review at 2, 5, and 10 years after diagnosis were 40, 28, and 14, respectively. The incidences of symptomatic progression related to the cyst were 0%, 0%, and 8% at 2, 5, and 10 years, respectively. No patient died suddenly during the follow-up interval. Two (6%) of 34 patients in whom follow-up imaging was performed either exhibited cyst growth (one patient) or experienced hydrocephalus (one patient) at a mean of 41 months after diagnosis (range 4–160 months).

Conclusions. Patients in whom asymptomatic colloid cysts are diagnosed can be cared for safely with observation and serial neuroimaging. If a patient becomes symptomatic, the cyst enlarges, or hydrocephalus develops, prompt neurosurgical intervention is necessary to prevent the occurrence of neurological decline from these benign tumors.

KEY WORDS • brain neoplasm • colloid cyst • natural history

The optimum management of cases of colloid cysts of the third ventricle remains unclear. A recent population-based study conducted over a 14.5-year period found a yearly incidence of 3.2 colloid cysts per 1,000,000 people.16 Previously, the histogenesis of colloid cysts was believed to be neuroepithelial;19 however, more recent studies have concluded that they are endodermally derived.17,23,26 Although the majority of patients who harbor colloid cysts typically present with a history of headaches lasting days to years,42 sudden neurological decline related to the blockage of cerebrospinal fluid flow (CSF) at the level of the foramen of Monro has been well established.3,4,6,8,16,24,25,27,30,38 Although neurosurgeons frequently debate the merits of various operative approaches for symptomatic patients, excellent patient outcomes have been reported after stereotactic cyst aspiration,11,20,33,37 stereotactic transcortical–transventricular resection,2,5,13,22 transcallosal–transventricular resection,6,24,30 and endoscopic removal.13,8,24

Because little information is available on the natural history of colloid cysts in patients in whom the cysts were incidentally discovered, surgical intervention is generally recommended to protect the patient from the development of acute hydrocephalus.24,27,30 Camacho and colleagues6 previously reported 24 cases of asymptomatic third ventricular colloid cysts that were diagnosed between 1974 and 1987 and managed conservatively at our institution. At an average follow-up interval of 19 months, none of these patients exhibited cyst-related symptoms. The present report updates that experience at our institution, focusing on 58 patients with asymptomatic, untreated colloid cysts who were observed over a 25-year interval during the modern neuroimaging era.

Clinical Material and Methods

Patient Population
A computer search of the Mayo Clinic and Foundation clinical and radiology databases in Rochester, Minnesota, was performed to identify all patients in whom a diagnosis of colloid cyst of the third ventricle had been made. Between January 1974 and June 1998, 162 cases of third ventricular colloid cysts were evaluated and managed. Ninety-four patients (58%) with these cysts were either symptomatic and underwent surgical resection of the cyst
or had previously undergone a surgical procedure for the cyst. In 68 patients (42%) colloid cysts were discovered incidentally and observation with serial neuroimaging was recommended rather than surgical intervention. Twenty-four of these patients were also included in an earlier study conducted at our institution on colloid cyst management. The indications for neuroimaging in these 68 asymptomatic patients are outlined in Table 1. Of note, 19 (28%) of these 68 patients had headaches as their primary complaint, which were thought to be unrelated to the cyst at the time of the patients’ neurological evaluation. The headaches were tension related in 10 patients, migrainous in seven, and posttraumatic in two patients. There were 36 men and 32 women. The mean patient age was 57 years (range 7–88 years) at the time of diagnosis.

**Diagnostic Neuroimaging**

The Mayo Clinic entered the modern neuroimaging era in late 1973 when computerized tomography (CT) scanning became available for clinical application. The actual scans obtained after 1988 were available for review; we relied on official radiology reports for information on scans obtained prior to that time. As part of their initial evaluation, 42 patients underwent CT scanning alone, 10 patients underwent magnetic resonance (MR) imaging alone, and 16 patients underwent both CT and MR imaging. In 46 (68%) of 68 patients, a contrast agent was administered either during the CT or MR imaging session. The neuroimaging characteristics of the 68 patients at the time of diagnosis are shown in Table 2.

**Patient Follow-Up Evaluation**

The clinical histories of all patients were reviewed. If patients had not been evaluated within the last year, every effort was made to locate them and conduct a telephone interview regarding clinical status and the most recent neuroimaging study. In cases in which the patient had died before the time of data retrieval, the local physician was contacted for information whenever possible. Three patients were excluded from the study because they died of unrelated causes (cardiac disease, cancer, and neurodegenerative disease in one patient each) within 6 months after diagnosis. Seven patients were lost to follow-up review. Clinical follow-up evaluation was available at a mean of 79 months (range 7–268 months) in the remaining 58 patients: a complete follow-up interval (until surgery, death, or telephone interview) was available in 43 patients (74%). The numbers of patients who participated in follow-up review at 2, 5, and 10 years after diagnosis were 40, 28, and 14, respectively. Neuroimaging follow-up review was available for comparison in 34 patients at a mean of 41 months (range 4–160 months) after their initial imaging study. The numbers of patients in whom follow-up imaging was obtained at 2, 5, and 10 years after diagnosis were 18, 10, and 2, respectively.

**Statistical Analysis**

A computerized database was compiled using all available patient information. Actuarial cyst-related symptom progression was calculated from the date of diagnosis by using the Kaplan–Meier method. Nonparametric variables were analyzed using the chi-square test; parametric variables were compared using the Student t-test.

**Results**

At last follow-up review, 30 patients (52%) were neurologically unchanged and three patients were clinically improved. One patient remained clinically stable, and repeated imaging performed 4 months later showed the cyst to be unchanged. He was evaluated at another institution and underwent surgical resection of his tumor 6 months after diagnosis. Twenty-four patients experienced a decline in their functional status that was unrelated to the colloid cyst. Thirteen patients died of unrelated causes: cancer in six patients, cardiac disease in three, neurodegenerative disease in three, and intracerebral hemorrhage in one patient. One patient (2%) had progressive symptoms related to the colloid cyst. This patient was a 57-year-old woman who presented with intermittent visual complaints and was found to have an 8-mm hyperdense lesion on CT scanning with partial contrast enhancement.
The patient remained asymptomatic, and her serial scans were unchanged until 101 months after the original diagnosis. At that time, the cyst was believed not to have changed in size, but the patient’s ventriculomegaly had progressed. The patient was evaluated by a neurosurgeon, and surgical resection of the colloid cyst was recommended. The patient refused to have surgery, and 5 months later acute obstructive hydrocephalus developed. The patient underwent emergency placement of bilateral external ventricular drains, which were later converted to ventriculoperitoneal shunts. Despite these urgent measures, the patient sustained a significant brainstem injury and required placement of a tracheostomy and gastrostomy tube. She died 4 years later in a nursing home, 160 months after the colloid cyst had been diagnosed. The 2-, 5-, and 10-year incidences of cyst-related symptom development in our group were 0%, 0%, and 8%, respectively (Fig. 1).

Thirty-two (94%) of 34 patients in whom follow-up neuroimaging had been performed experienced no change in either the cyst or ventricular size (Fig. 2). In addition to the patient already described, another patient’s cyst increased 2 mm on scanning performed 82 months after diagnosis. The patient’s ventricles remained of normal size, and she remained asymptomatic; further observation was recommended. The patient remains well almost 11 years later, 210 months after the initial diagnosis.

**Discussion**

*Management of Incidental Colloid Cysts*

Observation of patients in whom colloid cysts are incidentally diagnosed is rarely recommended because of the risk of acute neurological deterioration secondary to ventricular obstruction. Little and MacCarty\(^2\) reported that four (11%) of 38 patients with colloid cysts seen at the Mayo Clinic between 1929 and 1973 presented with sudden clinical deterioration and death. Although it is now recognized that sudden neurological decline is rare in patients with colloid cysts who do not exhibit preceding symptoms, reports of fatal patient outcomes continue even during the modern neuroimaging era.\(^3\)\(^,\)\(^4\)\(^,\)\(^6\)\(^,\)\(^24\)\(^,\)\(^27\)\(^,\)\(^30\) Physicians are also reluctant to recommend conservative management for patients with incidentally discovered colloid cysts because of the paucity of information available on the natural history of the cysts in this patient group. Hernesniemi and Leivo\(^16\) reported on outcomes in 40 patients with colloid cysts treated between 1980 and 1994. They had two patients with small cysts (3 mm and 7 mm) who did not undergo surgical resection and were alive and well 1 and 3 years after diagnosis, respectively. Kondziolka and Lunsford\(^21\) recommended the use of conservative management in six asymptomatic patients with small colloid cysts (< 7 mm in diameter) evaluated between 1984 and 1995. Their patients have not required intervention during follow-up intervals ranging from 3 to 7 years. Based on their experience, these authors believe that ob-
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Conservation with serial neuroimaging is possible for asymptomatic patients with small cysts and normal ventricular size. Mathiesen and associates reported on 37 consecutive patients with colloid cysts managed between 1984 and 1997. These authors found that four of seven patients in whom initial radiological follow-up studies were performed either became symptomatic or experienced an increase in their symptoms and underwent surgical resection 6 to 37 months after diagnosis. One additional patient had a slight increase (1 mm) in the size of her cyst noted at 2 years, but the patient was lost to any further follow-up evaluation. Mathiesen and associates concluded that most younger patients will become symptomatic during their lifetime and that expectant surgical resection is the preferred management strategy. In the current series, we have documented the long-term outcomes in 58 patients in whom incidental colloid cysts were diagnosed. In a mean follow-up period lasting longer than 6.5 years, one patient (2%) became symptomatic from the cyst but only after serial imaging had shown progression of her ventriculomegaly; surgical resection was recommended. Moreover, in only two (6%) of 34 patients was either cyst enlargement or progressive hydrocephalus demonstrated on follow-up neuroimaging. Consequently, we believe that observation with serial neuroimaging is a safe management strategy for use in patients with incidentally discovered colloid cysts and that the majority of such patients will not require any future neurosurgical intervention.

Of course, it is important to remember several vital points before recommending conservative therapy for patients in whom a colloid cyst has been diagnosed. First, the patients in our series at the time of their diagnosis were believed to be asymptomatic with regard to their cyst. The vast majority of our patients underwent an independent consultation with a staff neurologist who agreed that the cyst was an incidental finding. This is especially important because many patients (28% in our series) have headaches as one of their primary symptoms. Unless another cause for the headache could be explained (such as migraine or posttrauma), the headaches were considered cyst-related and surgery was recommended. For patients believed to be symptomatic, prompt neurosurgical care is indicated to minimize the likelihood of sudden clinical decline. Second, the patients in our series may represent a somewhat different cohort of patients when compared with reported patients undergoing surgery for their colloid cysts. Compared with 372 symptomatic patients whose cases have appeared in the literature during the past 25 years, the average age of our patients was older (57 years compared with 41 years, p < 0.001). Also, 49 (85%) of our 58 patients had cysts that appeared hyperdense on CT scanning, compared with 181 (70%) of 259 patients from an updated literature review conducted by Kondziolka and Lunsford during the modern neuroimaging era (p = 0.02).

Thus, in younger patients with iso- or hypodense colloid cysts, prophylactic neurosurgical intervention, as suggested by Macdonald, et al., may be reasonable because these patients are likely to become symptomatic within their lifetime. Third, the imaging characteristics of the lesion in question must be entirely consistent with those of a colloid cyst. The differential diagnosis of a round or oval well-circumscribed mass in the anterior third ventricle includes aneurysms of the basilar artery, hamartomas, primary or secondary neoplasms, and xanthogranulomas. In our series, each patient’s imaging was reviewed by a staff neuroradiologist and a colloid cyst was believed to be present in all cases.

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What are the factors involved in determining whether a patient with a colloid cyst will become symptomatic? Macaulay and colleagues postulated that in patients with colloid cysts, ectopic endodermal elements migrated into the velum interpositum during development of the central nervous system. Numerous pathological studies have shown colloid cysts to be composed of ciliated and nonciliated cuboidal, pseudostratified, or columnar epithelial cells interspersed with mucus-containing goblet cells. As the patient ages, these cells secrete an amorphous, proteinaceous material resulting in cyst formation and expansion. If the cyst enlarges rapidly, obstruction of CSF flow occurs and symptoms of increased intracranial pressure develop. Sudden death occurs in patients in whom CSF flow is abruptly blocked, resulting in increased intracranial pressure and brain herniation. If, however, the cyst enlarges more gradually, the patient can accommodate the enlarging mass at the foramen of Monro without disruption of CSF flow and the patient remains asymptomatic. At some point, it is likely that most cysts stop enlarging and a steady state of CSF flow and absorption is achieved. We believe that the majority of patients in our study had reached this later point and thus had little future risk of neurological deterioration related to their colloid cyst.

Several observations lend support to this hypothesis of colloid cyst development, growth, and related clinical symptoms. First, during a 40-year period, Macaulay and colleagues were unable to document a single case of an incidental colloid cyst in 10,000 autopsies performed in pediatric cases. Thus, although the ectopic tissue that later gives rise to colloid cysts is congenitally derived and not acquired, few if any patients are born with true colloid cysts. Second, in a review article on colloid cysts of the third ventricle associated with sudden death, the mean age of 21 patients reported after 1990 was 27 years (range 6–46 years). Similarly, symptomatic patients undergoing surgery during the modern neuroimaging era were significantly younger than the asymptomatic patients observed in our series. Third, the imaging characteristics of colloid cysts may change over time and correlate with the likelihood of future cyst growth. In our series of older patients, we observed a higher percentage of colloid cysts that were hyperdense on CT scans than that documented in the surgical literature, and further cyst growth was observed in less than 3% of our patients. Although the hyperdense appearance on CT scans has previously been attributed to calcium distributed within the cyst mucin, a more recent analysis of the elemental composition of colloid cysts found no difference in the amount of calcium contained within hypo- and hyperdense cysts. Urso, et al. postulated that the state of hydration of the cyst contents may correlate with CT density. If this postulate is correct, the desiccated contents of hyperdense colloid cysts would be
more solid and less capable of further growth. Fourth, almost one third (31%) of our patients demonstrated some degree of ventriculomegaly at the time of diagnosis, and yet only one patient (2%) demonstrated either the development or progression of clinically significant hydrocephalus. The probable explanation is that these patients had previously sustained some degree of CSF obstruction from the cyst, resulting in enlargement of their ventricles and a progressive loss of extracellular water from the brain parenchyma.\footnote{15,35} As water shifted out of the brain parenchyma, the viscoelastic properties of the brain were altered and the brain became less elastic. In this situation, the ventricles remained enlarged due to the lowered brain modulus,\footnote{15,35} and the newly established pressure–volume relationship allowed the coexistence of enlarged ventricles and low-to-normal intracranial pressures. Once the cyst stopped enlarging, a steady state was achieved between CSF production and absorption, and the patients remained asymptomatic.

**Conclusions**

Patients in whom asymptomatic colloid cysts are diagnosed can be cared for safely with observation and serial neuroimaging. If a patient becomes symptomatic, the cyst is enlarging, or hydrocephalus develops, prompt neurosurgical intervention is necessary to prevent the occurrence of neurological decline from these benign tumors.

**References**


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