High risk of acute deterioration in patients harboring symptomatic colloid cysts of the third ventricle

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Object. Patients harboring colloid cysts of the third ventricle can present with acute neurological deterioration, or the first indication of the lesion may appear when the patient suddenly dies. The risk of such an occurrence in a patient already identified as harboring a colloid cyst is unknown. The goal of this study was to estimate the risk of acute deterioration in patients with colloid cysts.

Methods. A retrospective study was made of a cohort of patients with newly diagnosed colloid cysts who were recruited in The Netherlands between January 1, 1993, and December 31, 1997. Seventy-eight patients were identified, all of whom displayed symptoms. Twenty-five patients (32%) presented with symptoms of acute deterioration; four patients died suddenly and the cysts were discovered at autopsy. The overall mortality rate was 12%. Results of a multivariate logistic regression analysis demonstrated that no subgroup of patients presenting without acute deterioration could be identified on the basis of patient age, duration of symptoms, cyst size, or the presence of hydrocephalus. The national incidence of colloid cysts in The Netherlands is 1/106 person-years; the prevalence was estimated to be 1800 asymptomatic colloid cysts.

Conclusions. Acute deterioration was a frequent presentation among a national cohort of Dutch patients harboring symptomatic colloid cysts. The risk of acute deterioration in a symptomatic patient with a colloid cyst in The Netherlands is estimated to be 34%. The estimated risk for an asymptomatic patient with an incidental colloid cyst is significantly lower. These results strongly advocate the selection of surgical treatment for patients with symptomatic colloid cysts.

KEY WORDS • colloid cyst • intraventricular tumor • risk factor • sudden death

The threat of sudden death, presumably due to acute obstructive hydrocephalus, is often a decisive argument for neurosurgical intervention in patients harboring colloid cysts of the third ventricle. Despite our increasing awareness of the natural history of colloid cysts, we do not know the risk of acute neurological deterioration in a patient harboring a colloid cyst. Recently, Pollock and Huston presented data on a group of selected patients with asymptomatic colloid cysts, who displayed no signs of deterioration during the follow-up period, although the cysts were left untreated. These authors, as well as others, demonstrated that selected patients with incidental and minimally symptomatic colloid cysts can safely undergo close observation. This finding is opposed to a vast body of reports on sudden deterioration of patients, with fatal outcome. Essential for case management decisions concerning a patient who presents with a colloid cyst is the perceived risk of acute deterioration. Estimates of the risk of acute deterioration in reported series, including two reviews on the subject, vary from 6 to 45%.

The goal of this study was to estimate the risk of acute deterioration on the basis of a population-based retrospective analysis of all patients in whom colloid cysts were diagnosed at neurosurgical consultation or revealed by autopsy during a recent 5-year period (1993–1998) in The Netherlands. The data obtained in this study will allow a first estimate of the national incidence of colloid cysts in our country.

Clinical Material and Methods

Patient Selection

A cohort of patients with colloid cysts was formed from two sources of patient data. To collect clinical data, a search was made of local medical record archives in all 13 neurosurgical centers located in The Netherlands. To collect
and consisted of a progressive headache cascade that developed within 48 hours before neurological symptoms lasting more than 48 hours that led to neuroimaging and subsequent cyst identification was considered to have stable symptoms. Patients were included in the fourth category if the colloid cyst was an incidental finding on neuroimages obtained in asymptomatic patients (for example, images obtained during screening of a systemic disease or in a volunteer participating in a neuroimaging study). For each patient the presentation category was determined.

Data on patient age at presentation (cutoff age 55 years) and duration (cutoff 3 months) and type of symptoms were retrieved for regression analysis to study deterioration (presentation Categories 1 and 2) as an independent variable. The neuroimages were centrally reviewed by investigators for colloid cyst size (cutoff 10 mm in diameter) and presence of hydrocephalus. Hydrocephalus was diagnosed when either transependymal cerebrospinal fluid resorption or enlarged temporal horns were present.

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**TABLE 1**

<table>
<thead>
<tr>
<th>Symptoms &amp; Signs</th>
<th>Stable Symptoms (40 patients)</th>
<th>Acute Deterioration (25 patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>headache</td>
<td>41 (84)</td>
<td>25 (100)</td>
</tr>
<tr>
<td>position dependent</td>
<td>5 (10)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>episodic</td>
<td>20 (41)</td>
<td>7 (28)</td>
</tr>
<tr>
<td>compromised consciousness</td>
<td>0 (0)</td>
<td>21 (84)</td>
</tr>
<tr>
<td>nausea or vomiting</td>
<td>23 (47)</td>
<td>16 (64)</td>
</tr>
<tr>
<td>visual disturbance</td>
<td>20 (41)</td>
<td>6 (24)</td>
</tr>
<tr>
<td>gait disturbance</td>
<td>19 (39)</td>
<td>4 (16)</td>
</tr>
<tr>
<td>cognitive impairment</td>
<td>16 (33)</td>
<td>6 (24)</td>
</tr>
<tr>
<td>amnesia</td>
<td>13 (27)</td>
<td>2 (8)</td>
</tr>
<tr>
<td>vertigo</td>
<td>17 (35)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>sensory disturbance</td>
<td>11 (22)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>drop attack</td>
<td>8 (16)</td>
<td>3 (12)</td>
</tr>
<tr>
<td>tinnitus</td>
<td>4 (8)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>epileptic seizure</td>
<td>2 (4)</td>
<td>2 (8)</td>
</tr>
<tr>
<td>urinary incontinence</td>
<td>2 (4)</td>
<td>3 (12)</td>
</tr>
<tr>
<td>parkinsonism</td>
<td>2 (4)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>dysphasia</td>
<td>1 (2)</td>
<td>1 (4)</td>
</tr>
<tr>
<td>hemiparesis</td>
<td>0 (0)</td>
<td>1 (4)</td>
</tr>
</tbody>
</table>

* Numbers do not total 100% because often multiple symptoms were observed at presentation.

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Pathological reports, personnel at PALGA performed a computer search for both autopsy and surgical specimens. Surgical specimen retrieval by PALGA was used to verify coverage of the medical record archive search results. The sole inclusion criterion was a third ventricular colloid cyst that was newly diagnosed on the basis of pathological and/or radiological studies between January 1, 1993, and December 31, 1997.

**Patient Population**

In this retrospective study 78 cases of newly diagnosed colloid cysts were culled from a medical database covering 77.1 × 10^6 person-years (mean 15,413,000 inhabitants followed up over a 5-year period; source: Dutch Central Bureau for Statistics, Voorburg/Heerlen, The Netherlands, 2000). The mean age of the 78 patients at the moment of colloid cyst diagnosis was 40 years (range 17–72 years) and there was a slight male preponderance of 54% (42 of 78 patients). Initial diagnostic neuroimaging was performed using CT scanning in 59 patients (76%) and MR imaging in 15 patients (19%). In four autopsy cases (5%) imaging was not performed. In nine patients (12%) neuroimages could not be reviewed because the patients’ radiology files were missing. Colloid cysts were histologically verified in 60 patients (77%).

**Presentation Data**

Four categories of colloid cyst presentation were distinguished. The first category consisted of patients who harbored a colloid cyst that was diagnosed as the cause of sudden, unexpected death at autopsy without prior cyst identification. Patients in the second category presented with acute deterioration, which was defined as a clinical cascade that developed within 48 hours before neurosurgical consultation and consisted of a progressive headache combined with vomiting, compromised consciousness, or papilledema, and for which a ventricular catheter had to be inserted. The third category consisted of patients in whom the colloid cysts were identified by diagnostic imaging that had been performed for stable symptoms. Any patient with neurological symptoms lasting more than 48 hours that led to neuroimaging and subsequent cyst identification was considered to have stable symptoms. Patients were included in the fourth category if the colloid cyst was an incidental finding on neuroimages obtained in asymptomatic patients (for example, images obtained during screening of a systemic disease or in a volunteer participating in a neuroimaging study). For each patient the presentation category was determined.

**Results**

**Presentation Categories**

Four autopsy cases (5%) of sudden death (presentation Category 1) were identified. In all four cases, the direct cause of death was cerebral herniation due to ventricular obstruction, which had been caused by blockage of the foramen of Monro. Another 25 patients (32%) presented with acute deterioration on admission (presentation Category 2). Emergency ventriculostomy was performed in all these patients. A wide variety of complaints were observed in the remaining 49 patients (63%) who presented with stable symptoms (presentation Category 3). The majority of them (at least) suffered from a headache. The patients’ symptoms and signs are presented in Table 1. No incidental cysts (presentation Category 4) were revealed in this cohort of patients.

**Incidence of Colloid Cysts**

Seventy-eight cases of newly diagnosed colloid cysts...
Acute deterioration in symptomatic colloid cysts

were culled from a medical database covering \(77.1 \times 10^6\) person-years. Therefore, the incidence of symptomatic colloid cysts among the Dutch population calculated on the basis of this cohort is \(1/10^6\) person-years.

**Estimated Risk of Acute Deterioration**

Acute deterioration developed in 25 (34%) of 74 patients admitted to the hospital in our cohort. This was calculated by dividing the number of patients presenting with acute deteriorations by the number of patients presenting with either acute deterioration or stable symptoms. Overall the mortality rate was 12%, consisting of four sudden deaths before diagnosis and five deaths subsequent to acute deterioration, despite acute application of ventricular drainage.

**Risk Factors**

The results of univariate analysis showed that hydrocephalus (relative risk 1.7; 95% confidence interval 1.3–2.2) and a 3-month-long or shorter history of symptoms (relative risk 2.2; 95% confidence interval 1.2–4.1) proved to have a statistically significant correlation with deterioration (Table 2). No stable multivariate logistic regression model could be fitted to the data.

**Discussion**

**Estimated Risk of Acute Deterioration in Patients With a Symptomatic Colloid Cyst**

Twenty-five (34%) of 74 patients presented with symptoms of acute deterioration and four with sudden death; the overall mortality rate in this study was 12%. The natural history of colloid cysts and the pathophysiology of acute deterioration are insufficiently known to calculate the risk for an individual patient based on these figures. If all patients harboring a symptomatic colloid cyst are at equal risk, a Dutch patient presenting for neurosurgical consultation has a 34% estimated minimum lifetime risk of acute deterioration; however, our cohort of symptomatic patients may constitute a composite of subgroups that have different risks. For instance, it has been suggested that colloid cysts smaller than 10 mm in diameter are associated with a minimal risk of acute deterioration. Other factors asserted to play a role in the relative risk are hydrocephalus, patient age, and duration of symptoms. We were unable to differentiate a subgroup of patients who did not present with acute deterioration based on time from onset of complaints, type of complaints, and cyst size (see also Table 2). Reviews of the literature lead one to conclude that duration of symptoms, cyst size, and evidence of hydrocephalus on neuroimages cannot be reliably used to indicate the risk of sudden neurological deterioration. Therefore, based on data obtained in our patients who presented for neurosurgical consultation, the generalized estimated risk of acute deterioration or sudden death is 34% for an individual patient with a symptomatic colloid cyst.

Of particular concern in our estimation of risk is combining patients who suddenly died (presentation Category 1) and those admitted after acute deterioration (presentation Category 2). Timing of hospital admission may actually be the only distinction between these patients. We believe that the same pathophysiological mechanisms are responsible for acute deterioration and sudden death. This is illustrated by the fact that five patients with acute deterioration died, despite emergency application of ventricular drainage. All five patients presented with irreversible cerebral herniation, which proved refractory to ventricular drainage. Nevertheless, our object was to estimate the risk to patients presenting for neurosurgical consultation and, therefore, we separated presentation Categories 1 and 2. This separation of categories slightly understimates our risk estimate (34% compared with 37%).

Recently, Pollock and colleagues proposed a theory of the natural history of colloid cysts. The occurrence of symptoms is thought to depend on the interaction of three factors: rate of cyst growth, development of cerebrospinal fluid obstruction, and arrested cyst growth in the older patient. According to this theory, all of our patients can be classified as Class III because they are symptomatic. Asymptomatic patients with (Class II) or without (Class I) hydrocephalus were not identified in our series. The theory posed by Pollock and colleagues does not identify subgroups of Class III patients with higher or lower risks of acute deterioration. Although asymptomatic colloid cysts will be encountered more frequently—as a result of the increasing availability of MR imaging—neurosurgeons are more frequently confronted with a symptomatic patient. A particularly difficult problem in the assessment of headache as the presenting symptom concerns whether the headache is caused by the colloid cyst. If the headache is thought to be unrelated to the colloid cyst, the patient is categorized as Class I or II; in these cases Pollock and colleagues suggest refraining from prompt neurosurgical intervention. It is generally agreed that headache can be unrelated to the cyst. In our series, however, only six patients in whom headache was attributed to the colloid cyst presented with headache as the solitary complaint. In the other patients headache was invariably accompanied by other symptoms. Therefore, all presentations were considered symptomatic (Class III). In our opinion, the high estimated risk of acute deterioration in symptomatic patients should be interpreted as a generalized risk for symptomatic patients, because a subgroup with a substantially reduced risk has yet to be discerned. This supports the use of surgical treatment of these symptomatic patients, even when the relationship between the cyst and the complaint is unclear. A description of the surgical treatment of patients in our cohort is beyond the scope of this paper.

The unexpectedly high incidence of acute life-threatening neurological disease in patients with symptomatic colloid cysts is striking. In recent discussions about patients harboring colloid cysts, the emphasis has been on the be...
nign character of this disease. In a 1996 review of the literature by Hernesniemi and Leivo, however, 21% of the 939 patients presented with compromised consciousness. In these authors’ own series, 13 patients (37%) presented with acute deterioration and five of these died. The relatively high incidence of acute deterioration and sudden death in this Dutch cohort can be explained by a number of factors. First, it is standard practice to ask for autopsy in a case of sudden, unexplained death. Second, there is a meticulous national registration of pathological diagnoses and autopsies. Third, no asymptomatic patients were identified, which perhaps suggests that more strictly applied neuroimaging indications and/or restrained referral patterns were operational. Nonetheless, there is unrestrained access to CT and MR imaging units throughout The Netherlands. Last, rapid access to neurosurgical care is guaranteed in all regions of our relatively small country, and delayed neurosurgical intervention does not appear to have been a factor in the deaths of patients displaying acute deterioration. This rapid access may actually play a role in the high incidence of acute deterioration in patients in our country; moribund patients are admitted to the hospital who would otherwise have died suddenly, before diagnosis.

**Prevalence and Incidence of Colloid Cysts**

The true prevalence of colloid cysts is unknown, but based on a series of consecutive CT scans it has been estimated to be lower than one in several thousand. Based on incidences calculated in autopsy series (three of 17,404 cases, one of 10,995 cases, one of 9,886 cases, one of 9,920 cases, and none of 7020 cases) and consecutive series of patients who underwent MR neuroimaging (none of 1000 asymptomatic volunteers and one of 3672 selected sexagenarians), a prevalence of 1 in 8500 persons can be estimated. Although the prevalence of colloid cysts is quite low, the incidence is even lower. Based on our data, the estimated incidence of symptomatic colloid cysts in the Dutch population is 1/10^5 person-years, whereas 3/10^6 person-years was the incidence rate demonstrated in a smaller Finnish study. Genetic variations in patients with colloid cysts or regional differences in presentation of symptoms, neuroimaging, or access to healthcare systems may explain the observed difference.

**Estimated Risk of Acute Deterioration in Patients With Incidentally Found Colloid Cysts**

Extrapolation of the previously estimated prevalence of colloid cysts to the Dutch population results in approximately 1800 persons bearing a colloid cyst. According to this calculation, the majority of persons harboring a colloid cyst in The Netherlands were not identified. In our series four of the presumed prevalence total of 1800 persons with a colloid cyst suddenly died. This suggests that the estimated risk of acute deterioration for incidentally discovered asymptomatic colloid cysts is only a fraction of the estimated risk for symptomatic patients. These results are in agreement with recent data on untreated asymptomatic patients and with a theory on the natural history of these cysts.

**Patient Selection Bias**

Various sources of selection bias may confound the results of this retrospective study. First, patients who were not referred to a neurosurgeon were not included in this analysis. Historically, however, a colloid cyst has been considered a neurosurgical disorder in The Netherlands, which makes management decisions without neurosurgical consultation most improbable in our country. Second, patients referred for neurosurgical consultation can be missed by the applied recruitment method. Nevertheless, the excellent agreement between our two patient identification sources, local medical record searches and retrieval of surgical specimens by PALGA, supports coverage of all patients with newly diagnosed cysts. Still, we cannot exclude the possibility that using the present recruitment method, we may have missed patients who were seen only as outpatients in a nonneurosurgical hospital by a consulting neurosurgeon. Third, presumably there is a considerable number of people harboring colloid cysts who experience only minor symptoms or express no complaint; this results in an underestimation of presentation Categories 3 and 4. We have assessed the effects of this bias by estimating the number of all prevalent colloid cysts based on consecutive autopsy and imaging series. Fourth, not all patients who suddenly died during the study period may have undergone autopsy. The four cases of sudden death due to colloid cyst that were identified during the 5-year period, however, constitute a high number (there are only 98 case descriptions in the world literature according to a recent review), whereas no colloid cysts have been identified in large series of unexpected deaths.

**Conclusions**

In our national cohort of patients harboring symptomatic colloid cysts, 25 (34%) of 74 patients presented with acute deterioration and four autopsy cases of sudden death prior to diagnosis were identified. The overall mortality rate in this study is 12% (nine of 78 patients), despite the availability of emergency surgery. Because no subgroups can be reliably identified, we estimate that the generalized risk of acute deterioration in a symptomatic patient with a colloid cyst presenting for neurosurgical consultation in The Netherlands is 34%. The estimated risk for patients in whom asymptomatic colloid cysts have been identified incidentally is considerably lower. On the basis of these estimated risks, we strongly advocate the use of neurosurgical intervention in patients presenting with symptomatic colloid cysts. Crucial for the perceived risk in the individual patient appears to be whether the presenting symptoms can be attributed to the diagnosed cyst.

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References


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