The colloid cyst of the third ventricle - a potential life threatening benign tumour

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Abstract: The colloid cyst of the third ventricle is a rare lesion, extremely interesting for forensic experts due to its potential in causing sudden death. Although not malignant in nature, this lesion may be life threatening as it can cause acute hydrocephalus by obstructing cerebrospinal fluid flow. Although the clinical, radiological and histological characteristics of colloid cysts are well known, their etiology and physiopathology continue to be a subject of debate. Further on, we present the case of a young woman who had a sudden death, on her admission to the hospital. She had had a several-year history of episodic headaches, but no CT scans performed prior to her death. The forensic pathology and microscopic examination revealed a colloid cyst of the third ventricle, resulting in a hydrocephalus involving the lateral ventricles and a massive pulmonary edema. The fulminant neurogenic pulmonary edema, following the increased intracranial pressure and the complete obstruction of the cerebrospinal fluid flow triggered death. This case report emphasizes that, although a rare disease, colloid cysts should also be taken into account when trying to establish the diagnosis of apparently harmless headaches in young adults. Furthermore, it stresses the importance of early diagnosis, generally done by computed tomography or magnetic resonance imaging.

Key words: colloid cyst, third ventricle, sudden death, hydrocephalus, forensic pathology

Colloid cysts are the most common lesions of the third ventricle [1]. They are rare benign lesions accounting for less than 1-2% of brain tumours [2]. These tumours are typically located in the anterior third ventricle, attached to its roof and between the columns of the fornix [3]. This is a critical location because the cyst can block the foramen of Monro, causing an impaired cerebrospinal fluid flow, internal hydrocephalus and increased intracranial pressure. The nature and severity of the obstructive symptoms depend both on the lesions’ size and position, and on their shape and consistence.

Therefore, cysts may remain asymptomatic and be incidentally discovered during autopsy [4], or may become symptomatic, usually in the third or fourth decades of life [3]. The most common clinical symptom, but not the only one, would be an episodic headache.

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Other symptoms may be: vertigo, seizures, memory deficit and behavioural disturbances. Sudden death from acute obstruction of the foramen of Monro has been well documented, especially with cysts larger than 1 cm [5-7], and occurs in only about 10% of the patients with a colloid cyst diagnosis [4].

Below, we report the case of a young female who suddenly died after a long history of headaches. The post-mortem examination revealed a colloid cyst of the third ventricle.

Case report
A 26-year-old woman was admitted to the hospital in cardio respiratory arrest due to a massive pulmonary edema. Despite intensive resuscitation efforts, she died four hours later under mechanical ventilation. In the last 12 hours before admission, she had had intermittent severe headaches, accompanied by vomiting and dyspnea.

Her medical history was common, except that two years before she was suspected of meningitis because of severe cephalgia. Moreover, one year before she saw a neurologist because of her repetitive headaches, but no definite diagnosis could be made.

Autopsy findings
The external examination was normal. On the other hand, the internal examination showed severe pulmonary edema and marked vascular congestion without other gross anomalies of the heart, kidneys, spleen, or liver. The brain was obviously swollen and edematous, with flattened gyri and narrowed sulci. It weighed around 1450 g. The coronal brain sections, placed at 1 cm distance from each other, revealed moderate dilation of ventricles, already filled with clear cerebrospinal fluid. Within the third ventricle, there was a smooth yellow-greyish cystic structure measuring 1x1.5x1.5 cm (Fig. 1). On the cut surface, the lesion revealed a viscous content and a thin fibrous capsule. There were no signs of cerebral or cerebellar herniations.

Histopathological findings
Multiple samples from the ventricular tumour, brain, lungs, kidney, heart, spleen and pancreas, were introduced in 10% neutral buffered formalin, embedded in paraffin and stained with haematoxylin-eosin, trichrome Masson, Periodic acid-Schiff and Alcian Blue.

The brain showed extensive interstitial edema. Large areas of the lungs were filled with a light eosinophilic substance. While alveolar walls presented an obvious capillary congestion, the other organs showed only moderate inflammation.
The ventricular tumour was cystic, a peripheral capsule delimitating an amorphous eosinophilic substance. The wall of the cyst was made up of two layers: an inner one formed of a ciliated or non-ciliated cuboidal or columnar epithelial cells and an outer thin layer of fibrous connective tissue (Fig. 2). The substance within the cyst contained some small calcifications and cellular debris and was positively stained with Periodic acid-Schiff and Alcian Blue.

![Figure 2 Cyst wall lined by a single flattened to cuboidal epithelium (black arrow) resting on a fibrous connective tissue (*). Cyst’s content is represented by an amorphous eosinophilic material (white arrow). Adjacent edema of the cerebral white matter (HE x200)](image)

![Figure 3 The cyst epithelium show strong positivity for pancytokeratin AE1/AE3 (Avidin-Biotin immunoperoxidase x 400)](image)

Immunohistochemical investigations were performed on 4-µm specimens, which had not been embedded into paraffin, according to the routine standard protocols for the avidin-biotin-complex-peroxidase method. The following antibodies were used: creatine kinase (CK) (clone AE1/AE3), vimentin (VIM) (clone Vim 3B4), epithelial membrane antigen (EMA) (clone E29/EP1), S-100A1 protein (Rabbit polyclonal), glial fibrillary acidic protein (GFAP) (clone 6F2) and neurofilament protein (clone 2F11).

All antibodies were from DAKO, Glostrup Denmark. On the one hand, within the intracytoplasmic cytoskeleton of epithelial tissue, cytokeratins came up positive (Fig. 3), as
well as weak and positive for epithelial membrane antigen. On the other hand, they were negative for vimentin (Fig. 4), S-100, GFAP and neurofilament protein.

![Figure 4](image.png)

**Figure 4** The cyst epithelium is completely negative for vimentin (Avidin-Biotin immunoperoxidase x 400)

According to histological criteria and immunohistochemical profiles, the intraventricular lesion was clearly diagnosed as a colloid cyst.

**Discussion**

The colloid cyst is a rare benign lesion of the third ventricle [8]. However, a number of studies prove that they can also be found in unusual locations within the central nervous system. Generally, incidence is equal in males and females. They are usually unique, but multiple colloid cysts have also been reported [9, 10].

Among the variety of colloid cysts tissues of origin proposed for examination, there were: primitive neuroepithelium [11], ependyma [12], choroid plexus epithelium [11] and paraphysal tissue [13]. Neither ultrastructural, nor immunohistochemical evidence could support the origin of the ependyma or of the choroid plexus epithelium. Similarly, paraphysis could hardly be supported either.

According to immunohistochemical staining and ultrastructural analysis, there is some evidence that colloid cysts take rise into the primitive foregut endoderm, where ectopic endodermal elements migrate towards the choroid plexus epithelium, during the development of the central nervous system [14-18].

There are exceptional reported cases of colloid cysts associated with congenital anomalies, which is an additional argument that colloid cysts are growth malformations [19]. Most colloid cysts occur sporadically although familial cases were rarely reported [19, 20].

Genetic factors may play a role in the familial occurrence of this lesion, although specific chromosomal anomalies have not yet been characterized [20, 21]. Some authors
argue that screening is indicated in families where two or more members are already affected [20].

The colloid cyst of the third ventricle may be asymptomatic, but they can also be responsible for neurological signs and sudden death caused by the obstruction of the foramen of Monro. The clinical image is not relevant and can be attributed to the increased intracranial pressure. The most common symptoms are headaches (68%), vertigo (47%), short term memory loss (37%), while the most common physical signs are papilledema (47%) and ataxia (32%) [22].

Colloid cysts are usually smooth, round, hyperdense structures, attached to the roof of the third ventricle. They can vary from a few millimetres to several centimetres in diameter. On the other hand, symptomatic cysts are typically at least 1-2 cm in diameter. Although cysts are usually light-coloured, they can sometimes get dark-coloured, when hemorrhagic [23]. Generally, a cyst is a homogenous colloid, gelatinous or dense substance.

From a histological point of view, colloid cysts are derived from the endoderm and composed of ciliated and non-ciliated cuboidal or columnar epithelial cells interspersed with mucus-containing goblet cells. This epithelium rests on an outer thin layer of fibrous connective tissue. The periodic acid-Schiff staining of the cyst came up positive for amorphous material, sometimes with cellular debris or cholesterol clefts [14, 15, 24].

The immunohistochemical test of the cyst tissue came up positive for cytokeratin, epithelial membrane antigen and carcinoembryonic antigen [25]. On the other hand, it came up negative for glial fibrillary acidic protein or vimentin [25], and only occasionally were there certain areas of epithelium weakly positive for S-100 [25].

In this case, the location, gross appearance, histopathological and immunohistochemical features of the intraventricular mass were similar to those of colloid cysts.

In forensic pathology, colloid cysts are rarely the actual cause of sudden death. In a series of 11,000 forensic autopsies, DiMaio et al. [26] barely found one case of sudden death caused by a colloid cyst of the third ventricle.

In our case, the patient had a rapidly installed respiratory failure, accompanied by cardiac arrest, secondary to a severe neurogenic pulmonary edema, which is a rare complication of the central nervous system. It is generally discovered in young patients and associated with subarachnoid haemorrhage, trauma, tumours, epilepsy, or infections. The condition is due to severe damage to the vascular tissue or a result of inadequate functioning of the heart [27].

Conclusions

This case report emphasizes that, although a benign entity, colloid cyst of the third ventricle may cause sudden death. Therefore, an early CT / MRI scan is a must for diagnosing patients with repetitive episodic headaches, even when they show no neurological disorder.

In cases of colloid cysts of the third ventricle, the neurogenic pulmonary edema may function as the mechanism triggering sudden death. Accordingly, physicians must be aware of and consider this clinical entity when caring for patients with acute respiratory distress following neurogenic causes.
References