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Huge familial colloid cyst of the third ventricle: An extraordinary presentation

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Abstract

Background: Since the use of computed tomography and magnetic resonance imaging, colloid cysts (CCs) are discovered more frequently and subsequently their true incidence exceeds the numbers previously estimated. In 1986, the first familial case was reported in two identical twin brothers. To date, a total of 17 of these cases have been reported, all differing in the pattern of affected family members.

Case Description: Here, we describe a unique presentation of a familial case and review the relevant literature on CCs and their natural history to improve our understanding of these cases.

Conclusion: Familial CC can present in various patterns, sizes, and forms. A genetic factor is likely to be responsible in these cases, and further research is warranted to clarify this phenomenon.

Key Words: Colloid cyst, familial, genetics, tumor

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INTRODUCTION

Colloid cysts (CC's) of the third ventricle are benign intra-cranial cysts that account for approximately 1% of all intra-cranial tumors. Considering the intraventricular lesions only, they comprise up to 20% of all tumors, and they are the most common mass found in the third ventricle.[4,10,22,27,29] The true incidence of CC's can only be estimated, because of the large cohort of asymptomatic individuals. Usually, the patients are middle-aged though the cysts can occur at virtually all ages.[9,17] The first case report dates from 1858 by Wallmann, who described the lesion both clinically and pathologically.[48] From there, it took several decades and progress in the field of neurosurgery to allow Dandy to successfully remove a CC in 1921.[13] Since this achievement, these lesions were considered curable as surgery offered a definite solution for the disease. Nowadays, CC's are not considered to be a neoplasm, rather a developmental malformation composed of a fibrous outer layer, internally bordered by a ciliated or mucus-producing epithelium. It is the activity of this very epithelium that determines their growth and expansion, leading to the capacity to cause the neurological decline. Although they are known for their slow growth and indolent character, their strategic position at the foramen of Monro not seldom gives them malicious traits.[36] This is often inconsistent with their usually small size. More precisely, they most often lay in the anterior part of the third ventricle, between the forniceal columns, obliterating the foramen of Monro and causing hydrocephalus.

They mainly present with signs and symptoms related to hydrocephalus such as headache and nausea, which are

too unspecific to pinpoint an exact etiology. On the other hand, we have the silent cases diagnosed incidentally by means of magnetic resonance imaging (MRI) or computed tomography (CT).[34] On imaging, these structures are seen as spherical isodense to hyperdense lesions on CT. On T2-weighted MRI, they usually appear hyperintense, and unless the surrounding fibrous capsule is vascular, they do not enhance on contrast agents. Finally CC's may incidentally be found at autopsy, as in the case of Dr. Harvey Cushing.[15]

To date, a total of 17 familial cases has been reported.[1-3,5-7,24,25,30,32,33,35,37,38,43,44,47] We would like to replenish the series with a case that is, unique, as it concerns two middle-aged nontwin brothers with large to gigantic CC's. The cyst sizes of all familial case reports are listed in Table 1. In our case descriptions, we also report the technical notes of how we surgically managed the cases.

CASE REPORTS

First case

In 2006, a 43-year-old Saudi man was referred to our institution, the International Neuroscience Institute in Hannover, for the treatment of a cystic intra-cranial lesion.

Table 1: Overview of the literature on familial CC of the third ventricle

Authors and year	Affected family members	Size on imaging (largest diameter)
Ibrahim *et al.* 1986	Identical male twins	25 mm and <10 mm
Bengtson *et al.* 1990	Two nontwin brothers	20 mm and 20 mm
Vandertop *et al.* 1995	Three sisters	Not available§
Akins *et al.* 1996	Father and son	18 mm and <10 mm
Mathiesen *et al.* 1997	Mother and son	15 mm and 13 mm
Stoodley *et al.* 1999	Brother and sister	13 mm and <10 mm
Aggarwal *et al.* 1999	Mother and son	16 mm and 20 mm*
Nader-Sepahi *et al.* 2000	Mother and two daughters	Not available, 10 mm and <10 mm§
Ahmad *et al.* 2002	Monozygotic twin brothers	13 mm and 4 mm
Socin *et al.* 2002	Two half-sisters	10 mm and 15 mm
Sadeghi *et al.* 2003	Brother and two sisters	18 mm, 14 mm and <10 mm*
Partington *et al.* 2004	Father and daughter	Not available§
Joshi *et al.* 2005	Nontwin sisters	Not available§ and <10 mm*
Bavil *et al.* 2007	Nontwin sisters	20 mm and 10 mm*
Romani *et al.* 2008	Dizygotic twin brothers	12 mm and 20 mm*
Salaud *et al.* 2012	Mother and daughter	17 mm and 13 mm
Benoiton *et al.* 2014	Mother and daughter	Not available§
Current report	Two nontwin brothers	52 mm and 25 mm

The presentation in terms of family members affected and cyst sizes are listed. *Cyst sizes were assessed on imaging when they were not explicitly mentioned in the paper. §Not mentioned and no imaging available. CC: Colloid cyst

During the week before admission, the primary complaint was sudden onset headaches accompanied by episodes of vomiting. At the time of evaluation, the headaches were described as constant, very severe and diffuse. Sensorimotor evaluation showed mild numbness in the right hand, with a slight weakness of the hand extensors on the right side. A CT-scan performed in the country of origin revealed a cystic lesion that appeared to be a CC of the third ventricle. On T1-weighted gadolinium-enhanced images a 25 mm × 25 mm × 20 mm measuring cystic lesion was seen [Figure 1] causing mild obstructive hydrocephalus. The mass itself was also strongly contrast enhanced, leading us to believe the cyst wall contained some aberrant vessels.

The patient underwent a right fronto-dorsal parasagittal craniotomy for a microsurgical extirpation of the lesion through a transcallosal approach. Total removal of the cyst and its colloidal content, together with its aberrant vascular steel was achieved.

Histological examination of the biopsy specimens confirmed the diagnosis of a CC. Surprisingly, the vascular steel consisted of a cluster of markedly abnormal arteries together with tortuous and dilated veins, in accordance with our pathological diagnosis of an arteriovenous malformation (AVM).

Postoperatively the patient recovered quickly and there were no complications. At discharge, the headaches and vomiting were no longer present and the patient was free of any other neurological deficits.

Second case

After a 6-year interval, the 39-year-old brother of our first patient was admitted to our clinic with a 1-month history of vertigo together with episodes of nausea and vomiting. One week prior to admission the patient had lost consciousness after having an acute onset headache and was transported to a local hospital. His past medical history and familial history were unremarkable for brain diseases. However, a detailed familial history was not obtained, nor were any other family members examined at our center. A CT-scan was performed showing hydrocephalus and a huge cystic lesion in the third ventricle. In the acute setting, he was treated by means of a ventricular drain. Preoperative gadolinium-enhanced T1-weighted MRI showed a huge, 52 mm × 42 mm × 39 mm measuring, hypointensive cystic lesion in the third ventricle that had progressively expanded upward to the corpus callosum, displacing the septum pellucidum and bulging in the lateral ventricles [Figure 2]. Diffusion tensor imaging (DTI) fiber tracking visualized a pronounced displacement of the fornices to the right [Figure 3]. Therefore, we planned a left frontal parasagittal craniotomy to gain access to the lesion through a transcallosal approach from the opposite side of the forniceal structures. The

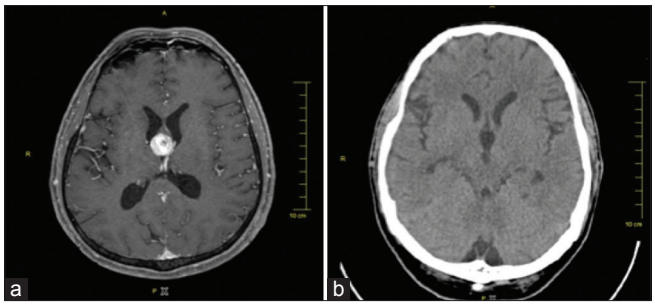

Figure 1: First case. (a) Preoperative gadolinium enhanced T1-weighted axial magnetic resonance imaging, showing an in homogenously enhancing mass in the third ventricle causing mild hydrocephalus. (b) Postoperative axial computed tomography-scan showing complete removal of the lesion and absence of hydrocephalus

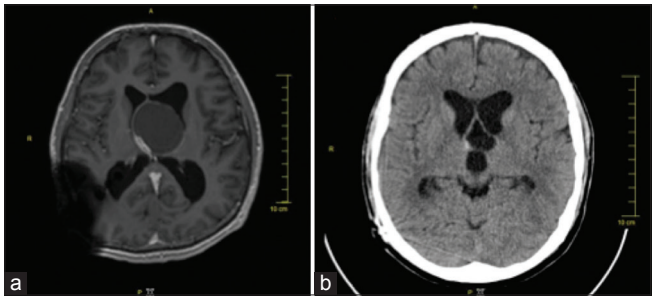

Figure 2: Second case. (a) Preoperative gadolinium enhanced T1-weighted axial magnetic resonance imaging, showing a gigantic cystic lesion in the third ventricle causing hydrocephalus. Note the enhancing vessels on the cyst wall. Artifact is due to the occipital venticuloperitoneal-shunt. (b) Postoperative axial computed tomography-scan showing extirpation of the cyst content and no signs of increased intra-cranial pressure

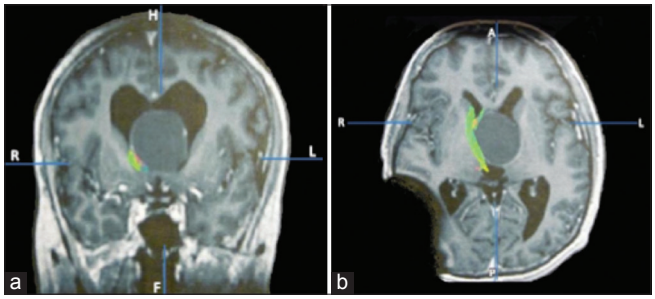

Figure 3: Second case diffusion tensor imaging (DTI). Preoperative DTI fiber tracking. Coronal (a) and axial (b) images showing a pronounced displacement of the fornices inferiorly and to the right. The artifact is due to the ventriculoperitoneal-shunt

surgery was performed under intraoperative MRI control with DTI fiber tracking in order to visualize the forniceal structures. After puncturing the cyst and aspirating the entire glue like the content, the capsule was partially removed. To restore the liquor flow a large and wide-opening was made in the cyst wall ventro-cranially, to ensure outflow to the lateral ventricles. Moreover, a second opening was created caudally in the area of the lamina terminalis, to form a connection between the third ventricle and the suprasellar cisterns. The foraminae of Monro were identified, as they were displaced more ventrally, and their patency was secured. Intra-operative MRI showed total extirpation of the cyst content as well as the artificial "cysto-cisternal" and "cysto-ventricular" openings. Finally, endoscopic inspection was performed to ensure hemostasis. There were no postoperative complications and no memory deficits were detected on subsequent serial examinations. Histology confirmed the diagnosis of a CC, showing a single layered AE1/AE3 positive ciliated epithelium.

DISCUSSION

The origin of colloid cysts

Ever since their discovery, CC's have remained a curious clinicopathological entity. More than a century ago Sjovall presumed the cysts originated out of the paraphysis cerebri, an evanescent vestigial embryonic structure.[42] This theory held state until the advent of the term "neuroepithelial cyst" in 1929 by Fulton and Bailey. They discussed the presence of cilia and certain cyst contents in their specimens along with the variability in the location of the cysts, holding both a pathological and an anatomical argument against a paraphyseal origin. In 1955 Kappers partially restored Sjovall's theory by explaining that an ectopic location of the cyst results from inclusion of peripheral paraphyseal "anlagen," which is of ependymal origin and may arise along variable locations along the ventricular axis.[26] Electron microscopy allowed Coxe and Luse to subscribe an ependymal epithelial origin in 1964 though their findings were based on a single case.[11] One year later Shuangshoti *et al.* introduced their theory of neuroepithelial origin.[41] Based on a review of the literature combined with embryological and comparative anatomical studies, they classified the paraphysis as the extraventricular choroid plexus. The suggestion that both choroid plexus and ependyma are derived from a common neuroepithelium can balance the arguments Fulton and Bailey held against the paraphyseal origin, somewhat unifying the former theories. Besides this, some authors have proposed an extraneural origin, namely out of the ectopic endodermal tissue. The argument for this theory is the similarity of the cyst epithelium to the respiratory mucosa, described by Tsuchida *et al.*[45] Concurrently Ho and Garcia found the presence of ciliated cells and goblet cells upon ultrastructural analysis of their specimens. In their arrangement, the cells were interconnected by desmosomes and met the criteria of an endodermal lineage.[23] These findings have led to the supposition that CC's and Rathke's cleft cysts may share the same pathophysiology and represent comparable lesions at different locations.[18] Still the true origin of the CC's remains a matter of debate.

Colloid cysts and genetics

Another approach of trying to clarify the mechanisms involved in the development of familial CC's is the search for a genetic abnormality that could lead to an inheritable disease. Interestingly in this respect, insights into the function of "paired"-like homeodomain transcription factor (Prop1) in the development of the Rathke's pouch, the pituitary primordium, have been described in mice. Prop1 seems to have a crucial role in cell proliferation and differentiation and thus in the organogenesis and function of the pituitary gland. A dysregulation in Prop1 expression is correlated with an increased susceptibility for pituitary tumors and Rathke's cleft cysts. The latter were found in 40% of the alpha glycoprotein subunit (αGSU)-Prop1 transgenic mice, which express a high level of Prop1 under the αGSU promoter (gain of function).[12] In humans the Prop1 gene fulfills the same function, and several loss-of-function mutations have been known to cause dysfunction and cystic dysplasia of the pituitary.[49,51] By analogy with Rathke's cleft cysts it is likely that a genetic factor is involved in causing CC's as well. Especially since these clinical conditions may constitute the same entity. The idea of an inheritable genetic factor involved in the pathophysiology of familial CC's of the third ventricle has already risen. This assumption is made, because of the improbable statistical chance of co-occurrence in first-degree relatives ($1:10^{11}$).[46] Despite the fact that this phenomenon can occur in a very variable way with regard to the family members affected, an autosomal dominant inheritance seems to be the most likely form of inheritance.[17,32,44] Our case shows that huge cysts, earlier described solely in individual cases,[20,50] can also arise in kinship. In addition, we found an AVM in the first case. Previous reports have mentioned the solitary occurrence of AVM in the third ventricle.[8,21,39] On the other hand, some intra-cranial anomalies have been described in association with CCs, such as craniopharyngioma,[28] xanthogranuloma,[19,31] astrocytoma,[16] and agenesis of the corpus callosum.[14] To the best of our knowledge, it is the first time that an AVM is reported in association with a CC of the third ventricle. These ascertainments, revealing an additional variable factor in how this phenomenon may present, advocate in favor of a developmental malformation.[40] Yet it remains worthwhile to invest in research to pinpoint a genetic defect that would offer an explanation for the cases observed.

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