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Case Report

Posterior fossa giant tumefactive perivascular spaces: 8-year follow-up in an adolescent

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Abstract

Background: Cystic masses in the posterior fossa are ominous appearing lesions with broad differential diagnosis. Giant tumefactive perivascular spaces (GTPS) are rarely occurring pathological findings in the posterior fossa with unclear etiology and ill-defined long-term prognosis.

Case Description: We present a case of a 15-year-old male diagnosed with posterior fossa GTPS. The patient remained asymptomatic during the 8-year follow-up after diagnosis with the serial magnetic resonance imaging (MRI) showing no change in the size and morphology of the lesion.

Conclusion: This case supports prior literature on supratentorial GTPS suggesting that the natural history of GTPS is mostly benign. Identification of GTPS in the posterior fossa could prevent the patient from unnecessary surgery or other aggressive treatment modalities.

Key Words: Cerebral cyst, giant tumefactive perivascular spaces, posterior fossa, prognosis

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INTRODUCTION

Posterior fossa cystic lesions can appear quite ominous when discovered on a patient's imaging workup, they may present a challenging differential diagnosis, and tend to be associated with a dismal prognosis. The identification and study of cerebral cysts has been advanced over the past few decades with the introduction of magnetic resonance imaging (MRI) into clinical practice. Presently the natural history and prognosis for many types of intracranial cystic lesions can be known based largely on imaging alone with the goal to identify those pathologies that need rapid medical or surgical intervention. In the same way it is extremely important to recognize benign pathological findings to prevent unnecessary interventions.

Posterior fossa giant tumefactive perivascular spaces (GTPS) are one such discovery, which has been divulged during the MRI era, but its natural history and pathogenesis remains uncertain.[11] Current knowledge suggests that GTPS are large, bizarre appearing clustered cystic structures formed from the perivascular (Virchow–Robin) spaces of the brain. The prognosis of GTPS is thought to be benign, such as that of an arachnoid cyst; however, as with other benign cysts surgical intervention may become necessary in order to relieve symptoms caused by mass effect. Few case reports have been published describing the characteristics of GTPS,

however, much of the etiology and natural history remains elusive. Here we present a case of GTPS in the posterior fossa followed over 8 years with serial imaging and clinical exams, detailing one of the longest observational records reported in the literature.

CASE REPORT

The patient was addressed to our institution for second opinion. His medical history started 8 years ago at his age of 15 when he was hospitalized with a 3-day history of dizziness, gait instability, nausea, and headaches. On clinical examination at that time, he had mild diplopia on left lateral gaze and convergence, incapacity of upward vertical gaze, mild right upper and lower extremity weakness (M4), right sided hypoesthesia, mild gait instability, but no cerebellar signs in the extremities.

The MRI of the brain revealed a well-defined lobulated cystic lesion in the right middle cerebral peduncle close to the forth ventricle with mild mass effect to the cerebellar vermis [Figure 1]. The lesion contained multiple thin septations (black arrow in Figure 1c) and followed cerebrospinal fluid (CSF) signal in all pulse sequences (Figure 1a: Axial T1-weighted image, Figure 1b: Axial postcontrast T1-weighted image, Figure 1c: Axial T2-weighted image, Figure 1d: Diffusion-weighted, Figure 1E: Apparent diffusion coefficient). There is no definite enhancement or diffusion restriction. Mild edema is noted in the right middle cerebellar peduncle (white arrow in Figure 1c). Single voxel proton magnetic resonance spectroscopy [Figure 1f] showed unremarkable concentration of *N*-acetylaspartate (NAA), choline (Cho), creatine (Cr) with normal Cho/Cr ratio and Cho/NAA ratio.

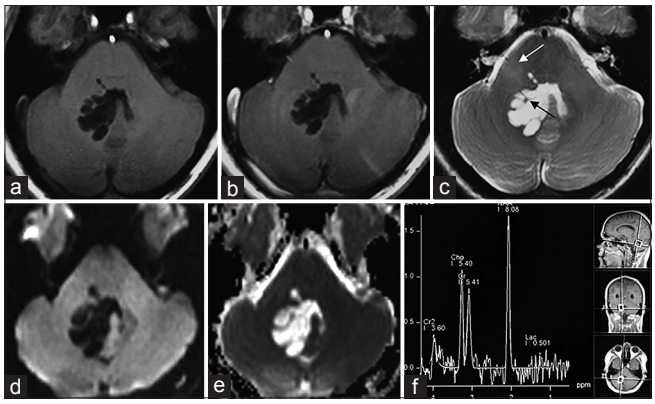

Figure 1: Magnetic resonance imaging (MRI) of the brain performed at the time of symptom onset 8 years ago demonstrated a well-defined lobulated cystic lesion in the right middle cerebral peduncle close to the forth ventricle with mild mass effect to the cerebellar vermis. The lesion contained multiple thin septations (black arrow in C) and followed cerebrospinal fluid (CSF) signal in all pulse sequences (a) axial T1-weighted image, (b) axial postcontrast T1-weighted image, (c) axial T2-weighted image, (d) diffusion-weighted, (e) apparent diffusion coefficient). There is no definite enhancement or diffusion restriction. Mild edema is noted in the right middle cerebellar peduncle (white arrow in C). Single voxel proton MR spectroscopy (f) showed unremarkable concentration of *N*-acetylaspartate (NAA), choline (Cho), Creatine (Cr) with normal Cho/Cr ratio and Cho/NAA ratio

During his hospitalization the patient underwent a craniotomy with biopsy of the cyst. Via the midline posterior fossa craniectomy and supracerebellar-infratentorial approach, the right ponto-mesencephalic region was identified. With the help of image guidance a cystic cavity containing xantochromic fluid was entered about 3–4 mm below the surface. Following biopsy of the cyst wall, the closure and immediate postoperative course were uneventful. The surgical pathology of the cyst revealed nontumoral edematous parenchyma without an epithelial lining containing signs of old hemorrhage and reactive astrocytes with glial satellitosis. The histologic reports were inconclusive and a nondefinitive diagnosis of pilocytic astrocytoma was given based on the history, imaging, location, and histology.

In the postoperative period, the patient completely recovered from upper gaze palsy and double vision, as well as his left hemiparesis and hemihypoesthesia resolved. He was followed on 2-year intervals and remained neurologically intact at the most recent 8-year follow-up. Serial MRI imaging revealed no change in the size and shape of the lesion (Figure 2a: At the time of diagnosis, Figure 2b: 2 years later, Figure 2c: 5 years later, Figure 2d: 8 years later).

DISCUSSION

GTPS typically appear as multiloculated cystic lesions located unilaterally within the thalamomesencephalic region and white matter of the cerebral hemispheres and

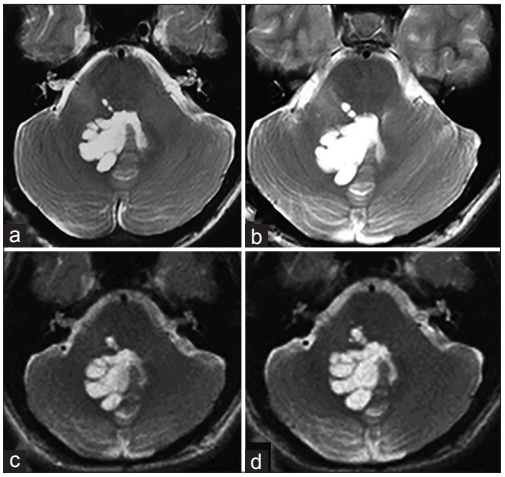

Figure 2: Serial annual brain magnetic resonance imaging (MRI), with representative axial T2-weighted images, has shown stability to slight increase in size of the lesion in the past 8 years. (a) MRI at the time of diagnosis, (b) Two years later, (c) Five years later, (d) Eight years later

less commonly within the cerebellar white matter, as they are thought to develop from the perivascular spaces of the perforating arteries in these areas.[3,4,7,10,11] Earlier reports have described this entity using the term 'expanding lacunae'.[7,10] Unique to the present case is the posterior fossa location of GTPS. Most cases of GTPS reported in the literature are located supratentorially. A review of the literature yielded few reported cases of GTPS within the posterior fossa [Table 1]. Histopathologic analysis of GTPS demonstrates a pial lined cyst in smaller lesions and a gliotic parynchmal lining without an observed pial layer in larger lesions.[4,11] No evidence of any ependymal or epithelial lining, neoplasia or infection is observed. Imaging features distinguishing GTPS from neoplasm or other disease are their isointensity to CSF on all sequences, no enhancement following contrast administration, no diffusion restriction, absence of calcification, and their characteristic locations.[11,12] These lesions are also believed to show stability over time. Similar to other benign pathologies, patients tend to develop symptoms and present as result of the mass effect created by a larger lesion.

While the exact etiology of GTPS remains elusive, several hypotheses have surfaced over the past decades. The first theory argues that GTPS are distensions of perivascular spaces, likely caused by a disorder of the permeability of the arterial wall. A permeable arteriole situated in the center of the cavity, as evidenced by the histologic presence of severe lesions of segmental necrotizing angeitis, may facilitate dilation of the Virchow–Robin space.[10] Furthermore, the proximity of ventricles is thought to explain the expanding character of these lesions in some cases by means of a hydrodynamic factor.[7,10] A second theory argues that GTPS may arise as result of impaired drainage of the cerebral interstitial spaces via the lymphatic pathways resulting in the dilation of the Virchow–Robin space.[7] Another theory suggests that GTPS might be formed through budding from the ventricular system, with subsequent loss of ependymal cells by stretching or pressure effects as the cyst distended with fluid.[14] Lastly, an argument that at some point in development, the ventricular wall ruptured to allow (CSF) to dissect into the adjacent brain parenchyma in a manner similar to the extension of CSF from the central canal into the spinal cord to form a syrinx.[8,14]

We should note that GTPS appear to be a separate process, although not unrelated, from dilated perivascular spaces or cerebral lacunes (also termed 'unidentified bright objects' on MRI T2-weighted sequences) associated with aging and cerebrovascular disease.[2,4,6,10,15] In the latter, perivascular dilations are relatively small, unclustered dilations that do not cause mass effect and appear symmetrically within the cerebral white matter, basal ganglia, and mesencephalon.[1,2,4,5,15] GTPS also appears to be a separate process from the more familiar simple cysts of the cerebellum, also termed vermian cysts, benign intracerebral cysts, and nonneoplastic gliotic cerebellar cysts.[9,13,14] Simple cysts of the cerebellum are reported more frequently in the literature and while histologic observations of the cyst wall also typically report gliotic parynchmal lining, all reports identify a single large midline or paramedian cyst involving the cerebellar vermis. Conversely, a characteristic multiloculated cystic structure has been described in all reports of GTPS.

Table 1: Reported cases of giant tumefactive perivascular spaces in the posterior fossa

Reference	Case	Age/sex	Clinical presentation	Appearance and location	Histology	Follow-up period
Salzman *et al.*[11]	1	17/male	Not available	Multiloculated giant perivascular spaces in the bilateral cerebellar hemispheres in area of bilateral dentate gyri	None	None
	2	6/male	Minor trauma	Multiloculated giant perivascular spaces in the left dentate gyrus adjacent to 4th ventricle	None	None
	3	35/male	Headaches	Midbrain and pons	A section through the cyst wall shows collagen in the leptomeninges on the outer aspect of the cyst wall coating the underlying brain tissue that forms the bulk of the cyst wall. No lining of pia matter is present on the inner aspect of the cyst. Extensive gliosis was observed in the cyst wall. No neurons were identified	1-year
Current report	4	15/male	Dizziness, gait instability, nausea, headaches, transitory left hemiparesis and lateral gaze deficit	Lobulated cystic mass in the right cerebellum and pontine peduncle	Nontumoral edematous parenchyma without epithelial lining, signs of old hemorrhage and reactive astrocytes with glial satellitosis	8 years

As our knowledge of GTPS increases, it is becoming evident that while these lesions can appear quite ominous, they hold a relatively benign prognosis. The difficultly herein for clinicians becomes ensuring that an accurate diagnosis is made, and that more malignant pathologies are not confused with GTPS and vica-versa. Within the differential diagnosis of posterior fossa cystic lesions we should consider: Parasitosis, abscesses, cystic glial and astrocytic tumors, craniopharyngioma, hemangioblastoma, dermoid and epidermoid cyst, arachnoid and Rathkes cleft cysts, porencephalic cysts, encephalomalacia, subependymal cysts, neuroepithelial cysts, metabolic deposition disorders.[7,9,11,12,14] The initial diagnosis given in the present case was likely incorrect. The patient remained symptom free and serial imaging showed stability over an 8-year follow-up period [Figure 2]. This illustrates the difficulty in diagnosing rare, poorly understood pathology, and highlights a need for raising awareness of posterior fossa GTPS along with its natural history. The patient in the present report presented acutely with symptoms, which may have either been related to the mass effect created by this cystic lesion or secondary to small amounts of hemorrhage within tissues adjacent to the lesion. However, the absence of symptoms and imaging in the 15 years prior to presentation, offers little insight into the onset of symptoms at this particular point in time. One possibility is that symptoms onset may have occurred as result of small areas of hemorrhage, similar to that seen in the natural history of cavernomas. Focal areas of old hemorrhage have been observed on histopathology taken from GTPS biopsy. In addition, one theory about the etiology of GTPS identifies a single leaky arteriole at the center of each cavity responsible for cavity enlargement; such a vessel may also be prone to hemorrhage on occasion. A second possibility could be that cyst enlargement in GTPS occurs during childhood or adolescence and slopes off in adulthood. Small areas of hemorrhage may occur adjacent to the cavity as it grows and displaces surrounding tissue, or as result of the cavity growing to a point where it is influenced by intracranial hydrodynamics.

An important insight into the pathology of GTPS is its benign nature. Our patient remained symptom free with a large cerebellar cystic lesion, which did not change in size over an 8-year follow-up period. No other report of GTPS located in the posterior fossa has documented a follow up period longer than 1 year. One report in the literature documents GTPS located in the frontal lobe, which remained stable in size and asymptomatic over a 17-year follow up.[12] The largest series of GTPS reported follow up on 17 patients ranging from 1 to 12 years after initial diagnosis, in all patients GTPS lesions remained stable in size and appearance over the course of their follow up.[11] While the etiology of posterior fossa GTPS remains elusive, it appears that this pathology is associated with a benign prognosis. Conservative management and observation tend to be the mainstay of treatment, while invasive therapies are reserved for obtaining tissue diagnosis and addressing symptoms of mass effect.

CONCLUSION

GTPS should be included into the differential diagnosis of cystic masses in the posterior fossa. Although differentiating GTPS from other benign pathologies may be challenging, it is important to keep this benign pathological entity on the forefront. As documented by our case, posterior fossa GTPS has a long-term favorable prognosis and its identification would prevent from unnecessary surgery or other more aggressive treatment modalities.

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