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# Surgical considerations regarding giant dilations of the perivascular spaces

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*Object.* Dilations of brain perivascular spaces (PVSs), also known as Virchow–Robin spaces, are routinely identified on magnetic resonance imaging studies of the brain and recognized as benign normal variants. Giant dilations occur only rarely and can be easily misdiagnosed as central nervous system tumors. The relevant surgical literature was reviewed to help establish indications for surgical intervention in these typically benign lesions.

*Methods.* Giant dilations of the PVSs in 12 patients who had undergone surgery for several different indications were identified. Both clinical and radiographic presentations of these patients were reviewed along with the surgical procedures.

*Conclusions.* Dilations of the PVSs can become giant lesions that may necessitate surgical intervention to relieve mass effect or hydrocephalus. The relationship of these lesions to neurological symptoms such as tremor and seizures remains unclear.

**Key Words • perivascular space • Virchow–Robin space**

The PVSs in the brain are complex pia mater–lined areas that follow penetrating arteries and arterioles into the cerebral cortex. They are lined by a single layer of pia in the cerebral hemispheres and two layers of pia along the lenticulostriate arteries.[17] The spaces are usually small (1–2 mm in diameter), but can be easily visualized on thin-section $T_2$-weighted MR imaging studies.[19] Perivascular spaces are filled with interstitial fluid, not CSF, and are thought to be a major pathway for interstitial fluid egress from the brain.[21] Furthermore, they play a role in immunological regulation because they harbor resident microglia.[13]

Giant dilations of the PVS are unusual anatomical variants that can be misdiagnosed as central nervous system tumors. Often these dilations are found in patients with nonspecific neurological complaints. The relationship between tumefactive PVS dilations and a variety of neurological symptoms has yet to be firmly established. Here, we reviewed the surgical literature regarding PVS dilations with an emphasis on the indications for intervention.

## Clinical Material and Methods

The clinical, radiological, and pathological records of patients with giant dilations of the PVS were reviewed. We identified 12 patients harboring tumefactive dilations of the PVS who had undergone a variety of surgical procedures, and these patients constitute the largest group of such patients in the medical literature to date (Table 1). Most (11 patients) had undergone either primary treatment or review at the University of Utah Hospital at the request of the treating physicians. One additional patient was treated primarily at the University of Southern California Hospital. All patients had dilations of at least 1.5 cm in diameter, which produced local mass effect.

Patients, seven of whom were men, ranged in age from 21 to 57 years, with a mean age of 42 years. Dilated PVSs were located in the thalamus, midbrain, and subcortical white matter. Lesions were situated in the left hemisphere in seven patients, right hemisphere in three, and both hemispheres in two. The majority of patients presented with headaches, and eight had obstructive hydrocephalus.

Six patients underwent biopsy. Eight patients required CSF diversion because of hydrocephalus. Three patients underwent VP shunt placement, whereas a fourth experienced a cystoperitoneal shunt placement. Four patients underwent ventriculocisternostomy. One patient had a cyst catheter-reservoir implanted to enable serial aspiration. Follow-up imaging studies from 2 to 9 years after the initial diagnosis were available in all patients. No enlargement of a cystic dilation was noted, except in the two patients described later.

## Illustrative Cases

### *Case 1*

This 39-year-old man presented with a 1-year history of severe headaches, which had become progressively more debilitating. These headaches initiated behind the left eye and evolved to encompass the entire head. Additionally, the patient experienced a coarse tremor of the right upper and lower extremities. Magnetic resonance images of the brain revealed a nonenhancing cystic lesion in the left insula and basal ganglia together with significant local mass effect (Fig. 1).

*Abbreviations used in this paper:* CSF = cerebrospinal fluid; FLAIR = fluid-attenuated inversion-recovery; MR = magnetic resonance; PD = Parkinson disease; PVS = perivascular space; VP = ventriculoperitoneal.

TABLE 1

*Characteristics in 12 patients with giant dilations of the PVS*

| Case No. | Age (yrs), Sex | Primary Symptom(s) | Procedure(s) Performed | PVS Location | Laterality | Hydrocephalus |
|---|---|---|---|---|---|---|
| 1 | 39, M | headache | biopsy | thalamus, white matter | lt | no |
| 2 | 35, M | headache, poor vision | biopsy, ventriculocisternostomy | midbrain | lt | yes |
| 3 | 57, M | lethargy, poor memory | biopsy, ventriculocisternostomy | midbrain | lt | yes |
| 4 | 44, F | poor balance, poor concentration | ventriculocisternostomy | midbrain | rt | yes |
| 5 | 46, M | headache | biopsy | midbrain, thalamus | rt | no |
| 6 | 56, F | headache, poor memory | fenestration, shunt placement | thalamus | lt | yes |
| 7 | 40, M | headache | biopsy | midbrain | rt | yes |
| 8 | 21, M | seizure | biopsy | white matter | lt | no |
| 9 | 47, F | headache | shunt placement | thalamus, midbrain | bilat | yes |
| 10 | 35, M | headache, confusion | shunt placement | thalamus | bilat | yes |
| 11 | 49, F | headache | ventriculocisternostomy | thalamus | lt | yes |
| 12 | 31, F | headache, hemiparesis | cyst catheter aspiration | midbrain | lt | no |

Craniotomy was performed for cyst fenestration and diagnostic purposes. A healthy small artery could be identified centrally in some of the cysts. The patient experienced resolution of headaches and improvement in tremor (Fig. 2). Histological analysis showed cystic dilations of healthy brain tissue with some reactive gliosis at the cyst edges.

Five months following his surgery the patient was involved in a motor vehicle accident and experienced a recurrence of the headaches. Brain imaging studies revealed reexpansion of the fenestrated cysts with some hemorrhage. Along with the headaches, the patient also developed some intermittent dystonic movements of the right arm. Endoscopically assisted placement of a VP shunt was performed because of the symptomatic enlargement of the cysts. The patient again experienced relief of the headaches and resolution of the movement abnormalities. He remains asymptomatic 1 year following shunt placement.

*Case 6*

This 56-year-old woman presented on multiple occasions to local emergency rooms and to her primary physician with a variety of complaints. She had suffered headaches and gait instability. These were accompanied by new memory and intermittent speech difficulties. She also had a history of panic attacks and depression. Her symptoms were believed to be nonspecific and were originally managed using medical therapy. After several episodes of worsening symptoms, brain imaging studies were performed.

Both computerized tomography scanning and MR imaging studies revealed that the patient had a left posterior thalamic cyst causing obstructive hydrocephalus (Fig. 3). The patient underwent cyst fenestration via a supracerebellar, subtentorial approach. Initially, she had a good response to surgery; 4 months later, however, many of her symptoms returned. Imaging studies demonstrated that the cyst had returned to its original size with resultant hydrocephalus. The patient therefore underwent placement of a ventriculoatrial shunt. Again, initially she responded well, with improvement in her hydrocephalus. Unfortunately, despite this improvement in the hydrocephalus, some of her symptoms, including headache and dizziness, persisted.

## Discussion

Dilations of the PVS could be visualized on $T_2$-weighted MR imaging in up to 95% of patients in a recent study.[19] It has been asserted that PVS dilations are a normal part of aging and occur primarily in the elderly.[9] Such dilations have been noted in nearly 30% of healthy children, however,

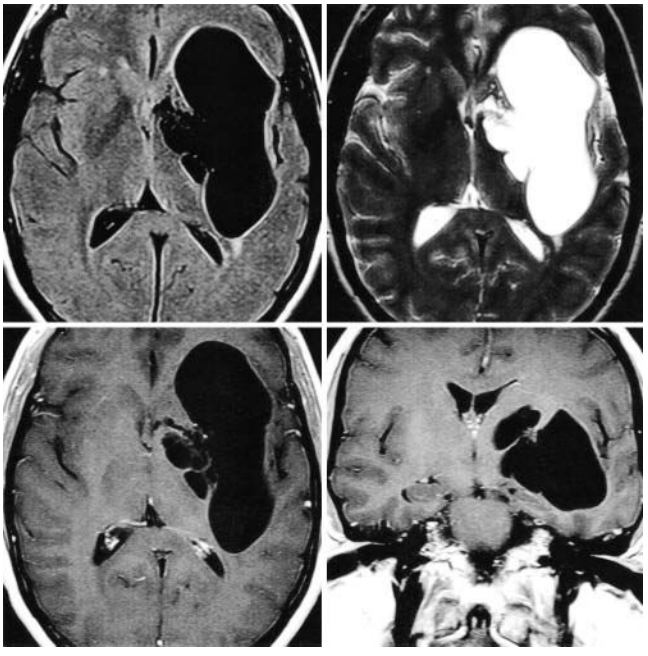

FIG. 1. Case 1. Axial FLAIR-weighted *(upper left)*, $T_2$-weighted *(upper right)*, and contrast-enhanced $T_1$-weighted *(lower left)* and coronal contrast-enhanced $T_1$-weighted *(lower right)* MR images revealing the tumefactive dilations of the PVS in the left basal ganglia and insula. Note that the lesion follows CSF signal intensity and does not enhance following administration of a contrast agent. This large multilocular lesion produces mass effect on the basal ganglia, thalamus, and third ventricle. The thin rim of high signal on the $T_2$- and FLAIR-weighted images surrounding the enlarged PVS is consistent with the small amount of gliosis identified on histological examination.

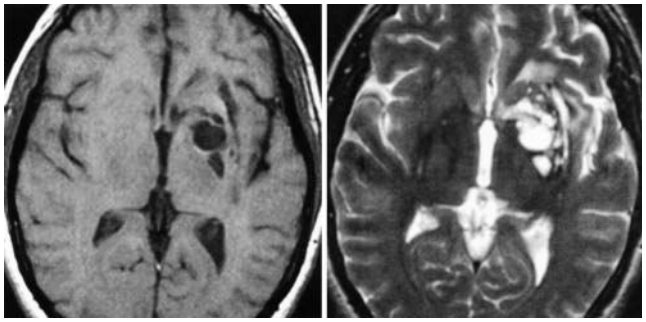

FIG. 2. Case 1. Axial $T_1$- *(left)* and $T_2$-weighted *(right)* MR images obtained following cyst biopsy and fenestration, demonstrating greatly reduced mass effect with reexpansion of the third ventricle to normal dimensions.

and have been associated with normal development, even in macrocephalic children.[2,18] Small dilations of the PVS are now considered to be a normal imaging variant with a benign prognosis. In fact, small PVS dilations are now visualized in nearly all patients when 3-tesla imaging is used (AG Osborn, unpublished data).

Case reports of extreme dilations of the PVSs have been published previously and will be described later. Often the cases of tumefactive PVS dilation come to surgical attention because of their unusual appearance and concerns regarding possible pathological features. A variety of indications for surgical intervention exist in association with these lesions. To help clarify these issues, we review the surgical indications regarding treatment of hydrocephalus, treatment of tremor or seizure, and the need to perform biopsy.

*Treatment of Hydrocephalus*

Cystic dilation of the PVS within the midbrain can cause obstructive hydrocephalus by limiting CSF flow through the cerebral aqueduct. In 1983 Poirier, et al.,[15] described a 54-year-old patient with mesencephalic lacunae who had experienced neurological deterioration with symptoms similar to those in normal-pressure hydrocephalus, including progressive gait disturbance, incontinence, and worsening mental status. Improvement occurred after ventriculocisternostomy. Similarly, Homeyer, et al.,[10] reported on a 42-year-old man who had experienced worsening headache in association with 10 years of progressive diplopia and paresthesias in both upper extremities. On MR imaging, PVS dilations in the right mesencephalon and thalamus with resultant hydrocephalus were visualized. Eventually, a VP shunt was placed, with improvement in the patient's paresthesias and headaches, although his diplopia remained. No change in the PVS dilation was noted on MR imaging studies performed at 6 months.

As these two cases illustrate, patients become symptomatic from hydrocephalus very slowly and the symptoms may mimic those that occur in normal-pressure hydrocephalus. More recent literature confirms these initial reports. Mascalchi, et al.,[14] have described two patients. The first, a 58-year-old woman, presented with a decreased mental status (as documented on the Mini-Mental State Examination), Parinaud phenomena, gait difficulty, and rubral tremor. All symptoms improved after a shunt was placed to relieve hydrocephalus. The second patient, a 55-year-old man, received a diagnosis of a "frontal lobe syndrome" consisting of memory loss, decreased mental status, and ataxic gait. A ventriculocisternostomy was performed and the patient's symptoms improved. Again, the size of PVS dilation was unchanged on MR images obtained 6 months later. In a more recent study,[11] a 35-year-old man was described as experiencing slowly developing symptoms of forgetfulness, confusion, and somnolence. Aside from these symptoms, results of his neurological examination were unremarkable. He was found to have left midbrain PVS dilations with hydrocephalus, although his symptoms improved with the placement of a shunt.

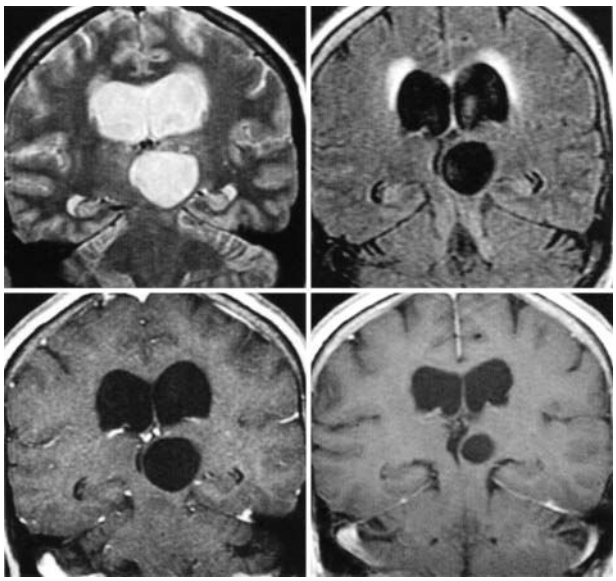

FIG. 3. Case 6. Coronal $T_2$- *(upper left)* and FLAIR-weighted *(upper right)* and contrast-enhanced $T_1$-weighted *(lower left)* MR images of the dilated PVS revealing severe compression of the third ventricle with resultant hydrocephalus. Transependymal edema is demonstrated, but there is no evidence of contrast enhancement. The coronal contrast-enhanced $T_1$-weighted image *(lower right)* obtained after cyst fenestration reveals a decrease in both the size of the giant PVS and hydrocephalus.

The development of hydrocephalus necessitated surgery in the majority of patients included in our study. Eight patients required CSF diversion procedures. Three patients underwent insertion of VP shunts, one patient received a cystoperitoneal shunt, and four patients underwent ventriculocisternostomy procedures. One patient had small serial aspirations of a midbrain cyst with no further treatment. In all cases the cystic PVS dilation remained stable or decreased in size on subsequent MR imaging studies.

Although PVSs are filled with interstitial fluid and not CSF, one might postulate that CSF drainage alone could decrease the size of dilated PVSs. In all cases published to date in which CSF drainage was used to treat hydrocephalus, the PVS dilations remained stable in size. In the patients in this study the PVS dilations only decreased in size when they were directly fenestrated or subjected to shunt placement.

Clearly, some degree of enlargement of the cystic PVS dilation occurred in each patient who later developed hydrocephalus. Longitudinal studies of PVS dilations have not been performed, but follow-up imaging studies in cases

published to date have yet to demonstrate an increase in PVS size. Given that the number of patients who harbor undiagnosed tumefactive dilations of the PVS is likely to be large, the few published cases of lesions causing hydrocephalus indicate that lesion growth is rare.

*Tremor and PVSs*

When multiple small dilations of the PVSs are present in the striatum, they can be classified as état criblé or type III lacunae in the classification system of Poirier and Derouesné.[16] These were first described in 1843 and in 1929. Critchley[5] described this condition as being a form of arteriosclerotic parkinsonism. The contribution of multiple small PVS dilations to symptoms of PD is still a matter of debate. This subject is reviewed by Fénelon and associates,[8] who also reported on two patients with état criblé, based on imaging and histological studies. Although both patients displayed signs of PD, only one patient had the usual changes in the substantia nigra, indicating that dilated PVSs may play a role in causing or modifying PD.

The surgical implications of état criblé have also been investigated recently. Desaloms and colleagues[7] prospectively studied the outcome of posteroventral medial pallidotomy in patients with PD, noting that patients who had status cruciformis or lacunae prior to surgery had less improvement in their off-medication condition at 6 months posttreatment. Patients with both conditions had a higher incidence of transiently altered mental status. Nonetheless, Laitinen, et al.,[12] reported no difficulty or lack of effect of pallidotomy in patients harboring dilated PVSs. In fact, the majority of their patients harbored dilated PVSs predominately in the posteroventral regions of the globus pallidus. The patients' preoperative motor symptoms were noted to be more severe on the side of the body contralateral to the side of the brain having the least number of dilated PVSs. These findings indicate that there may be a functional consequence to multiple PVSs. When the majority of dilations are in the posteroventral pallidum, however, they may lessen the effects of PD.

The effect of a massive PVS dilation on tremor is unknown. The case of a patient harboring mesencephalic cystic dilations with resultant triventricular hydrocephalus was presented by Mascalchi and colleagues.[14] This patient displayed a right-sided rubral tremor along with symptoms of hydrocephalus. Although many of the hydrocephalic symptoms improved with CSF diversion, the patient's tremor did not. In contrast, one of the patients in the present study displayed upper- and lower-extremity coarse tremor that dramatically improved with decompression. In this case, the extensively dilated PVS was causing mass effect on the basal ganglia, which, according to neuroimaging studies, improved following shunt placement. The experience of this patient demonstrates that tremor may sometimes be improved if it is caused by basal ganglia compression.

*Seizure and PVSs*

The functional relationship between tumefactive dilation of the PVS and seizures is unclear. Only one case report demonstrates a causal link.[3] This patient, a 64-year-old man, experienced right temporal lobe seizures very late in life. Evaluation revealed a large PVS dilation in the right hippocampus. It is possible that this lesion expanded over years and led to the development of seizure. Other case reports indicating a link between dilations and seizures are unable to offer clear causal explanations.[1,4]

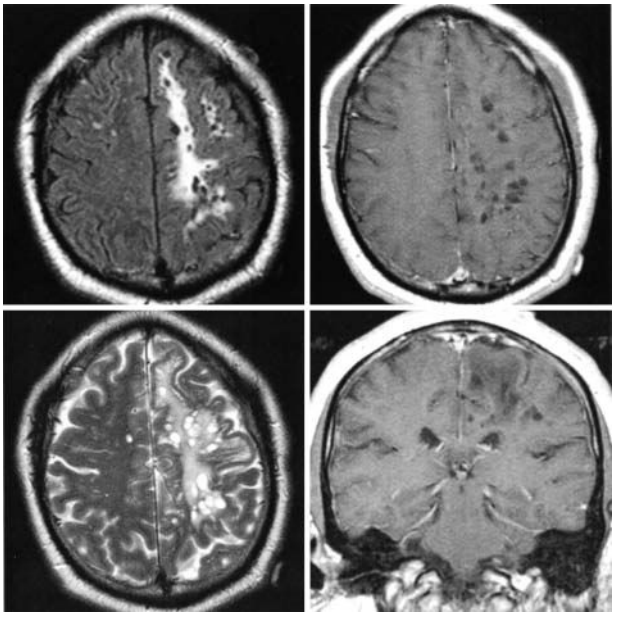

FIG. 4. Magnetic resonance imaging performed in a patient with multiple cystic dilations of the PVS demonstrating a pattern that could at first appear to be a neoplasm. Axial FLAIR- *(upper left)* and $T_2$-weighted *(lower left)* images reveal abnormal increased signal within the adjacent white matter; however, the signal characteristics of the giant PVS always follow CSF signal intensity and no contrast enhancement is demonstrated. *Right:* The $T_1$-weighted images.

One patient in our series experienced seizures. This patient, a 21-year-old man, had a history of generalized seizures with no clear origin. Magnetic resonance imaging studies revealed cystic dilations in the cortical and subcortical white matter on the left side. The patient underwent biopsy sampling for what proved to be PVSs. The patient was also found to have cortical dysplasia, a known contributory factor to seizures. Follow-up imaging performed 6 years after biopsy revealed the PVS dilations to be unchanged.

It is unclear whether there is any functional consequence to PVS dilations. As discussed earlier, there is some evidence indicating that the condition of état criblé may contribute, in either a positive or negative way, to parkinsonian symptoms. The functional consequence of extreme PVS widening has been studied in only one patient.[20] This 60-year-old woman with extreme widening of subcortical PVSs in the right frontal and parietal areas underwent somatosensory evoked potential and transcranial magnetic motor evoked potential monitoring. No laterality of testing or other functional consequences could be demonstrated. Analysis of data currently available indicates that PVS dilations do not often contribute to seizure activity. Patients harboring dilated PVSs and demonstrating seizures should be thoroughly evaluated for a more common cause of seizure.

*Biopsy for Tissue Diagnosis*

The ominous appearance of tumefactive PVS dilations will often lead to a differential diagnosis that includes neoplasm. The majority of case reports published to date fea-

ture patients who have undergone a brain biopsy procedure. A typical case was recently reported from Australia; MR imaging results revealed large right frontal cystic structures with mass effect. A biopsy was performed, revealing the masses to be dilated PVSs.[6] Six of the patients in our series had undergone biopsy procedure for diagnostic purposes.

With the high-resolution capability of modern 1.5-tesla MR imaging, there is now little need for tissue biopsy sampling to diagnose even a dramatically enlarged PVS. Note that PVSs are filled with interstitial fluid,[21] which has the imaging characteristics of CSF on all MR imaging and computerized tomography scanning sequences.[19] Enhancement does not occur following administration of a contrast agent (Fig. 4). Evaluation of this series of patients reveals consistent imaging characteristics, as described earlier, in all lesions subject to biopsy sampling.

In patients with small dilations of the PVS the surrounding brain parenchyma has normal imaging characteristics. In some patients with massive dilations of the PVSs, however, increased $T_2$ and FLAIR signals are noted surrounding the dilations (Figs. 2 and 4). The presence of the increased $T_2$ signal has been viewed as a worrisome finding and in some cases has prompted the performance of tissue biopsy. In patients who have been followed up with serial imaging we have not identified a case in which this $T_2$ signal worsened over time or masked an underlying malignancy. Our series of patients indicates that this abnormal signal stems from reactive gliosis surrounding the enlarged PVS and is not an ominous finding.

After reviewing this series of patients and the relevant surgical literature, we adopted the following approach to patients presenting with massive dilations of the PVS. Patients presenting with symptomatic hydrocephalus are treated with the aid of CSF diversion. Patients presenting with focal symptoms related to PVS mass effect undergo cyst drainage and fenestration. If the cyst symptomatically recurs, shunt placement is undertaken. Incidentally noted PVS dilations are evaluated using high-resolution MR imaging and are not subject to biopsy sampling.

## Conclusions

Extreme or tumefactive dilations of the PVS are unusual anatomical variants often found during imaging evaluation for a variety of neurological symptoms. These lesions are benign and do not require biopsy sampling for diagnosis when high-resolution MR imaging studies can be performed. Nonetheless, a rare subset of these lesions will slowly expand over time and may produce neurological sequelae or hydrocephalus if they arise in critical areas. Cerebrospinal fluid diversion procedures successfully alleviate symptomatic hydrocephalus. The relationship of these unusual dilations to seizures or tremor remains unclear.

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