Editorial

Neuroimaging aspects and clinical significance of giant perivascular spaces in the brain

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The cerebral vasculature represents a major component of the brain, constituting 25–30% of the total brain volume (1) and providing essential support to the cells of the nervous system. The blood vessels penetrating or leaving the brain parenchyma present unique anatomical properties, including the presence of a fluid-filled perivascular compartment, known as perivascular space (PVS) or Virchow-Robin space. PVS physiological function is still not completely understood, but is thought to be related to the cerebrospinal/interstitial fluid circulation and the clearance of cerebral waste products. In fact, in recent years, PVS have been described as main pathways in clearance system models of the brain (2), and numerous studies reported the association between PVS alterations and several neurological diseases.

As PVS follow the course of the penetrating blood vessels and have a tubular shape, they appear on magnetic resonance imaging (MRI) as lines or dots, based on the orientation of the PVS with respect to the image acquisition plane (parallel or perpendicular, respectively), and have a signal intensity similar to the cerebrospinal fluid (i.e., hypointense on T1-weighted images and hyperintense on T2-weighted images). PVS cross-sectional diameter is usually less than 2 mm and on MRI they are most commonly seen in the centrum semiovale and basal ganglia (3,4). Thanks to the improved resolution and signal-to-noise ratio, modern MRI scanners and sequences currently allow to visualize PVS in practically all individuals, including healthy young adults (5). It is important to emphasize that these PVS do not necessarily represent a pathological finding.

In rare occasions, however, large PVS with size even higher than 15 mm, can be found in certain brain regions as solitary lesion or in clusters on neuroimaging data [both on computed tomography (CT) and more clearly on MRI] (6). This rare entity has been defined "giant tumefactive PVS" and, due to its size and configuration, can be associated with mass effect in the brain and also mistaken for other types of lesions such as brain cysts or cystic neoplasms (6).

In their article, Cheraya *et al.* described and discussed an interesting case of giant PVS: the patient, a 70-year-old woman with history of diabetes and hypertension, presented to the emergency department with acute onset of dizziness and difficulty in ambulation (7), a relatively uncommon symptom compared with those reported in previous case reports of giant PVS (6,8). In fact, patients with giant PVS usually present with nonspecific symptoms not necessarily attributable to the giant PVS, the most common of which is headache (6,8).

Cheraya *et al.* additionally reported the neuroimaging data acquired on this patient, including CT and multiple MRI sequences, describing the radiological characteristics of this case of giant PVS: the lesion was located in the white matter underlying the right parietal cortex, and appeared as a circumscribed, multiseptated, non-enhancing cystic lesion, with signal intensity similar to cerebrospinal fluid and no mass effect (7). The location of the giant PVS in this patient is also relatively uncommon, as giant PVS have been described more frequently in the mesencephalo-thalamic region (6,8). The pathophysiological reason for

this preferential occurrence is unclear, but it is possible that lesions in this location might be more likely associated with symptoms or hydrocephalus, which lead the patients to seek medical attention, compared with giant PVS in the white matter and centrum semiovale, which might instead be more frequently silent.

In the case described by Cheraya *et al.* (7), the fluid-attenuated inversion recovery (FLAIR) MRI sequence showed only a minor perilesional hyperintense area, as was also described for other similar cases of elderly patients with giant PVS in the white matter (6). On the other hand, younger patients with giant PVS in the white matter tend to have more diffuse and extended areas of abnormal FLAIR signal (i.e., not limited to the perilesional region), and this was hypothesized to be secondary to gliosis or spongiosis (6). These observations suggest that the mechanisms leading to the formation of giant PVS might differ not only based on the location of the lesion, but also based on the age of the patients.

The etiology of giant PVS is unknown, but several hypotheses have been proposed. For example, recent studies have shown that PVS dilation is associated with vascular accumulation of amyloid-β in the overlying cortex (9), which could possibly lead to impairment of the perivascular clearance and engorgement of fluid in PVS with subsequent dilation. Another hypothesis suggests that altered vascular permeability might lead to the enlargement of PVS induced by the accumulation of blood-derived products and subsequent obstruction of PVS, as shown in preclinical and pathological studies (9,10). It is also possible that the dilation of PVS might be consequent to ex-vacuo dilation secondary to brain atrophy (11) and/or the mechanical stress caused by high blood pressure on the arterioles and their periarterial compartment, as hypertension is associated with higher PVS burden, especially in the basal ganglia (12-14). Further studies are required to elucidate the mechanisms underlying the dilation of PVS in humans.

Conveniently, Cheraya *et al.* summarized the neuroimaging characteristics that could facilitate the correct diagnosis of giant PVS and described how to discriminate them from common differentials, such as lacunes, neurocysticercosis, and cystic neoplasms (7), which is particularly important for the appropriate management of the patient and the clinical outcome. In fact, giant PVS are typically benign and, if the MRI characteristics allow the diagnosis of giant PVS, biopsy sampling is not required, even in case with perilesional abnormal hyperintense signal on T2-weighted FLAIR images. While asymptomatic cases do not need surgical treatment, cystic dilation of PVS causing hydrocephalus and/or mass effect may prompt a surgical intervention. Specifically, cerebrospinal fluid diversion is recommended in patients presenting with symptomatic hydrocephalus, which is often caused by giant PVS located within the midbrain which can obstruct the cerebral aqueduct (15). On the other hand, patients experiencing focal symptoms related to mass effect may be treated with cyst drainage and fenestration, which can lead to improvement or full resolution of symptom (15). Nonetheless, the giant PVS and symptoms can recur, and in that case a shunt placement should be considered as therapeutic option (15). For asymptomatic cases, periodic clinical visits and MRI are recommended, as in some cases giant PVS can slowly expand over time and cause hydrocephalus and/or symptoms (15).

In conclusion, the case report by Cheraya *et al.* describes both by a clinical and neuroradiological point of view a rare case of giant tumefactive PVS, with important information that could assist clinicians in the correct diagnosis of this entity and its differentiation from lesions with similar appearance on neuroimaging. This study adds to the series of previous case reports on giant PVS and helps the further clinical and imaging characterization of this uncommon lesion.

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