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Review

Tumefactive Virchow-Robin spaces

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ABSTRACT

Objective: To systematically review the clinical manifestations, MRI appearance, and management of tumefactive Virchow-Robin spaces (VRs).

Methods: A systematic MEDLINE literature search was performed. Data were extracted per tumefactive VRs location (type 1: along lenticulostriate arteries entering the basal ganglia; type 2: along perforating medullary arteries; type 3: mesencephalothalamic region; and other locations).

Results: Ninety-nine articles were included, comprising 164 patients. There were few reports on type 1 tumefactive VRs (n = 5 patients) and tumefactive VRs at other locations (n = 16 patients). In type 2 tumefactive VRs (n = 62 patients), clinical manifestations were reported in 12.9%, signal abnormalities of adjacent brain parenchyma were reported in 32.3%, and MRI follow-up of 23/24 asymptomatic tumefactive VRs showed no change (mean follow-up of 3.2 years). In type 3 tumefactive VRs (n = 80 patients), clinical manifestations were reported in 75.0%, signal abnormalities inside VRs or adjacent brain parenchyma were reported in 3.8%, and neurosurgical outcome (59 reported patients) was generally good. Type 3 tumefactive VRs may increase after neurosurgery (5/59 [8.5%] reported patients; 0.5–14 years follow-up) or spontaneously (2/5 [40%] reported patients; 2 and 9 years follow-up), requiring (repeated) neurosurgery.

Conclusion: In type 2 tumefactive VRs, clinical manifestations and signal abnormalities of adjacent brain parenchyma occur in a minority of cases, and follow-up of asymptomatic patients seems unnecessary. In type 3 tumefactive VRs, clinical manifestations are common, concomitant signal abnormalities occur infrequently, and neurosurgical outcome is generally good. Follow-up of type 3 tumefactive VRs is suggested. There are limited data on other types of tumefactive VRs.

1. Introduction

Virchow-Robin spaces (VRs) or perivascular spaces are pial-lined interstitial fluid-filled spaces which surround the walls of vessels as they course from the subarachnoid space through the brain parenchyma [1]. VRs are routinely seen at magnetic resonance imaging (MRI), and slightly dilated VRs are highly prevalent in healthy elderly people [2]. Such “normal” VRs have a signal intensity that is equal to cerebrospinal fluid (CSF) on all pulse sequences and do not enhance after intravenous contrast agent administration [1]. Furthermore, the surrounding brain parenchyma generally has normal signal intensity [1]. Moreover, they are usually asymptomatic and considered as “leave me alone lesions” [1].

A very unusual phenomenon is extreme enlargement of VRs, which is also referred to as tumefactive VRs [3]. Tumefactive VRs are poorly understood entities whose pathogenesis is unclear. Furthermore, little is known about the clinical manifestations, MRI appearance, and management of tumefactive VRs. The lack of systematic data on tumefactive VRs may lead to diagnostic confusion and variable non-evidence-based management of patients who have these anomalies in their brain. Importantly, the clinical significance and MRI appearance of tumefactive VRs may depend on their location in the brain, which can be divided into three main types. Type 1 appears along the lenticulostriate arteries entering the basal ganglia through the anterior perforated substance (Fig. 1), type 2 is found along the paths of the perforating medullary arteries (Figs. 2 and 3), and type 3 appears in the mesencephalothalamic region (Fig. 4) [1].

The purpose of this study was to perform a systematic review of published articles on tumefactive VRs.

2. Methods

This systematic review followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) guidelines [4]. We

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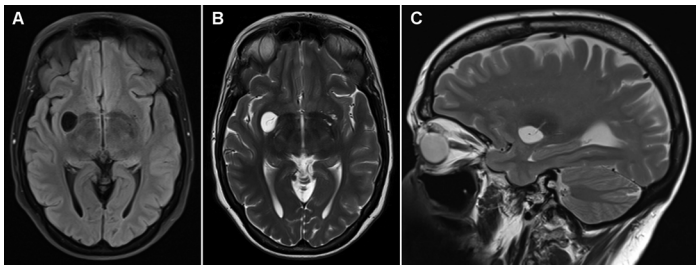

Fig. 1. Type 1 tumefactive VR space in a 56-year-old female with atypical symptoms of headache, nausea and dizziness. Axial fluid attenuated inversion recovery (A), axial T2-weighted (B), and sagittal T2-weighted images show a cystic-appearing lesion with a diameter of 1.6 cm in the right anterior perforated substance, which is traversed by a lenticulostriate artery. There are no signal intensity changes in the adjacent brain parenchyma.

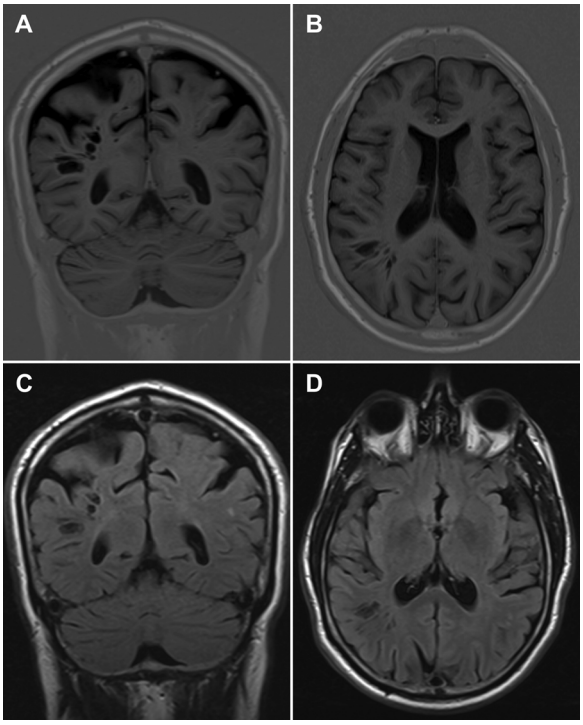

Fig. 2. Type 2 tumefactive VR spaces in the right cerebral white matter in a 60-year-old man. Axial and coronal T1-weighted inversion-recovery images (A and B) and axial fluid attenuated inversion recovery images (C and D) show cystic-appearing lesions in the right cerebral white matter, without signal intensity changes in the adjacent brain parenchyma and no mass effect.

searched for relevant articles in the MEDLINE database. The specific search strategy is displayed in supplemental Table 1. In the first stage, two researchers (R.M.K. and T.C.K., both academically trained radiologists who have ample of experience in performing systematic reviews) independently reviewed the titles and abstracts of the retrieved articles. Articles were included if they 1) were published in a peer-reviewed journal; 2) reported on VRs which were named either "giant", "tumefactive", "extreme", "extensive", "expanding", "markedly dilated", "cystic", or "unusual", were more than 1.5 cm in diameter [3], and/or caused symptoms because of mass effect; 3) performed brain MRI; and 4) were written in English, French, or German language. With use of the aforementioned selection criteria, titles and abstracts of the retrieved articles were reviewed. Articles were rejected if it was already obvious from the title and abstract that they did not fulfil the selection criteria. In the second stage, the same researchers (R.M.K. and T.C.K.) independently evaluated the full-text version of all articles that were found to be potentially eligible for inclusion, using the same inclusion and exclusion criteria as mentioned above. When data were presented in more than one article, the article with the largest number of patients was chosen. Reference lists of included articles were hand-searched for published reports missed by the electronic MEDLINE database search. At all stages, disagreements between the two researchers (R.M.K. and T.C.K.) were discussed and resolved by consensus.

For each included article, data were extracted by one researcher (R.M.K.) who used a structured record form, concerning publication year and country of origin, number of patients, age and sex, locations of tumefactive VRs, presence of symptoms and symptoms attributed to the presence of tumefactive VRs, signal alterations of the adjacent brain parenchyma, treatment and outcome, and follow-up. Data were categorized by VRs location: type 1 (along the lenticulostriate arteries entering the basal ganglia through the anterior perforated substance) (Fig. 1), type 2 (along the paths of the perforating medullary arteries) (Figs. 2 and 3), type 3 (in the mesencephalothalamic region) (Fig. 4), and other locations.

3. Results

3.1. Literature search

The flowchart of the literature search is presented in Fig. 5. Reviewing titles and abstracts from the MEDLINE database resulted in 74 articles that were potentially eligible for inclusion [1,3,5–76] and the full-text versions of these articles were retrieved. After reviewing the full articles, one article [53] was excluded because tumefactive VRs were not observed and one article [59] was excluded because the same data were used by the same group in another study with a larger number of patients [3]. Screening the reference lists of full articles resulted in another 27 articles which were included [77–103]. Among these 27 articles, there were 15 articles [89,78–103] which reported on cystic lesions in the mesencephalon. Although these cystic lesions were not specifically named tumefactive VRs, their location and appearance were characteristic [1], and therefore these articles were also included in this systematic review. Data from one article [102] were also used in another article from the same group, comprising a larger number of patients [103]. However, the article with less patients [102] was also included, because it reported more follow-up details. Thus, eventually 99 articles were included [1,3,5,78–103], published between 1989 and 2018, and comprising 164 patients (86 females [sex of 3 patients was not reported]; mean age 44.1 years; age range 3–86 years) with tumefactive VRs. The median number of patients per article was 1 (range 1–37). Salzman et al. [3] reported the largest series of patients (n = 37).

Type 1 tumefactive VRs

There were 5 patients (3 females; mean age 53.8 years; age range 41–71 years) with type 1 tumefactive VRs.

Presenting symptoms are displayed in Table 1. In 2/5 (40%) patients, symptoms were attributed to the presence of tumefactive VRs. In one patient, homonymous quadrantanopsia was attributed to the mass effect of tumefactive VRs [9]. Because of worsening symptoms and enlargement of the tumefactive VRs on MRI 9 months later, this patient underwent cyst fenestration, which resulted in immediate shrinking of the tumefactive VRs with marked clinical improvement [9]. In one other patient, bilateral chorea was attributed to the presence of bilateral tumefactive VRs [37]. This patient was treated with benzodiazepines, reducing the movements mildly at 3 months follow-up [37].

No signal alterations in the adjacent brain parenchyma were

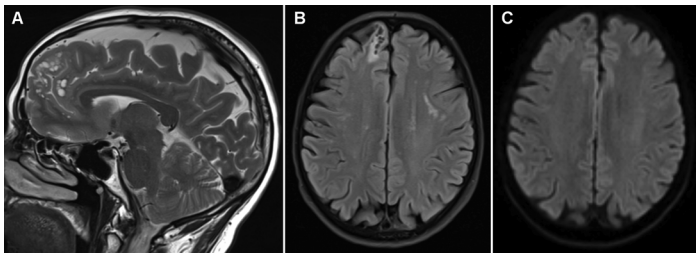

Fig. 3. Type 2 tumefactive VR spaces in a 69-year-old woman with a history of migraine and fibromyalgia who presented with two fainting episodes preceded by autonomous symptoms. Sagittal T2-weighted (A), axial fluid attenuated inversion recovery (B), and axial diffusion-weighted (C) images show multiple cystic lesions in the subcortical white matter of the right frontal lobe, with high signal intensity of the adjacent white matter on T2-weighted (A) and FLAIR (B) images. The overlying cortex appears normal, there is no mass effect, and no impeded diffusion (C). These findings and absence of associated symptoms are compatible with type 2 tumefactive VR spaces, surrounded by gliosis. There are incidental white matter lesions in the centrum semiovale, especially on the left side.

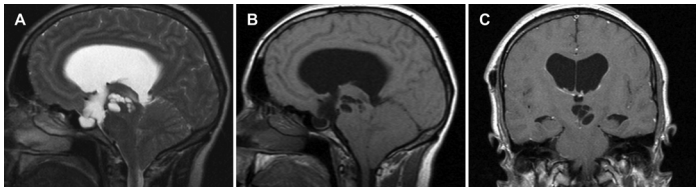

Fig. 4. Type 3 tumefactive VR spaces in a 19-year-old man (previously reported in reference [1]). Sagittal T2-weighted images (A), sagittal T1-weighted images (B), and axial postgadolinium T1-weighted images (C) show a multicystic-appearing lesion in the mesencephalothalamic region, with content equal to CSF, and no pathological enhancement. The tumefactive VR spaces have caused obstruction of the Sylvian aqueduct, resulting in hydrocephalus. The patient has been treated with a ventriculoperitoneal shunt. There is an incidental Chiari type 1 malformation.

Table 1
Presenting symptoms in 5 patients with type 1 tumefactive VR spaces.

Study and publication year	Presenting symptoms	Presenting symptoms attributed to the presence of tumefactive VRs
Naganawa et al. [8], 2017	Left tinnitus and vertigo attacks	No
Rivet et al. [9], 2017	Homonymous quadrantanopsia and left arm weakness	Yes
Zacharia et al. [37], 2011	Bilateral chorea	Yes
Salzman et al. [3], 2005	Not specified (2 patients)	Not specified (2 patients)

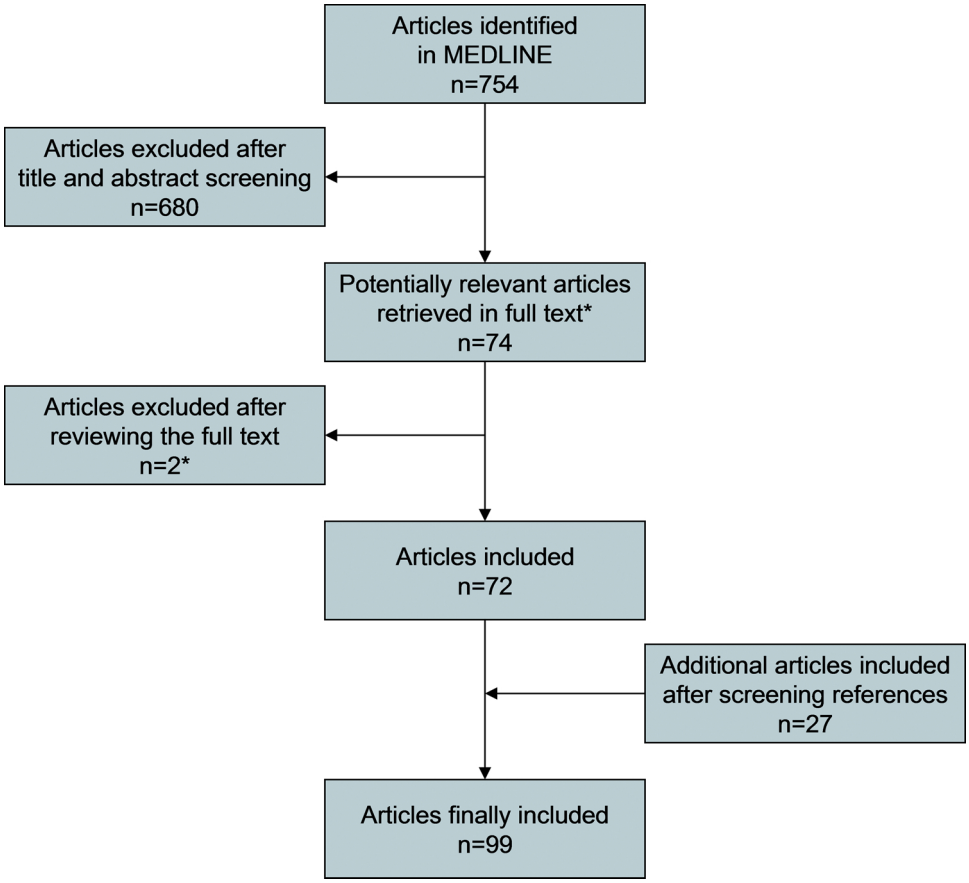

Fig. 5. Flowchart of articles included in our systematic review.
* One article [53] was excluded because it did not report on tumefactive VR spaces and one article [59] was excluded because the same data were used in another article by the same group, comprising a larger number of patients [3].

Table 2
Presenting symptoms in 62 patients with type 2 tumefactive VR spaces.

Study and publication year	Presenting symptoms	Presenting symptoms attributed to the presence of tumefactive VRs
Mahboobani et al. [83], 2017	Seizure and status epilepticus	No
Lahiri et al. [82], 2017	Tinnitus	No
Lee et al. [86], 2015	Bradykinesia and memory disturbances	Yes
Zafar et al. [14], 2015	Intermittent hemianopsia on the left side	Yes
Warner et al. [87], 2015	Seizures	Not reported / unclear
Datta et al. [13], 2015	3-month history of intermittent word-finding difficulty and prosopagnosia	No
Li et al. [18], 2014	Left leg pain (in a patient with NF tyoe 2)	No
Matalia et al. [79], 2014	Right superior quadrantanopsia	Yes
Mölzer et al. [21], 2014	Clumsiness of the left hand and headaches	No
Omidi et al. [20], 2014	Slowness in daily activities and walking	Not reported / unclear
John et al. [30], 2013	2-day history of acute-onset headache	No
Tseng et al. [27], 2013	None	Not applicable
Gronier et al. [26], 2013	- Left-sided paresis	- Not reported / unclear
	- Bravais-Jackson-like somatosensory epilepsy of the left body half	- Not reported / unclear
	- Partial epileptic seizure, secondarily generalized, with postictal right-sided paresis	
Sankararaman et al. [88], 2013	None	Not applicable
Jhawar et al. [33], 2012	Headache	Not reported / unclear
Tortora et al. [32], 2012	Generalized seizure	No
Bayram et al. [80], 2012	Developmental delay	Not reported / unclear
Buerge et al. [35], 2011	Cognitive decline, left hemianopsia, and mild left-sided pyramidal signs	Yes
Wani et al. [39], 2011	Headache	No
Wong et al. [42], 2010	Orbital apex syndrome	No
Cohen et al. [44], 2009	None (in a patient with NF type 1)	Not applicable
Fumal et al. [47], 2009	Headache	No
Brockmann et al. [45], 2009	- Mild general clumsiness	- No
	- Delay in speech development and clumsiness	- No
Stephens et al. [46], 2008	None	Not applicable
Caner et al. [49], 2008	- Ringing in the left ear	- No
	- Hydrocephalus symptoms	- Yes
Lefranc et al. [48], 2008	Numbness of left arm and of both legs	Not reported / unclear
Mathias et al. [50], 2007	- None	- Not applicable
	- Stability disorders	- No
Kim et al. [52], 2007	Memory impairment and gait disturbance	Yes
Salzman et al. [3], 2005	Not specified (14 patients)	Not specified (14 patients)
Härtel et al. [58], 2005	- Psychonmotor retardation and macrocephaly	- No
	- Psychonmotor retardation and macrocephaly	- No
Saeki et al. [60], 2003	Transient dizzy sensations	Not reported / unclear
Davis et al. [77], 2002	Left upper and lower limbs weakness and numbness that resolved 12 hours following admission	Yes
Shiratori et al. [63], 2002	Single, nonspecific fainting attack	No
Eichhorn et al. [65], 2001	Left ear pain	No
El Quessar et al. [69], 1999	History of a pituitary adenoma	No
Sawada et al. [70], 1999	Slight dizziness and headache in the right temporo-parietal region	No
Ohta et al. [67], 1999	Transient muscular weakness of the extremities	Not reported / unclear
Ugawa et al. [71], 1998	None	Not applicable
Komiyama et al. [73], 1998	- Frontalgia, floating sensation, dysarthria, and left hand weakness and numbness	- No
	- Posterior neck pain	- No
Vital et al. [74], 1997	Slowly progressive disturbances of cognitive function (dementia)	Yes
Ogawa et al. [76], 1995	- Ringing in the left ear	- No
	- Positional vertigo	- No

reported in any of the 5 patients (0%) [3,8,9,37].

Follow-up MRI was performed in only one (untreated) patient, which showed no change of the tumefactive VRs after one year [3].

Type 2 tumefactive *VRs*

There were 62 patients (33 females; mean age 42.9 years; age range 3–83 years) with type 2 tumefactive VRs.

Presenting symptoms are displayed in Table 2. In 8/62 (12.9%) patients, symptoms were attributed to the presence of tumefactive VRs. In 4 patients, symptoms of parkinsonism and dementia were attributed to the presence of disseminated tumefactive VRs [35,52,74,85]. One of these patients was temporarily treated with medication for dementia without improvement [52]. In three other patients, the presenting symptoms of intermittent hemianopsia [14], quadrantanopsia [79], and temporary unilateral weakness and numbness [77] were attributed to the mass effect of more focally located tumefactive VRs; the first patient underwent endoscopic cystoventriculostomy of periventricular tumefactive VRs near the optic radiation, postoperative MRI showed tumefactive VRs reduction and intermittent hemianopsia was resolved [14]; the latter patient underwent tumefactive VRs resection in the medial frontal lobe, no postoperative outcome data were given [77]. In yet another patient, hydrocephalus symptoms were caused by tumefactive VRs between the left temporal lobe and supraventricular area compressing the foramen of Monro [49]. This patient underwent cyst fenestration, resulting in relief of symptoms and uneventful later clinical course [49].

Hyperintensity of the adjacent brain parenchyma on fluid-attenuated inversion recovery (FLAIR) / T2-weighted images (Fig. 3) was reported to be present in 20/62 (32.3%) patients.

In one study, an asymptomatic tumefactive VRs in the pre-Rolandic area completely disappeared at MRI after 6 months [32]. Sixteen other studies [3,23,26,44–46,60,67,70,73,74,76,80,83,85,88] which followed the natural course of 23 asymptomatic tumefactive VRs reported no change with a mean follow-up period of 3.3 years (range 1 month - 17 years).

Table 3
Presenting symptoms and presence of hydrocephalus in 80 patients with type 3 tumefactive VR spaces.

Study and publication year	Presenting symptoms	Hydrocephalus	Presenting symptoms attributed to the presence of tumefactive VRs
Al Abdulsalam et al. [5], 2018	Headache and right foot numbness	Yes	Yes
Ferrer et al. [6], 2017	Supranuclear palsy-like parkinsonism	No	Not reported / unclear
El Damaty et al. [101], 2017	Hemiparesis and Parinaud syndrome	Yes	Yes
Donaldson et al. [7], 2017	Unilateral right-sided pulsatile tinnitus with severe headaches	Yes	Yes
Kao et al. [10], 2016	Intermittent deviation of the eyes to the left and weaknes of the right extremities	No	Yes
Roelz et al. [85], 2015	Mild and very slowly progressing weakness of the left arm and leg	Yes	Yes
Revel et al. [15], 2015	Intermittent urinary incontinence, right leg weakness, progressive cognitive decline accompanied by memory loss	Yes	Yes
Smith et al. [78], 2015	Right eye pain, blurred vision, occasional diplopia, headache and gait difficulty with frequent falls due to imbalance	Yes	Yes
Kumar et al. [11], 2015	headache, poor attention and concentration, forgetfulness, polyuria, urinary incontinence, and hypersomnia	Yes	Yes
Yilmaz et al. [19], 2014	Not reported / unclear	Yes	Not reported / unclear
Young et al. [24], 2014	Headaches, memory loss, and confusion	No	No
Choh et al. [84], 2014	Headache and unsteadiness	Yes	Yes
Fiorindi et al. [92], 2013	- Resting tremor and weakness of the left arm, later extending to the left leg - Visual disturbance and progressive tremor of the right hand - Diplopia in the left lateral gaze and anisocoria - Unilateral tremors, gate instability, dizziness and diplopia	- Yes - No - Yes - Yes	- Yes - Yes - Yes - Yes
Ottenhausen et al. [25], 2013	Syncope, fatigue, slight gait disorder, stomach pain, and intermittent diplopia	Yes	Yes
Prieto et al. [98], 2013	Upward gaze palsy, progressive headache, nausea, and vomiting	Yes	Yes
Rocha et al. [28], 2013	Worsinig cognitive difficulties, gait imbalance with occasional falls, and urinary urgency	Yes	Yes
Fujimoto et al. [34], 2012	Headache and nausea at initial presentation, double vision and nausea 14 years after initial presentation	Yes*	Yes
Algin et al. [31], 2012	- Psychoorganic syndrome with dysphoric symptoms and complete morpheic epilepsy with secondary generalization - Right lower limb deficit and diplopia - Loss of vision	- Yes - Yes - No	- Not reported / unclear - Yes - Not reported / unclear
Cherif El Asri et al. [100], 2012	Intermittent headaches and paresthesia of the of the upper left limb	No	Yes
Baldawa et al. [81], 2011	Headache and gait imbalance	Yes	Yes
Sturiale et al. [38], 2011	Left hemiparesis, hemiataxia, and rubral tremor	Yes	Yes
Chudy et al. [36], 2011	Headaches and left arm weakness	No	Yes
Flors et al. [43], 2010	Headache	Yes	Yes
Fayeye et al. [40], 2010	Ataxia, deterioration of visual acuity, upward gaze palsy, and multiple cranial nerve involvement	Yes	Yes
Endo et al. [96], 2009	Slight vertigo, followed by headache and double vision two years later	Yes	Yes
Conrad et al. [102] and van Lindert et al. [103], 2008	- Cranial nerve 3 palsy, headache, gait disturbance, vertigo, slight hemiparesis - Parinaud syndrome, gait disturbance, headache, hemiparesis, facial palsy - Vertigo, headache, gait disturbance, lack of concentration - Tinnitus, headache - Headache, left hemihypesthesia, left hemiparesis, anosmia, gait disturbance - Somnolence, headache, gait disturbance, diplopia, anisocoria - Diplopia, gait disturbance, incontinence, hearing loss - Parinaud syndrome, vertigo, double vision	- Yes - Yes - Yes - Yes - Yes - Yes - Yes - Yes - Yes	- Yes - Yes - Yes - Yes - Yes - Yes - Yes - Yes - Yes
Ahmad et al. [51], 2007	Headache and vomiting	Yes	Yes
Kwee et al. [1], 2007	Symptoms related to hydrocephalus	Yes	Yes
Brkic et al. [97], 2006	Headache, diplopia and ataxia	Yes	Yes
Kumar et al. [99], 2006	- Headache, short sighted vision, and concentration problems - Dizzy spells, frequent falls, leg fatigue, lower leg paresthesia, and urinary incontinence and urgency	- Yes - Yes	- Yes - Yes
Krause et al. [55], 2005	Right hand tremor and difficulties in writing	Yes	Yes
Pialat et al. [56], 2005	Left hemiparesis and hypesthesia	No	Yes
Rohlfs et al. [57], 2005	- Right hemihypesthesia - Progressive tremor of the left hand	- Yes - No	- Yes - Yes
Salzman et al. [3], 2005	Not specified (19 patients)	- Yes (9 patients) - No (10 patients)	Not specified (19 patients)
Papayannis et al. [62], 2003	Depression, emotional lability, bradykinesia, gait disturbances, and tremor of the jaw	Yes	Yes
Longatti et al. [90], 2003	Resting tremor and weakness of the left arm, extending to the left leg	Yes	Yes
Cakirer et al. [61], 2003	Headache	Yes	Not reported / unclear
Mandrioli et al. [93], 2003	Right facio-brachial hypesthesia and paresthesia	No	Yes
Romi et al. [64], 2002	Symmetrical tremor in both hands, postural vertigo and mild stiffness of the lower limbs	No	Not reported / unclear
Kanamalla et al. [66], 2000	- Depression and occasional headache - Headache, forgetfulness, confusion, and somnolence	- Yes - Yes	- Not reported / unclear - Not reported / unclear

(*continued on next page*)

Table 3 (*continued*)

Study and publication year	Presenting symptoms	Hydrocephalus	Presenting symptoms attributed to the presence of tumefactive VRs
Mascalchi et al. [68], 1999	- Gait disturbance and tremor of the right arm, accompanied by urinary urgency and sudden falls - Memory loss and gait unsteadiness	- Yes - Yes	- Yes - Yes
Schroeder et al. [89], 1996	Headache and weakness and clumsiness of the right arm and hand	No	Yes
Homeyer et al. [75], 1996	Headache associated with blurred vision and diplopia	Yes	Yes
Ono et al. [91], 1994	Headache, slight dementia, gait disturbance and urinary incontinence	Yes	Yes
Eggenberger et al. [94], 1993	Vertical diplopia and mild balance difficulty	No	Yes
Nishioka et al. [95], 1989	Sensory disturbance in the right half of the face and body, and blurring of vision	Yes	Yes

* At initial presentation.

Type 3 tumefactive VRs

There were 80 patients (41 females [sex of 2 patients was not reported]; mean age 44.0 years; age range 6–86 years) with type 3 tumefactive VRs.

Presenting symptoms are displayed in Table 3. In at least 60/80 (75.0%) patients, symptoms were attributed to the presence of tumefactive VRs, and 59 of these 60 patients underwent neurosurgery, consisting of either treatment of hydrocephalus by diversion of CSF flow and/or direct surgery of the tumefactive VRs (Table 4). In the majority of patients, symptoms caused by space-occupying tumefactive VRs diminished or resolved after neurosurgery, without occurrence of complications. In one patient who underwent cyst fenestration, surgery was complicated by intracystic bleeding of a small intracystic artery, resulting in worsening of right hemiparesis [92]. An intracystic catheter with an Ommaya reservoir was inserted [92]. At discharge, the previous hemiparesis had only slightly worsened and improved at follow-up [92]. One patient developed a slight left brachiofacial hemiparesis due to a small hemorrhage in the surgical trajectory [57]. Subsequent clinical course was uneventful and hemiparesis resolved [57]. In one patient who was treated with a ventriculoperitoneal shunt, symptoms recurred immediately after slight head trauma [75]. Despite shunt revision and a valve change, fluctuating diplopia persisted [75]. Seven months after initial presentation, headache and visual disturbances increased and temporarily became worse as a result of slight head injuries [75]. One patient who was treated with a ventriculoatrial shunt presented with hyperdrainage symptoms and subdural hematoma one month later, which was evacuated without further complications [15]. In the majority of patients who underwent direct surgery of tumefactive VRs (mainly by cyst fenestration), the tumefactive VRs reduced and remained stable during follow-up. However, in 5 patients, the tumefactive VRs increased in size within 6 months up to 14 years, requiring new surgery [3,34,92,97]. In one other patient in whom only a ventriculoperitoneal shunt was placed (no direct surgery of tumefactive VRs), the tumefactive VRs also increased, with accompanying symptoms [69].

In 76/80 (95.0%) patients, no signal abnormalities of the adjacent brain parenchyma and no internal signal intensities of the tumefactive VRs other that CSF were reported. In a 15-year-old female patient, there was signal abnormality of the adjacent right mesencephalic parenchyma, corresponding with acute stroke [56]. In a 57-year-old female patient, a subtle hyperintense signal partially surrounded the VRs on FLAIR images [62]. In a 51-year-old female patient, there was hemorrhage in one of the cystic components of the tumefactive VRs [93]. This intracystic hemorrhage was attributed to mild head trauma and resulted in right faciobrachial hypesthesia and paresthesia [93].

Five studies [24,31,66,93,96] followed the natural course of 5 untreated tumefactive VRs. In three patients, the tumefactive VRs showed no change 3 months [93], one year [66], > 1 year [24], and 2 years [31] after initial presentation. In 2 patients, the tumefactive VRs increased in size with a follow-up period of 2 [96] and 9 [31] years, leading to more cerebral aqueduct compression and (increased) hydrocephalus.

Tumefactive VRs at other locations

There were 16 patients (8 females; mean age 45.1 years; age range 6–86 years) with tumefactive VRs at other locations. These locations were the middle cerebellar peduncle and/or pons region (n = 3) [16,29,54], cerebral peduncle, pons, middle cerebellar peduncle, and dentate nucleus (n = 1) [49], dentate nucleus (n = 1) [3], anterior temporal pole (n = 9) [12,21,22,41], hippocampus (n = 1) [72], and widespread locations (left temporal and occipital lobe, bilateral basal ganglia and thalami, along subependymal lining of temporal, occipital horn and body of left lateral and fourth ventricle, left periventricular white matter, left cerebellar hemisphere and vermis) (n-1) [51].

Presenting symptoms are displayed in supplemental Table 2. In 5/17 (29.4%) patients, presenting symptoms were attributed to the presence of tumefactive VRs [16,17,22,29,72]. A 15-year-old male patient underwent biopsy of tumefactive VRs in the middle cerebellar peduncle; in the postoperative period, the patient completely recovered from upper gaze palsy and double vision, as well as his left hemiparesis and hemihypesthesia [16]. Follow-up MRI up to 8 years showed no change of the tumefactive VRs [16]. In a 47-year-old female patient, temporal lobe seizures completely resolved after surgical excision of tumefactive VRs in the anterior temporal pole [22]. In a 47-year-old female patient, headaches were probably attributable to tumefactive VRs in the anterior temporal pole; the headaches were successfully treated with divalproex medication [21]. Follow-up MRI after 2 years showed no change, MRI after 3 years showed complete resolution, and MRI after 4 years showed recurrence of the tumefactive VRs [21]. In a 76-year-old female patient, follow-up MRI 3 and 4 years after resection of a symptomatic parafalcine meningioma showed disappearance of asymptomatic tumefactive VRs in the anterior temporal pole [41]. In one patient with trigeminal neuralgia caused by tumefactive VRs in the dorsal pons (extending into the middle cerebellar peduncle), the symptoms were well controlled by carbamazepine medication [29]. In a 64-year-old male patient with tumefactive VRs in the right hippocampus causing temporal epilepsy, seizures were suppressed with phenytoin medication [72]. Follow-up MRI after 5 months showed no change of the tumefactive VRs [72]. Hyperintensity of the adjacent brain parenchyma on FLAIR / T2-weighted images was reported to be present in 10 patients [12,16,21,22,51,54].

4. Discussion

This is the first systematic review on tumefactive VRs. We identified 164 patients with tumefactive VRs who were evaluated by MRI, in reports published in the past 30 years. Large population-based studies in adults [104] and children [105] did not report tumefactive VRs as incidental findings on brain MRI. Therefore, tumefactive VRs can be considered rare. However, the exact prevalence based on available data remains unclear. It should be noted that the prevalence also depends on

Table 4
Neurosurgical treatment, postoperative clinical outcome, and postoperative imaging findings of 57 patients with type 3 giant VRs.

Study and publication year	No. of patients, age and sex	Hydrocephalus treatment	Direct giant VRs surgery	Postoperative clinical course	Postoperative imaging findings
Abdulsalam et al. [4], 2018	1, 35, F	Ventriculoperitoneal shunt	None	Symptoms improved. After 6 months presentation with acute hydrocephalus. Uneventful clinical course after shunt revision.	CT: regression of hydrocephalus VRs size reduction. CT after shunt revision: regression of hydrocephalus and slight VRs size reduction.
El Damaty et al. [89], 2017	1, 42, F	Third ventriculostomy	Cyst fenestration	Resolution of hemiparesis and upward gaze palsy, follow-up of 5 years.	MRI after 5 years: regression of VRs
Donaldson et al. [5], 2017	1, 30, M	Third ventriculostomy	None	Almost complete resolution of unilateral pulsatile tinnitus and improvement of headache. After 12-months, symptoms almost completely resolved.	MRI: reduction of hydrocephalus and no change of VRs
Roelz et al. [72], 2015	1, 55, M	None	Cystoventricular catheter placement	Near-complete resolution of left hemiparesis. The patient remained without problems upon regular outpatient visits at 6 months after diagnosis and surgery.	MRI after 2 days: slight reduction of the VRs and unchanged hydrocephalus. CT 3 days: resolution of hydrocephalus. MRI after 2 weeks: slight VRs reduction.
Revel et al. [10], 2015	1, 74, M	Ventriculoatrial shunt	None	Positive immediate outcome. One month later hyperdrainage symptoms and subdural hematoma, which was evacuated. Good clinical evolution on gait and cognitive functions at follow-up	CT after one month: signs of hyperdrainage with ventricular collapse and a subacute subdural haematoma of the left hemisphere.
Smith et al. [65], 2015	1, 50, M	Third ventriculostomy	Cyst fenestration	Patient was able to ambulate without assistance and perform daily activities of living independently. Cognition remained intact, and he conversed appropriately. At 5 months, headache, and diplopia had essentially resolved.	MRI: decrease of hydrocephalus and some decrease in size of VRs. CT after 5 months: well decompressed VRs and disappearance of hydrocephalus.
Kumar et al. [8], 2015	1, 30, M	Ventriculoperitoneal shunt followed by third ventriculostomy	None	Temporary resolution of symptoms; recurrence of symptoms after 1 month because of shunt malfunction. After third ventriculostomy, symptoms completely resolved and patient is doing well at 4 months follow-up.	MRI after 3 months: decrease of hydrocephalus and no significant change of VRs.
Choh et al. [71], 2014	1, NR, M	Ventriculoperitoneal shunt	None	Dramatic resolution of symptoms.	MRI after two years: no change of VRs.
Fiorindi et al. [80], 2013	4, −43, F −52 F −29, M −19, M	- Third ventriculostomy - Third ventriculostomy - None - None	- Cyst fenestration - Cyst fenestration and intracystic catheter placement - Cyst fenestration - Cyst fenestration	- Transient disturbance of convergence and limitation of lateral eye deviation, which resolved spontaneously on day 3. At 8-year follow-up, the patient was neurologically normal except for a mild resting tremor of the left hand. - Intraoperative bleeding due to a small intracystic artery, complicated the operation. Postoperative worsening of right hemiparesis. An intracystic catheter with an Ommaya reservoir was inserted. At discharge, the previous hemiparesis had only slightly worsened and improved at follow-up. - No immediate postoperative neurological worsening. - Satisfactory clinical recovery. One year later dizziness recurred with new onset tremors and right 3rd cranial nerve deficit. After new endoscopic fenestrations, signs and symptoms regressed, except for the 3rd cranial nerve deficit.	- MRI: mild reduction of VRs volume and a reduction in ventricular size. - CT: intracystic bleeding. MRI after 5 years: reduction of VRs volume. - MRI: marked reduction of VRs size. - MRI: reduction of VRs. MRI one year after initial cyst fenestration: VRs re-expansion. MRI after new multiple cyst fenestrations: significant reduction of VRs volume.
Ottenhausen et al. [16], 2013	1, 43, F	Third ventriculostomy	None	Discharged in good condition. After 12 months, the patient reported substantial improvement of symptoms.	MRI after one year: no change of VRs and an open third ventriculostomy.
Prieto et al. [86], 2013	1, 30, M	Ventriculoperitoneal shunt	Cyst fenestration	Uneventful postoperative period. Upward gaze palsy remained 6 months postoperatively.	MRI after 6 months: partial collapse of VRs and a patent aqueduct with reestablishment of physiological CSF flow.

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Table 4 (*continued*)

Study and publication year	No. of patients, age and sex	Hydrocephalus treatment	Direct giant VRs surgery	Postoperative clinical course	Postoperative imaging findings
Fujimoto et al. [23], 2012	1, 17, M	Third ventriculostomy (initial treatment)	Cyst fenestration (initially and after 14 years)	Headache and nausea improved. Fourteen years later, the patient presented with left oculomotor and right trochlear nerve palsies. After repeated cyst fenestration, the symptoms and neurological disorder improved. Six months postoperatively, the patient remained symptom free.	MRI: marked improvement in hydrocephalus and no change of VRs. MRI after 14 years: increase of VRs without hydrocephalus. Postoperative MRI: slight VRs reduction. MRI after 6 months: slight VRs reduction.
Algin et al. [21], 2012	1, 63, F	None	Cyst fenestration	Stable postoperative course, improvement of limb deficit. Improvement of the right upper limb fine motility functions and diplopia after 2 months.	MRI: VRs reduction and decrease of hydrocephalus.
Cherif El Asri [88], 2012	1, 42, F	None	Cyst fenestration	Improvement of symptoms.	CT after 18 months: almost complete disappearance of VRs.
Baldawa et al. [68], 2011	1, 46, F	Third ventriculostomy	None	Significant relief from headache and gait imbalance improved.	MRI: resolution of the hydrocephalus and no change of VRs.
Sturiale et al. [27], 2011	1, 38, M	Ventriculoperitoneal shunt	None	After 2 years follow-up, the patient never experienced any symptom suggestive of shunt malfunction.	MRI: decrease in ventricular size and in VRs tension.
Chudy et al. [25], 2011	1, 13, M	None	Cyst fenestration	Gradual resolution of monoparesis which completely resolved in one month. During 14 months follow-up, the patient remained symptom free.	MRI: reduction of VRs. MRI after 14 months: persistent reduction of VRs.
Flors et al. [32], 2010	1, 10, F	Ventriculoperitoneal shunt	None	Prompt improvement of headache. Clinical follow-up examinations revealed no change.	CT: resolution of hydrocephalus.
Fayeye et al. [29], 2010	1, 6, M	Temporary external ventricular drain	Cyst fenestration	Improvement of left third cranial nerve palsy and resolution of symptoms at 6 months follow-up. Gait improved and was normal at 6 months' follow-up.	MRI: VRs size reduction and hydrocephalus redcution after 7 days. Stable VRs and no hydrocephalus after 4 months.
Endo et al. [84], 2009	1, 54, M	Third ventriculostomy	Cyst fenestration	Immediate improvement of vertical eye movement disturbance and headache. Uneventful postoperative course. No recurrence of symptoms after 3 years.	MRI: VRs shrinkage and hydrocephalus resolution. Persistent VRs shrinkage and open third ventriculostomy after 3 years..
Conrad et al. [90] and van Lindert et al. [91], 2008 and 1998	8, −35, F −53, F −54, F −56, F −60, F −35, F −36, M −22, F	- None - Third ventriculostomy - Third ventriculostomy (after cyst fenestration) - None - None - Third ventriculostomy - None - Ventriculoperitoneal shunt (before cyst fenestration)	- Patient 5: cystocisternostomy (, 6 years before cyst fenestration) and cyst fenestration. - All other patients: cyst fenestration	Improvement of headache and neurological deficits in all patients shortly after surgery. Patients 1, 2, 4, and 6 were symptom free, and the other four improved significantly after a mean follow-up of 38.5 months (range 5–119). Residual symptoms were headache (patients 3 and 5), gait disturbance (patient 7), and double vision (patient 8).	- MRI after 12 months: collapse of VRs. - MRI showed no change of VRs. - MRI: collapse of VRs. MRI after 4 months: hydrocephalus. - MRI after 14 months: significant reduction of VRs size, an open aqueduct and unchanged ventricles. - MRI after 7 months: decrease of VRs size and unchanged hydrocephalus. - Not reported. - CT: collapse of VRs. - MRI: collapse of VRs
Ahmad et al. [12], 2007	1, 40, F	Ventriculoperitoneal shunt	None	Complete relief of symptoms.	MRI after 7 days: resolution of hydrocephalus and no change of VRs
Kwee et al. [1], 2007	1, 19, M	Ventriculoperitoneal shunt	None	NR	MRI after two years: no change of VRs
Brkic et al. [85], 2006	1, 10, F	Ventriculoperitoneal shunt (second surgery)	Cyst fenestration followed by cysto-cisternostomy	Recovery after initial and second surgery was good but trochlear palsy was still present. One year later, the patient presented with ataxia, nystagmus and mild left-sided paresis. Recovery after third surgery was good. Follow-up after 11 years showed partial trochlear palsy.	CT after initial surgery: VRs regression but hydrocephalus was still present. CT after second surgery: resolution of hydrocephalus. CT after 6 months: recurrent VRs. CT after 3rd surgery: VRs regression. MRI after 6 years: VRs collapse
Kumar et al. [87], 2006	2, −36, M −40, F	- Third ventriculostomy - Third ventriculostomy	- Endoscopic cyst fenestration - Endoscopic cyst fenestration	- Uneventful recovery with immediate improvement of headache. At 3 months' follow-up, the patient remained well without headache and had returned to work. - Uneventful recovery. At 3 months' follow-up, the patient's mobility improved and she no longer complained of falling tendency. Upward gaze failure persisted.	- MRI after 3 months: reduction of hydrocephalus and reduction of VRs size. - No imaging follow-up (patient did not show up).

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Table 4 (*continued*)

Study and publication year	No. of patients, age and sex	Hydrocephalus treatment	Direct giant VRs surgery	Postoperative clinical course	Postoperative imaging findings
Rohlfs et al. [44], 2005	2, −50, M −51, M	- None - None	- Cyst fenestration - Cyst fenestration	- Hemihypesthesia improved and normal neurological function was restored. - Slight left brachiofacial hemiparesis. Subsequent clinical course was uneventful and hemiparesis resolved. Left upper limb tremor was also treated successfully.	- MRI one year postoperatively: marked reduction of VRs volume and resolution of hydrocephalus. - MRI: small hemorrhage in the surgical trajectory and slight reduction of VRs size.
Salzman et al. [3], 2005	9, NR	- Third ventriculostomy (5 patients) - Ventriculoperitoneal shunt (3 patients, including one who first underwent cyst fenestration)	Cystoperitoneal shunting (1 patient) Cyst fenestration (1 patient)	. In the patient who was treated with a cystoperitoneal shunt, headache improved. - Not specified for the other 8 patients.	- In two patients with a ventriculoperitoneal shunt VRs size was stable. - In one patient with a cystoperitoneal shunt, VRs size decreased. After minor trauma, VRs enlarged. - In one patient who underwent cyst fenestration followed by ventriculoperitoneal shunting, VRs returned to original size. - Not specified for the other 5 patients.
Papayannis et al. [49], 2003	1, 57, F	Ventriculoperitoneal shunt	None	Prompt improvement of gait difficulties, urinary incontinence, and bradykinesia. Stable condition for the following 6 months.	MRI directly and 6 months postoperatively: resolution of hydrocephalus and no change of VRs
Longatti et al. [78], 2003	1, 43, F	Third ventriculostomy	Cyst fenestration	Transient disturbance of convergence and limitation of lateral eye deviation. Neurologically normal except for mild left hand resting tremor at 18 months.	MRI 3 months postoperatively: mild reduction of VRs volume and moderate reduction of hydrocephalus.
Kanamalla et al. [53], 2000	1, 35, NR	Ventriculoperitoneal shunt	None	Gradual, progressive improvement.	MRI after 3, 6 and 12 months: no change of VRs
Mascalchi et al. [55], 1999	2, −58, F −55, M	- Ventriculoperitoneal shunt - Third ventriculostomy	- None - None	- Prompt amelioration of gait difficulties and bradykinesia. Four years later, there was a dorsal midbrain syndrome and right hand rubral tremor. - Normal gait and a negative Romberg's sign after 6 months. The patient was more attentive, collaborative, and there was no cognitive impairment.	- MRI after 4 years: resolution of hydrocephalus and an increase in VRs number and size. - MRI after 6 months: resolution of hydrocephalus and no change of VRs.
Schroeder et al. [77], 1996	1, 32, F	Third ventriculostomy	Cyst fenestration	Neurological examination was unremarkable. This improvement maintained after 13 months.	MRI after 2 months: regression of some VRs. MRI after 13 months showed no change of VRs.
Homeyer et al. [62], 1996	1, 42, M	Ventriculoperitoneal shunt	None	Paresthesia disappeared, visual symptoms improved. After 7 months, headache and visual disturbances increased as a result of slight head injuries.	MRI: no change of VRs.
Ono et al. [79], 1994	1, 26, M	Ventriculoperitoneal shunt	Cyst fenestration	Involuntary movement, left oculomotor nerve palsy, and right hemiparesis drastically improved, and the patient was ambulatory when discharged.	MRI: marked reduction of VRs size and a marked reduction of hydrocephalus.
Eggenberger et al. [82], 1993	1, 56, F	None	Cyst fenestration	Orthoptic assessment one day after surgery demonstrated resolution of the previously observed exotropia and a decrease in the right hypertropia.	CT: decrease in VRs size.
Nishioka et al. [83], 1989	1, 38, F	Ommaya reservoir	Cyst fenestration	Sensory and visual disturbances improved immediately.	CT: reduction of VRs and resolution of hydrocephalus.

CT: computed tomography.
F: female.
MRI: magnetic resonance imaging.
M: male.
NR: not reported.
VRs: Virchow-Robin spaces.

the definition of tumefactive VRs, for which there is no uniform consensus yet.

Type 2 tumefactive VRs (along the paths of the perforating medullary arteries) and type 3 tumefactive VRs (in the mesencephalothalamic region) were the most commonly reported types. Our results suggest that type 2 tumefactive VRs uncommonly cause clinical manifestations. However, when type 2 tumefactive VR spacers are disseminated, they may cause symptoms of parkinsonism and/or dementia [35,52,74,86], possibly because of reduction of normal brain tissue as shown by positron emission tomography [85], cerebral blood flow SPECT [35], and magnetic resonance tractography [42] studies. Pyramidal tract symptoms caused by type 2 tumefactive VRs are rare, with only one reported case [14]. Notably, type 2 tumefactive giant VRs have also been observed in patients with neurofibromatosis [18,44] and psychomotor retardation [58], which may suggest a genetic cause in these patients. Type 3 tumefactive VRs seem more likely to cause clinical manifestations: in at least 60/80 (75.0%) patients, symptoms were attributed to the presence of type 3 tumefactive VRs. Type 3 tumefactive VRs can cause hydrocephalus (by compression of the cerebral aqueduct or third ventricle) and/or symptoms due to local mass effect on the mesencephalon.

MRI findings pathognomonic for tumefactive VRs are a typical location along the path of a penetrating vessel and visual signal intensity identical to CSF on all pulse sequences [1]. In patients with small to moderate dilatations of the VRs, the surrounding brain parenchyma generally has normal signal intensity [1]. This also appears to apply to type 3 tumefactive VRs. However, hyperintensity of the adjacent brain parenchyma on FLAIR / T2-weighted images (Fig. 4) appears to be common in type 2 tumefactive VRs, as it was reported to be present in 19/56 (33.9%) patients. This abnormal signal intensity stems from reactive gliosis and is not an ominous finding [1,59,62,89]. If the imaging findings are pathognomonic for tumefactive VRs, no further work-up is needed. Biopsy should be avoided, as there is a risk of hemorrhage by damaging the penetrating vessel in the tumefactive VRs [34]. However, careful review of clinical history and MRI is crucial to make a correct diagnosis of tumefactive VRs. Symptomatic type 2 tumefactive VRs may be considered uncommon. Pathologic processes causing pyramidal symptoms, such as watershed cerebral infarctions (Fig. 6), should not be mistaken for type 2 tumefactive VRs. Another notable finding is that we identified only 6 patients with tumefactive VRs in the posterior fossa, which may therefore be considered an atypical location. When cystic lesions are identified in the posterior fossa, gadolinium-enhanced T1-weighted images may be required to exclude the presence of a cystic neoplasm (Fig. 7).

There were some reports of tumefactive VRs at other uncommon locations or with uncommon presentation. Bastos et al. [72] reported a case of tumefactive VRs in the hippocampus with associated temporal seizures. Mandrioli et al. [93] reported a case of posttraumatic symptomatic hemorrhage in type 3 tumefactive VRs. The anterior temporal lobe is a preferred location for dilated VRs [22], but their cause and clinical significance still remains to be elucidated. In 6 of the 7 reported cases, symptoms were not attributed to the presence of anterior temporal lobe tumefactive VRs (supplemental Table 2), whereas in one symptomatic case temporal lobe seizures completely resolved after surgical resection [22]. In 4 reported cases, tumefactive VRs in the anterior temporal lobe did not change after follow-up of 7, 11, 34 and 112 months [12,22]. However, Eluvathingal Muttikkal et al. [21] and Cerase et al. [41] reported cases of tumefactive VRs in the anterior temporal lobe, which disappeared after 3 years. In Eluvathingal Muttikkal et al.'s case [21], the tumefactive VRs recurred again after 4 years. In Cerase et al.'s case [41], a parafalcine meningioma was resected before the tumefactive VRs disappeared. Causative mechanisms may have been obstruction of tumefactive VRs [21] or changes in CSF fluid pressure [41].

We identified 59 patients who underwent neurosurgery for symptomatic type 3 tumefactive VRs, consisting of either treatment of hydrocephalus by diversion of CSF flow and/or direct tumefactive VRs surgery. In general, clinical outcome after either type of surgery was good. As there is no randomized controlled trial, the best treatment remains unclear. CSF flow diversion by third ventriculostomy or ventriculoperitoneal shunting may be sufficient if there are only symptoms caused by hydrocephalus. In one report [89], third ventriculostomy was performed to prevent the possibility of hydrocephalus by aqueduct obstruction of type 3 tumefactive VRs. Cyst fenestration or placement of an intracystic catheter may be performed if there are symptoms of mesencephalon compression. However, both surgical procedures carry a risk of hemorrhage by damaging the penetrating vessel in the tumefactive VRs [34,92], which may be catastrophic in a highly eloquent area such as the mesencephalon.

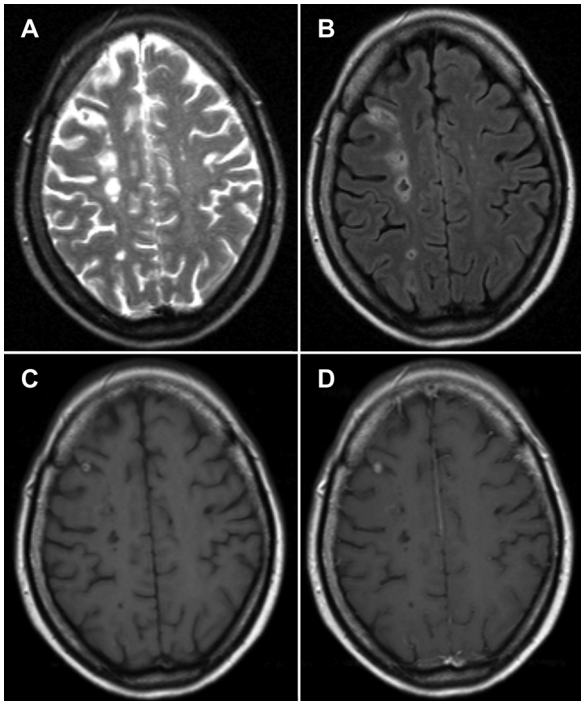

Fig. 6. Chronic watershed cerebral infarctions in a 46-year-old woman with a history of left-sided sensory disturbances and weakness. Axial T2-weighted (A), fluid attenuated inversion recovery (FLAIR) (B), pregadolinium T1-weighted (C), and postgadolinium T1-weighted (D) images show lacunes in the deep white matter of the right centrum semiovale, extending into the right frontal cortex. There is hyperintensity of the surrounding brain parenchyma on FLAIR images, representing gliosis. The patient history and the location of lesions in a watershed area with involvement of the cortex are consistent with chronic watershed cerebral infarctions and not with tumefactive VR spaces.

For type 1 tumefactive VRs (along the lenticulostriate arteries entering the basal ganglia through the anterior perforated substance) and tumefactive VRs at other locations than types 1–3, there were too little data to give follow-up recommendations. We identified 23 asymptomatic type 2 tumefactive VRs, which all remained stable with a mean follow-up period of 3.3 years (range 1 month - 17 years). Therefore, follow-up of asymptomatic type 2 tumefactive VRs by MRI seems unnecessary. Type 3 tumefactive VRs can increase in size, cause increased local mass effect and acute hydrocephalus [25,96,98], even up to 14 years after previous cyst fenestration [34]. Therefore, follow-up of type 3 tumefactive VRs is suggested, especially in patients who did not undergo CSF flow diversion surgery yet. However, the optimal frequency and duration of follow-up by MRI is still unclear.

A limitation of our systematic review is that we only identified case reports and case series. Therefore, publication bias is a possible confounder. First, we identified more reports on type 2 and 3 tumefactive VRs than on type 1 tumefactive VRs, but it is unclear whether there is a

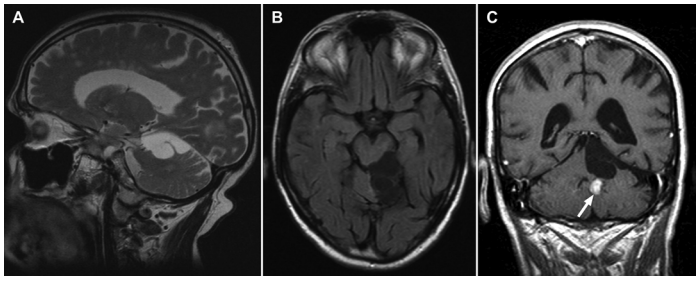

Fig. 7. Hemangioblastoma in a 65-year-old man. Sagittal T2-weighted (A), axial fluid attenuated inversion recovery (B), and coronal postgadolinium T1-weighted show a multicystic-appearing lesion in the superior part of the left cerebellum, causing mass effect on the left cerebral peduncle. There in an enhancing mural nodule at the caudal part of the lesion (arrowhead in C). Findings are consistent with hemangioblastoma in the left cerebellum (pathologically proven) and not with tumefactive VR spaces. It should also be noted that tumefactive VR spaces in the cerebellum are very rare, with only 4 reported cases identified by our systematic review.

true difference in prevalence or whether this is due to publication bias. Second, there may be an overrepresentation of symptomatic tumefactive VRs in the literature, either because asymptomatic tumefactive VRs less likely undergo brain MRI or also as a result of publication bias. Third, although general clinical outcome after direct type 3 tumefactive VRs surgery was good, this should also be interpreted with caution due to possible publication bias. Furthermore, we could not meaningfully apply a methodology assessment tool to the articles that were included in this systematic review, because the contents of the included studies were very heterogeneous and usually descriptive.

In conclusion, tumefactive VRs can be considered rare. Type 2 and type 3 tumefactive VRs are the most commonly reported types. In type 2 tumefactive VRs, clinical manifestations and signal abnormalities of adjacent brain parenchyma occur in a minority of cases, and follow-up of asymptomatic patients seems unnecessary. In type 3 tumefactive VRs, clinical manifestations are common, concomitant signal abnormalities occur infrequently, and neurosurgical outcome is generally good. Follow-up of type 3 tumefactive VRs is recommended, especially in patients who did not undergo CSF flow diversion surgery yet. There are limited data on type 1 tumefactive VRs and tumefactive VRs at other locations; no generalized conclusions can be made for these groups.

Conflicts of interest

All authors have no conflicts of interest to declare.

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