THE VENOUS MALFORMATIONS OF THE BRAIN

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The venous malformations are the most common congenital intracranial vascular lesions but the exact prevalence of them is unknown. Between 2001 and 2012, in our neurosurgery clinic there had been hospitalized a number of 70 patients with this kind of lesions. The patients’ ages ranged from 15 to 66 years old (mean age, 42.3 years; 38 female and 32 male). In 46 (65.71%) patients, the venous malformations had supratentorial localization. The most important symptoms encountered in these patients had been hemorrhage in 14 (30.43%), epilepsy in 10 (21.73%), hemiparesis and aphasia in 12 (26.08%) and headache in 42 (91.30%). In 24 (34.29%) of the patients, the venous malformations had been located at the level of the posterior fossa. The most important of their symptoms had been hemorrhage in 8 patients (33.33%), ataxia in 10 (41.66%), dizziness in 9 (37.5%), headache in 15 (62.5%), diplopia in 2 (8.33%), trigeminal neuralgia in 2 (8.33%) and peripheral facial palsy in 1 case (2.16%). As associated lesions, 5 (7.14%) of the patients had cavernous malformations which had been treated surgically with very good results. In 2 of the patients (2.85%) with epileptic seizures and with cerebellar venous malformations there had also been ascertained supratentorial arteriovenous malformations (temporal and frontal). The imaging methods used to reveal their presence had been magnetic resonance imaging and angiography. Out of the total of 70 analyzed patients, 46 (65.72%) had a stationary condition, while 24 (34.28%) of them had been improved. The patients with venous malformations associated with cavernous malformations had been subjected to surgery. The rest of the patients had received conservative and symptomatic treatment. None of the patients’ condition had aggravated and there had been no deaths.

Key words: venous malformations, arteriovenous malformations, cavernous malformations.

INTRODUCTION

The venous malformations (VMs) of the brain are congenital anomalies of the normal drainage veins. They are composed of dilated veins which converge in a single bigger drainage vein, or of more dense venous networks with multiple efferent vessels.

In 1887, Pfannenstiel published pathological descriptions of venous malformations, but McCornick presented the classic description in 1966.3

The venous malformations of the brain had been acknowledged for the first time as distinct pathological entities by Cushing and Bailey in 1928.3

The cause of their development is insufficently understood, but it had been alleged that they emerge in the late stages of the fetal maturation.

Saito and Kobayashi (1981)4 and Toro et al. (1988)5 implicated an intrauterine accident with resultant ischemia during the formation of medullary veins, resulting in collateral venous channels.

According to Mullan et al. (1996), all cerebrovascular malformations have a common origin, being related to a failure in the formation of the venous system, and that they differ only in that some are more and others less fistulized.

In some cases, the small veins from the cavernous malformations drain directly in the venous malformations.6

Rigamonti et al. (1990)\(^8\) had suggested that the cavernous malformations and the capillary telangiectasias are not separate entities, but rather variations of the same type of vascular malformation. The data obtained by Larson et al. (1998)\(^9\) support this theory. Therefore, these two malformations represent two extremes of the same pathological process, and a teleangectasia can develop in a cavernous malformation.

Mullan et al. (1996)\(^6\) proposed a similar model. In both paradigms, the venous malformations represent the anatomically abnormal, but a physiological normal venous outflow pathway for the involved portion of the brain.

They are known in the specialized literature under the name of venous angiomas or developmental venous anomalies.

According to Dănilă, these terms are inadequate and all they do is to complicate the pathology of the cerebral vascular malformations. If in the current, established literature there are the terms of arterial malformation, of arteriovenous malformation and that of capillary malformation, it is only fair to assign the same term to the abnormally developed veins, namely that of venous malformation.

Wolf et al. (1967)\(^10\) had made the first angiographical description of the venous malformations of the brain, and McCormick (1996)\(^11\) and then Dănilă et al. (2005)\(^12\) had made their first hystopathological descriptions. It had been shown that a venous malformation of the brain is composed of dilated subcortical veins with a radial layout which converge towards a transcortical or subependimal venous collector with a greatly increased caliber.

The venous malformations can be associated with other vascular anomalies, such as, cavernous malformations, arteriovenous malformations and capillary telangiectasias.

Because of the progresses made in the investigation of the brain, they can be now diagnosed with a higher frequency\(^13\)\textsuperscript{–}17.

The coexistence of the different types of vascular malformations in the same lesion suggests a common pathogenesis. Nevertheless, the pathogenic factors which are important for their development and build-up had not been ascertained yet. The natural history of the venous malformations of the brain is also unclear, this making difficult the establishing of the long term prognosis for the asymptomatic and symptomatic patients, for the treated and for the not treated ones.

MATERIALS AND METHODS

Clinical presentation

Between 2001 and 2012, in the neurosurgery clinic of The National Institute for Neurology and Neurovascular Diseases there had been hospitalized a number of 70 patients with venous malformations of the brain. Out of them, 46 (65.71\%) had a supratentorial localization, while in 24 (34.29\%) it had been an infratentorial one.

The patients’ ages ranged from 15 to 66 years old (mean age 42.3 years; 38 female and 32 male).

The patients’ ages ranged from 15 to 66 years old (mean age, 42.3 years; 38 female, 32 male), the conclusion being that the respective malformations had been present in approximately equal proportions in both men and women.

In 46 (65.71\%) patients, the venous malformations had supratentorial localization.

Out of these, 32 (45.71\%) had been found in the frontal lobe (Figure 1), 4 (5.71\%) in the parietal lobe (Figure 2), 8 (11.43\%) in the temporal lobe (Figure 3) and 2 (2.86\%) in the occipital lobe (Figure 4).

Fig. 1. This 30-year-old man presented with headaches and seizures. The anteroposterior (a) and left lateral (b) views of the angiogram shows, in the late phase, a frontal venous malformation.
Fig. 2. The patient FN, aged 35 years old, had been admitted in our clinic for subarachnoid hemorrhage and generalized epileptic seizures. The left lateral carotidian angiography had been normal in the arterial phase (a) but in the late, venous phase revealed the presence of a left parietal venous malformation (b).

Fig. 3. This 28-year-old man had presented for medical care with headache and vomiting. The early-phase on the lateral internal carotid angiography was normal (a). The late-phase on the lateral angiogram (b) reveals a small venous malformation in the tip of the temporal lobe.

Fig. 4. The late-phase on the anteroposterior view of the right internal carotid angiography reveals a large venous malformation. This 59-year-old woman presented with headache and without neurological deficits.

Therefore, they had been most often unilateral and tended to occur especially in the frontal lobes.

In 24 (34.29%) of our patients, the venous malformation had developed at the level of the posterior fossa (in 7 (29.16%) cases on the right side and in 17 (70.83%) cases on the left) (Figures 5–7).
Fig. 5. This 45-year-old man presented with headache, dizziness and right cerebellar syndrome. The late-phase angiogram shows a venous malformation localized in the right cerebellum.

Fig. 6. A 61-year-old woman presented with headache, dizziness and left cerebellar syndrome. The late-phase angiogram shows a venous malformation localized in the left cerebellum.

In a large study (Garner et al., 1991) the distribution of the VMs was as follows: frontal (42%), parietal (24%), occipital (4%), temporal (2%), basal-ventricular (11%), cerebellum (14%) and brainstem (3%).

Infratentorial VMs are virtually always in the cerebellum. They are most common solitary, but several cases of multiple VMs have been reported (19).

VMs are typically located at the junction of the superficial and deep venous systems or near the ependymal surface of the ventricle.

Fig. 7. A 19-year-old woman presented with headache and right cerebellar syndrome. The late-phase angiogram shows a venous malformation in the right cerebellum.

Clinical findings

The clinical features of the 70 patients with venous malformations of the brain are presented in Tables 1 and 2.

In the 46 (65.71%) patients with supratentorial venous malformations, the most important symptoms had been hemorrhage in 14 (30.43%), epilepsy in 10 (21.73%), focal deficits (hemiparesis and aphasia) in 12 (26.08%) and headache in 42 (91.30%) cases.

<table>
<thead>
<tr>
<th>The age group</th>
<th>The number of patients</th>
<th>Male gender</th>
<th>Female gender</th>
</tr>
</thead>
<tbody>
<tr>
<td>15 - 20 years</td>
<td>6 (8.57%)</td>
<td>4 (5.71%)</td>
<td>2 (2.87%)</td>
</tr>
<tr>
<td>21 - 30 years</td>
<td>10 (14.28%)</td>
<td>6 (8.57%)</td>
<td>4 (5.71%)</td>
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<tr>
<td>31 - 40 years</td>
<td>14 (20%)</td>
<td>10 (14.28%)</td>
<td>4 (5.71%)</td>
</tr>
<tr>
<td>41 - 50 years</td>
<td>20 (28.57%)</td>
<td>7 (10%)</td>
<td>15 (21.42%)</td>
</tr>
<tr>
<td>51 - 60 years</td>
<td>12 (17.14%)</td>
<td>4 (5.71%)</td>
<td>6 (8.57%)</td>
</tr>
<tr>
<td>61 - 66 years</td>
<td>8 (11.42%)</td>
<td>2 (2.86%)</td>
<td>6 (8.57%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>70</strong></td>
<td><strong>33 (47.14%)</strong></td>
<td><strong>37 (52.85%)</strong></td>
</tr>
</tbody>
</table>
Table 2

<table>
<thead>
<tr>
<th>Frontal</th>
<th>Parietal</th>
<th>Temporal</th>
<th>Occipital</th>
<th>Cerebellum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right</td>
<td>Left</td>
<td>Right</td>
<td>Left</td>
<td>Right</td>
</tr>
<tr>
<td>22 (31.42%)</td>
<td>10 (14.28%)</td>
<td>0</td>
<td>4 (5.71%)</td>
<td>6 (8.57%)</td>
</tr>
<tr>
<td>Total</td>
<td>32 (45.71%)</td>
<td>4 (5.71%)</td>
<td>8 (11.43%)</td>
<td>2 (2.86%)</td>
</tr>
</tbody>
</table>

Therefore, 14 (30.43%) patients had experienced symptomatic hemorrhage, with acute onset of the symptoms in eight, and chronically evolving complaints in six of them (Table 3). Generally, the hemorrhages had been small and they did not require surgical evacuation (Figure 8).

The gender, the localization and the dimensions of the venous malformation did not influence the risk of hemorrhage.

In one study, Rigamonti and Spetzler (1988) noticed that two patients sustained hemorrhages attributed initially to the venous malformations. The presence of cavernous malformation was suggested on MRI in one case, but not clearly. Both patients underwent surgery for hemorrhage and were found to have pathologically confirmed cavernous malformations associated with VMs.

Before the introduction of the modern neurodiagnostic techniques, the venous malformation were identified only after the complications they generated.

According to Mc Cormick et al. (1968) and Malik et al. (1988), the risk of hemorrhage is between 8% and 43%. The increased utility of MRI had led to changes of the above statistical data.

Therefore, Garner et al. (1991) had calculated that the risk of hemorrhage is 0.22% per year (1 hemorrhage in 4498 person-years). Less than 20% were considered with hemorrhage, and in only one case this was attributed to the venous malformation.

Likewise, the previous studies had showed that the risk for the occurrence of hemorrhages is higher in the patients with venous malformations localized in the posterior fossa, as well as in the pregnant women.

Mc Laughlin et al. (1988) retrospectively reviewed 80 patients with VMs and prospectively followed them over a mean of 3.6 years. There were 16 hemorrhages at the time of initial registration and 2 additional hemorrhages in the subsequent follow-up. They calculated a retrospective hemorrhage rate of 0.61% per year (18 bleeds in 2949 patient-years). In the prospective group, the annual rate was 0.34% (2 bleeds in 298 patient-years). The risk of hemorrhage was no greater in the posterior fossa, in contrast to previous suggestion that lesions in this location bleed more often.

These data emphasized that if a patient with a venous malformation is diagnosed with hemorrhage, a second lesion must be sought.

The risk of recurrent bleeding from venous malformations has not been well defined.

A review of 27 cases from the literature revealed that 5 cases (18.5%) had documented recurrence.

The annual rate of bleeding of 0.68% estimated by Mc Cormick et al. (1968) seems to be in consensus with the pertinent medical literature according to which they must not be treated surgically. In most of the authors there is the fear of the occurrence of cerebral infarctions after the surgical removal of the respective venous malformations. However, in the literature there are still present doubts about the possible effects of the venous malformations in causing thrombotic or hemorrhagic incidents during their evolution. The natural history of the venous malformations of the brain is unclear, this making difficult the establishing of the long term prognosis for the asymptomatic and symptomatic patients, both treated and not treated.

However, several authors suggest their removal or obliteration whenever the hemorrhage is life threatening, while others advocate for the surgical treatment of the accessible venous malformations, of the clinically symptomatic

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**Fig. 8.** Computed tomography scan in a 43 year-old male patient shows a small hemorrhage in the right frontal lobe (a). The early-phase angiogram is normal (b). The late-phase angiogram shows a right frontal venous malformation (c and d).
ones, of the angiographically occult, or when these are intimately associated and cannot be separated during the surgical intervention.

Some of our patients had different complaints and manifestations, but the epileptic seizure had been present in 10 (21.73%) of our patients with frontal VMs (Figure 9).

In the study conducted by Saito and Kobayashi (1981), the electroencephalographic localization was consistent in 3 of the 11 cases.

In the study of Garner et al. (1991), 5 out of 23 patients presenting with seizures had an electroencephalographic localization consistent with the VMs.

In the 45 patients with supratentorial venous malformations there had been present a number of 5 (10.86%) focal deficits.

In 4 (8.7%) of the patients, they had been manifested through discrete hemiparesis on the side opposite to the venous malformation, in 1 (2.7%) through aphasia and in 1 (2.17%) through central facial palsy. The respective deficits had appeared in the patients who had hemorrhages and in those in whom the VMs had been localized in the highly functional cerebral areas.

Out of the 24 (34.29%) patients with venous malformations of the posterior fossa, 8 (33.33%) had hemorrhage, 10 (41.66%) ataxia, 4 (16.66%) focal deficits, 9 (37.5%) dizziness and 15 (62.5%) headache, 2 (8.33%) diplopia, 2 (8.33%) trigeminal neuralgia and 1 (2.16%) peripheral facial palsy. However, cerebellar lesions may be more likely to cause focal deficits. In one study, 10 out of 12 patients with cerebellar VMs had signs or symptoms attributable to the lesion, such as ataxia, diplopia, or dizziness.

Not always the symptoms the patients are complaining of are caused by the respective venous malformations.

Because of this, before involving the venous malformation for generating the symptoms, the clinicians should also investigate other possible causes.

Generally, the patients complain of non-specific symptoms such as, hemorrhage, seizures, neurological deficits, vomiting, ataxia, dizziness, headache, etc.

However it is difficult to ascertain the relationship of the venous malformation to a neurological deficit in the absence of hemorrhage or thrombosis.

No pathological evidence of ischemic changes or microhemorrhage had been demonstrated. In addition, the MRI findings rarely show a mass effect unless there is associated bleeding. Despite this, the focal deficits are occasionally attributed to VMs.

Eight patients in one series were found to have VMs potentially causing focal deficits in the absence of hemorrhage, none of which was disabling.

Kondziolka et al. (1991) found two patients with focal deficits potentially related to VMs. One had hemiparesis and a venous malformation in the contralateral posterior internal capsule. The other presented with a movement disorder had an associated contralateral caudate nucleus VM.

Headache had been encountered in 42 (91.30%) of our patients with supratentorial venous malformations and in 15 (62.5%) of those with infratentorial lesions.

Anyway, headache had been present in 57 (81.42%) of the 70 patients analyzed by us (Tables 3 and 4).

<table>
<thead>
<tr>
<th>No.</th>
<th>The type of symptoms</th>
<th>Frontal</th>
<th>Parietal</th>
<th>Temporal</th>
<th>Occipital</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Hemorrhage</td>
<td>11 (23.91%)</td>
<td>1 (2.17%)</td>
<td>2 (4.35%)</td>
<td>0</td>
<td>14 (30.43%)</td>
</tr>
<tr>
<td>2</td>
<td>Seizures</td>
<td>10 (21.73%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>10 (21.73%)</td>
</tr>
<tr>
<td>3</td>
<td>Focal deficit</td>
<td>4 (8.7%)</td>
<td>1 (2.17%)</td>
<td>0</td>
<td>0</td>
<td>5 (10.86%)</td>
</tr>
<tr>
<td>4</td>
<td>Headache</td>
<td>32 (69.56%)</td>
<td>3 (6.52%)</td>
<td>5 (10.86%)</td>
<td>2 (4.35%)</td>
<td>42 (91.30%)</td>
</tr>
</tbody>
</table>

The clinical symptoms in the different lobes at presentation for the 46 patients with supratentorial venous malformations.
Table 4

The clinical symptoms in the different lobes at presentation for the 24 patients with venous malformations in the posterior fossa

<table>
<thead>
<tr>
<th>No.</th>
<th>The type of symptoms</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Hemorrhage</td>
<td>8 (33.33%)</td>
</tr>
<tr>
<td>2</td>
<td>Ataxia</td>
<td>10 (41.66%)</td>
</tr>
<tr>
<td>3</td>
<td>Focal deficit</td>
<td>4 (16.66%)</td>
</tr>
<tr>
<td>4</td>
<td>Dizziness</td>
<td>9 (37.5%)</td>
</tr>
<tr>
<td>5</td>
<td>Headache</td>
<td>15 (62.5%)</td>
</tr>
<tr>
<td>6</td>
<td>Diplopia</td>
<td>2 (8.33%)</td>
</tr>
<tr>
<td>7</td>
<td>Trigeminal neuralgia</td>
<td>2 (8.33%)</td>
</tr>
<tr>
<td>8</td>
<td>Peripheral facial palsy</td>
<td>1 (4.16%)</td>
</tr>
</tbody>
</table>

So, headache is a common symptom in patients undergoing imaging studies. The causal relationship to VMs is difficult to assess, as definitive proof would require treatment⁴⁰. Therefore, VMs rarely cause symptoms and are often incidental findings. They may be considered symptomatic if the location is consistent with signs and symptoms of the presenting illness or if a hemorrhage occurs within the VM.

The neurological symptoms include headache, seizure, focal deficit, and intracerebral or subarachnoid hemorrhage.

Rarely, trigeminal neuralgia and hydrocephalus have been described as presenting symptoms²⁶, ⁴¹, ⁴².

In large clinical series, less than 25% of the symptoms are attributable to the venous angioma, so other pathological conditions should be sought⁸.

Generally, the symptomatology caused by the cerebrovascular malformations may be acute or may have an insidious onset; it may be related to intrinsic growth bleeding, thrombosis or perilesional iron depositions and perilesional atrophy⁴³.

In 5 (7.14%) of our patients, the venous malformation had been associated with cavernous malformations.

In 2 female patients with epileptic seizures and a cerebellar VM it had also been discovered big temporal and front supratentorial arteriovenous malformations.

According to the data in the literature, the associated malformations have a more aggressive clinical evolution compared with the isolated lesions⁷, ¹³, ¹⁵, ¹⁷, ³², ⁴⁴–⁴⁹.

Imaging

**Computed Tomography Scans**

More commonly, patients undergo contrast enhanced computed tomography (CT) scans or magnetic resonance imaging (MRI).

On an infused CT scan, the most common finding is a linear or curvilinear enhancement after contrast administration. Delineation of the medullary veins sometimes can be seen on these imaging studies.

We had performed a CT scan as the first examination in all the symptomatic patients. With the help of this examination we had been able to reveal especially the hemorrhages (Figure 10).
The venous malformations of the brain

Magnetic Resonance Imaging

The Magnetic Resonance Imaging (MRI) is equally sensitive and more specific than CT, with the important finding being a linear or curvilinear hypointensity on the T1-weighted and the T2-weighted images. Therefore, MRI is the diagnostic method of choice, showing a starburst pattern of white matter veins converging on a large draining vein in the case of a venous malformation. The venous malformations enhances brightly with contrast administration (Figure 11).

Fig. 11. The computed tomography scan in a 36-year-old man shows a small hemorrhage in the right frontal lobe (a). The MRI reveals a venous malformation in the right frontal lobe (b). The late-phase angiogram shows a venous malformation on the anteroposterior (c) and lateral (d) views of the right frontal lobe.

The draining vein is better seen on the T2-weighted sequences. Because of the slow flow, there is good definition of the draining vein and of the perimedullary caput medusae veins. Early reports suggested that the area of a developmental venous anomaly was often hyperintense on T2-weighted images. However, it had been ascertained subsequently that the hyperintensity was artifactual. Latter studies had reported a hyperintensity surrounding the venous malformations in 50% of cases. However, not all of the studies reported this hyperintensity. Additionally, the pathological MRI image was proved to be an area of acute demyelination surrounding a developmental venous anomaly.

In conclusion, MRI is an extremely sensitive imaging method for the detection of venous malformations and cavernous malformations. The T2-weighted gradient-echo (GRE) sequences are the most important MRI techniques for the detection of the cavernous malformations. Hemorrhage and/or calcification lead to susceptibility effects, and the T2-weighted GRE is the most sensitive tool to visualize these effects.

A contrast-enhanced T1-weighted three-dimensional data set, such as magnetization prepared rapid acquisition gradient echo, is of advantage when delineating small venous malformations because of its high resolution.

Angiography

The first angiographic description of venous malformations was made by Wolf et al. (1967), and the golden standard for diagnosing the venous malformations is conventional cerebral angiography. The venous malformations are visualized in their entirety during the late venous phase. There is no early filling of a draining vein as in the arteriovenous malformations (AVMs).

The classic angiographic picture is described as a caput medusae lesion because of the lesion’s resemblance to the snakes on the head of the mythical character. The images
also have been likened to a spider, a hydra, spoked wheels, umbrellas, and a sunburst and are referred to by Mullan et al. (1996) as star clusters (Figures 12–14).

These findings are pathognomonic for a developmental venous anomaly.

Fig. 12. The late-phase right common carotid angiogram showing a frontal venous malformation. The venous drainage is through the deep venous system via the basal vein of Rosenthal.

Fig. 13. A 30-year-old woman presented with headache, dizziness, ataxia and diplopia. The angiography revealed in the late-phase a left cerebellar venous malformation.

Fig. 14. A 40-year-old woman presented with headache, vomiting and left hemiparesis. The angiography revealed in the late-phase a profound right-side venous malformation which drained in the internal cerebral vein. The CT scan revealed a hemorrhage around this venous malformation.

Venous malformations and other lesions

Mixed vascular malformations

With the increasingly sensitive and specific diagnostic yield of MRI and the growing clinical experience, the number of patients reported to harbour multiple malformations is increasing.

The natural history of these lesions is unknown because they have not been studied in a longitudinal fashion.

Little is known about their prevalence, their natural history, or, more importantly, their pathogenesis.

However, it had been established the association of the venous malformations with other vascular anomalies.

There had been observed associations with arteriovenous malformations (AVM) with cavernous malformations, as well as with capillary telangiectasia.

Venous malformations and arteriovenous malformations

Only 2 (2.85% of our patients had associations of venous malformations and arteriovenous malformations (Figure 15).

Mullan et al. (1996) hypothesized that the association of VMs and AVM may be related to failure of the development of cortical venous mantle. Komiyama et al. (1999) reviewed 31 patients with AVMs and VMs and found no difference in the prognosis of those with or without associated AVMs.

Venous malformations and cavernous malformations

We had only 5 (7.14%) patients in whom VMs had been associated with cavernous malformations. In 4 patients, the associated cavernomas had been supratentorial, while 1 in the mesencephalus (Figure 16). A female patient had multiple cavernomas. All of them had been treated surgically with very good results. None of our patients with associated lesions had any similar ailments in the family.
The venous malformations of the brain

Figure 15. A 32-year-old man presented with seizures in the left side of the body and headache. The angiography revealed in the early-phase a right temporal arteriovenous malformation (a) and in the late-phase a left cerebellar venous malformation (b).

Fig. 16. A 21-year-old man presented with the sudden onset of coma. The MRI revealed a bilateral ponto-mesencephalic hemorrhage triggered by a cavernoma (a). After the total resection of the cavernoma and hematoma (b), the patient’s condition has improved significantly, showing only a remaining right side weakness and hemisensory deficit. Now the patient is a student and has an excellent health condition. The late-phase angiogram reveals a venous malformation in the left cerebellum (c).
In the female patient with multiple cavernomas, only the frontal cavernoma had been removed, the associated temporal venous malformations being left in place (Figure 17).

The association of VMs with cavernous malformations and occult vascular malformations is also well documented. The cavernous malformations are well-circumscribed, multilobulated, angiographically occult vascular anomalies. Pathologically, they are composed of sinusoidal vascular channels (caverns) lined by a single layer of endothelium. The lack of intervening brain parenchyma is a characteristic pathological marker. The surrounding parenchyma consistently exhibits evidence of prior microhemorrhage, hemosiderin discoloration, and hemosiderin-filled macrophages.

Abe et al. (1998) found that 23% of the patients with occult vascular malformations also had VMs. There is a subgroup of cavernous malformations develops de novo in the vicinity of a venous malformation.
Russel (1930–1931) had been the first to hypothesize that the cavernous malformations may be derived from capillary telangiectasias.

Rigamonti et al. (1991), who studied the histopathological characteristics, admitted a single pathological entity and found that there is normal parenchyma between the dilated vascular channels in 35% of the cavernous malformations. It is hypothesized that the regional venous hypertension may facilitate the development of cavernous malformations through red cell diapedesis and release of vascular endothelial growth factor. The above mentioned argumentation does not explain the development of cavernomas at a distance, or in the contralateral hemisphere to that with the venous malformation.

Theoretically, the factors underlying the growth or the de novo formation of cavernous malformations would be involved in the transformation of a capillary telangiectasia to a cavernous malformation. Various angiogenic factors, including the basic fibroblast growth factor and the platelet-derived growth factor, can be influential in the initiation and propagation of this change.

Fig. 18. Female patient aged 45 years old who had been hospitalized with headache, vomiting and balance disorders. The angiography of the 4 cerebral blood vessels had revealed the presence of a complex venous malformation and the thrombosis of the superior sagital, of the right transverse and of the right sagital sinuses (Figure 18). Normal left transverse and sigmoid sinuses (a, b, c, d).

Venous malformations and capillary telangiectasias

Wolf and Brock (1935–1936) had been the first to observe the definite presence of a vein within a capillary telangiectasia, suggesting that the venous malformations might have developed from the capillary telangiectasias. Blackwood (1941) made an early observation regarding the similarity between the capillary telangiectasias and the venous malformations. Challa et al. (1995) stated that the two cannot be distinguished unless a draining vein is seen.

Blawwood (1941) provided the first classic histological descriptions. Microscopically, there are small tufts of capillaries, which are not structurally different from the normal capillaries.

There is no smooth muscle and a noted absence of classic fibers.
There are no feeding or draining vessels\textsuperscript{56}. Normal parenchyma is present between the dilated capillaries and a mild gliosis can surround the parenchyma. Hemosiderin and other evidence of prior hemorrhage are unusual. In rare case it is calcified and referred to as hemangioma calcifications\textsuperscript{88,12}.

The pathogenesis of these lesions is unknown. The imaging studies often miss capillary telangiectasias due to their size and the absence of hemorrhage. These lesions are nearly always angiographically occult\textsuperscript{85,32}.

The CT scan is often normal\textsuperscript{56} but it may display variable enhancement without mass effect\textsuperscript{85}. The MRI may reveal small enhancing lesions with a brushlike pattern, particularly in the pons, but they are often undetectable on standard T1- and T2- weighted images\textsuperscript{67,88}.

In a patient with hemorrhage from a capillary telangiectasia associated with a venous malformation, Mc Cormick et al. (1993)\textsuperscript{89} suggested that the capillary telangiectasia may develop as a result of venous hypertension within the venous malformation and it may be a transitional early form of a cavernous malformation.

Van Roost et al. (1997)\textsuperscript{90} reported a patient with a coexisting venous malformation and capillary telangiectasia.

A complex venous malformation had been discovered in a female patient aged 45 years old who had been admitted in hospital for headache, vomiting and balance disorders.

The angiography of the 4 cerebral blood vessels had revealed the presence of a complex venous malformation and the thrombosis of the superior sagital sinus, of the right transverse and of the right sigmoid ones (Figure 18). The left transverse and sigmoid sinuses had been normal.

Other pathologies, including infarctions and tumors, are found in 10\% to 20\% of patients with venous malformations\textsuperscript{18,29,91}.

In addition, there had been a case report describing a venous anomaly associated with facial hemangioma\textsuperscript{92}.

**Pathology and physiopathology**

On gross examination, one finds a radially arranged pattern of medullary veins converging centrally on single draining vein, which in turn drains ether superficially or deeply. This configuration has been described as a star cluster\textsuperscript{6}.

However, the venous malformations of the brain are congenital ant they consist of veins with angiogenically mature walls. At their level there cannot be found any arterial or capillary elements. Nevertheless, here and there they have the tendency to burgeon and to generate new veins. We are talking here about neurogenesis (Figure 19).

Fig. 19. Venous malformation with the development of new vessels through *in situ* loop formation in the wall of a large vein – an early stage with an evagination (arrow) (neo-venogenesis) (a).

Sometimes, these veins have minimal smooth muscle or elastic tissue, and the anomaly is found predictably with normal parenchyma\textsuperscript{2,80,83,93}.

Hemodinamically, these venous malformations have a low flow and a low resistance and they present only a small likelihood of hemorrhage\textsuperscript{29}.

**RESULTS**

Out of the total of 70 analyzed patients, 46 (65.72\%) had a stationary condition, while 24 (34.28\%) of them had been improved.

None of the patients in our series had died, nor had presented significant morbidities.

A number of 65 patients had presented the classic appearance of caput medusae, with the dilated medullary veins converging towards a large draining vein with connections to the deep venous system or to the cortical veins.

Five patients had presented with pathological large draining veins, but without a caput medusae appearance.

The clinical follow-up period ranged from 3 month to 6.2 years. The postoperative radiological follow-up investigations after a mean period of 25.8 months included computed tomography scans and MRI scans.

The three patients with venous malformations associated with cerebral cavernous malformations were treated surgically. Evidence of previous hemorrhage was found intraoperatively in all the patients.

The surgical removal of the cavernous malformations during the operation had been radical only in two cases, and it included the removal of the surrounding hemosiderin-stained gliotic tissue.
In the female patient with multiple cavernomas, only the right frontal lesion had been excised, and subsequently the seizures became sensibly less frequent.

Major postoperative morbidity and mortality had been absent.

However, there is the need for further experience with the treatment options and the post-surgery follow-up of single and associated lesions.

**DISCUSSION**

**Epidemiology**

The venous malformations are the most common intracranial vascular lesions but the exact prevalence of the VMs is unknown.

In one autopsy series of 4069 consecutive patients, 105 (2.6%) were found to have venous malformations\(^1\).

The autopsy studies also revealed that VMs are the most common type of vascular malformations, accounting for up to 65% of cases\(^9,4\).

One series found that 50% of the patients with vascular malformations diagnosed by MRI had venous angiomas\(^18\).

The prevalence varies among studies, but typically it ranges from 0.5 to 0.7% in retrospective imaging studies\(^34\) and is about 2.6% in autopsy studies\(^9,4\).

In a population-based study\(^95\) the incidence of VMs was second only to that of AVMs (arteriovenous malformations), with an age and sex-adjusted detection incidence rate of 0.41 per 100000 person-years. The initial diagnosis is typically made in the third decade\(^18,29,37\) but VMs have been reported also in children, as well as in adults in the eighth decade. There is an equal prevalence in men and women\(^18,37\).

No evidence suggests that the venous malformations are familial\(^8\).

A growing number of patients with symptomatic or incidental venous malformations are addressing to the neurosurgical clinics and raise the question of whether to operate on these lesions or to keep them under surveillance\(^17\).

The knowledge of the neural history of distinct venous malformations is crucial in clinical practice, because decisions on further treatment recommendations have to be based on the estimated risk of further morbidity in each patient\(^17\).

The prevalence of associated vascular malformations

According to Abdulrauf \textit{et al.} (1999)\(^15\) and Porter \textit{et al.} (1999)\(^96\), autopsy and MRI-based studies have shown that the cavernous malformations (CMs) occur in the population with a prevalence ranging from 0.47 to 0.9%, while the VMs has a prevalence of up to 3%\(^29\).

An association between CMs and VMs was first reported in 1974 by Robertson \textit{et al.}.

Since then, Wurm \textit{et al.} (2005)\(^17\) have found 294 cases of associated lesions and a percentage of 2.1 to 100% reported in the literature\(^13, 15, 16, 17, 39, 74, 96\).

In 1999, Porter \textit{et al.} reported a 100% coalescence of CMs with VMs in brainstem cases.

The patient series of Wurm \textit{et al.} (2005)\(^17\) is one of the largest series comparing the surgical treatment strategies of associated vascular malformations ever reported in the literature\(^13, 65, 96\).

Small venous malformations are sometimes encountered at surgery. They cannot be identified even on the best magnetic resonance images\(^15\). This is the cause why the prevalence of this co-occurrence is underestimated.

In the patient series of Wurm \textit{et al.} (2005)\(^17\), the MRI showed a 93.3% sensitivity for associated venous malformations.

The physical proximity of discrete subtypes of vascular malformations and the pathological heterogeneity within the lesions support the assumption of a common origin for distinct vascular malformations\(^8, 13, 14, 97\).

Some authors suggest that, whereas a venous malformation is a congenital lesion, any associated malformation is a dynamically acquired anomaly. They start from the supposition that the alteration of the blood flow of the VMs by hemodynamic turbulence, progressive obstruction, venous hypertension, and diapedesis of blood cells through leaky capillaries stimulate the angiogenic factors and thus favor the development of associated malformations\(^45, 46, 48, 49, 97–99\), with some forms representing transitional forms or precursors of other lesions\(^6, 8\).

It is known that several mechanisms mediating the growth of new blood vessels in the adult resemble those during embryogenesis\(^100\).

**The de novo lesions**

The de novo formation of cavernous malformations, with and without radiotherapeutical induction, has been reported in cases of both familial and sporadic cavernous malformations.

Although some of the newly discovered CMs could represent the growth of preexisting or
residual lesions that might have been missed on previous poorer-quality imaging, other actually represented true recurrent or novo lesions. The de novo lesions seem to be triggered by the cascade in the venous hypertension: microhemorrhage; growth factor release as a repetitive veno-occlusive disease develops over a long period of time, with fluctuating venous pressure. The diapedetic microhemorrhages resulting from the venous overload may cause a reactive angiogenesis with new vessel formation and coalescence, the so-called “hemorrhagic angiogenetic proliferation.” Alternatively, a hemodynamic disturbance such as a venous outflow restriction might open preexisting arteriovenous connections, resulting in minute arteriovenous shunts that can enlarge over time.

In 1992, Wilson noted that arteriovenous connections exist normally in the brain, and they can be opened temporarily under particular circumstances. In the case of an outflow restriction and a venous overload from a VM, this fact might be the pathway for newly developing malformations. The description by MRI contrast enhancement of the surrounding brain parenchyma in two cases of associated malformations as a sign of blood-barrier supports both theories.

Anyhow, the pathogenic mechanism of the development of a mixed VM and AVM lesion is only in the stage of hypothesis. The description of the genes which are crucial in the formation of the capillary-venous side of the vascular system or the mutation of these genes as an underlying cause still remains speculative.

The angiogenesis mechanisms intervene not only in the genesis of the AVMs, but also in their development or recurrence. The arteriovenous malformations develop as a consequence of certain aberrations of the process of vasculogenesis of the capillary bed, and the resulting arteriovenous shunt leads to the vascular recruitment and the enlargement of the lesion. The venous malformations associated with cerebral cavernous malformations.

Although the biological behavior of the cerebral cavernous malformations (CMs) seems to be relatively benign in most of the cases, their potential for a more aggressive course has been recognized in the case of a size of at least 10 mm, with an infratentorial location.

A dynamic and more aggressive behavior of CMs with growth, higher risk of hemorrhage, and recurrent and de novo development of lesions has been observed under the following circumstances: associated venous malformation, multiplicity of lesions, familial occurrence, after radiotherapy or after incomplete surgical removal.

Treatment

Some of our patients with venous malformations of the brain had been asymptomatic. In others, the symptoms had been caused by the associated lesions, such as arteriovenous malformations (Figure 14) and cavernomas (Figure 15) situated at a distance from the venous malformation or within it.

In the majority of the patients with epilepsy and venous malformations, the seizures had been controlled very well using only the anticonvulsivant medication.

None of the cases, both ours or in the literature, had refractory epilepsy which required a surgical intervention. In the 12 (17.14%) patients with hemorrhage at the level of the venous malformations, the surgical drainage had not been necessary as they had been small. All the hemorrhages found at the level of the supratentorial venous malformations had received conservative treatment.

Many authors have described surgery as treatment for these hemorrhages. Although the patients may do well after surgery, the potential for catastrophic complications or death exists if the normal venous drainage is interfered with.

However, most of the surgeons would recommend a conservative approach.

The cerebral edema, the infarction and the hemorrhage occur after the obliteration of these venous malformations. They are similar to the complications occurring after the spontaneous thrombosis of the respective lesions and of the venous channels that ensure the drainage of the normal brain. This occlusion leads to venous hypertension and eventually to venous infarction.

Lindquist et al. (1993) hypothesized that the gradual occlusion of these channels through the use of radiosurgery would allow the slow recruitment of other venous channels and would
prevent this complication. In their study of 13 patients, however, most of the venous malformations were incompletely obliterated, and the incidence of the neurological morbidity was high.

Based on this study and its subsequent criticism\textsuperscript{112-114}, the stereotactic radiosurgery is not recommended for venous malformations.

Most of the authors recommended that no intervention should be intended for the venous malformations.

In the patients with hemorrhages situated outside the area of the venous malformation we should also consider other associated causes which we must treat accordingly.

**The surgical treatment**

Even though the symptomatic annual bleeding rate of venous malformations has been reported to be between 0.22%\textsuperscript{18}, and 0.68%\textsuperscript{29}, with a calculated lifetime risk of up to 23%\textsuperscript{29}, most of the authors are of the opinion that no treatment can be provided in the cases of a symptomatic venous malformations\textsuperscript{17}.

A review of the literature disclosed only seven reported cases\textsuperscript{31, 39, 62, 96, 111, 119}, in which had been observed adverse events after surgery, while all the other authors had deduced their opinions based on these few cases\textsuperscript{17}.

Rigamonti and Spetzler (1988)\textsuperscript{61} reported on one additional case in which the cerebellar hemisphere began to swell after the excision of the central trunk with the first few branches of the venous malformation; however, the patient had a complete recovery.

The variability of the results following the surgery of the venous malformations is caused by the confuse descriptions of the surgical techniques\textsuperscript{17}.

They concern the total ablation of the venous malformation through precise dissection and bipolar coagulation\textsuperscript{56}, the excision of the malformation\textsuperscript{51}, the excision of the first branches and of the central trunk\textsuperscript{61}, the complete ablation of the venous malformation\textsuperscript{38}, its surgical removal\textsuperscript{22}, the excision of the entire lesion\textsuperscript{120}, the compromising of the venous malformation during surgery\textsuperscript{36}.

Following the total and partial surgical resections, as well as after the coagulation of the venous malformation, the following authors had reported good results: Odom et al. (1961), Constans et al. (1968), Scotti et al. (1975), Preising et al. (1976), Cabanese et al. (1979), Iraci et al. (1979, Nagata et al. (1983), Rothfus et al. (1984), Inagawa et al. (1985), Lobato et al. (1988), Malik et al. (1988), Rigamonti and Spetzler (1988), Rapacki et al. (1990), Lupert et al. (1993), Brunken et al. (1999), Chandra et al. (1999), Yamada et al. (2001), Abe et al. (2003)\textsuperscript{120, 128, 36, 119, 27, 38, 22, 61, 69, 16, 39}.

Neurological sequela, such as hemiparesis, aphasia, etc. after the surgical treatment of the venous malformations, had been reported by the following authors: Sadeh et al. (1982), Nagata et al. (1983), Meyer et al. (1995), Abe et al. (2003)\textsuperscript{25, 119, 62, 39}.

Chandra et al. (1999)\textsuperscript{16} had supposed that in these patients there are present alternative channels of venous drainage.

According to Wurm et al. (2005)\textsuperscript{17}, the surgical risk of VMs might have been considerable overestimated.

The following authors had reported the death of their patients after the clipping, coagulation or resection of the venous malformations: Senegor et al. (1983), Biller et al. (1985), Porter et al. (1999)\textsuperscript{111, 31, 96}.

After radiosurgery, Dias et al. (1988)\textsuperscript{129} had achieved good results in one patient, while 3 of the 13 patients treated by Lindquist et al. (1993)\textsuperscript{118} had developed radionecrosis. In one of the patients it had been necessary the excision of the radionecrosis.

However, encouraged by the literature research, Wurm et al. (2005)\textsuperscript{17} decided to coagulate and divide the large transcerebral vein of the venous malformation during surgery of the recurrent cavernous malformations. They had considered that the large drainage veins cause flow disturbances, diapedetic microhemorrhages resulting from the venous overload, and neoangiogenesis. Moreover, the risk of recurrence of bleeding from the newly developed malformations in the vicinity of VMs might exceed the risk of infarction\textsuperscript{17}. In all the 9 patients, the above mentioned authors had not encountered intraoperative brain swelling, neither postoperative neurological deficits.

In opposition to Abe et al. (2003)\textsuperscript{39}, who considered that only the angiographically occult venous malformations (those without a typical caput medusae appearance) can be surgically treated, Wurm et al. (2005)\textsuperscript{17} had successfully coagulated the typical transcranial draining vein in six patients with a caput medusae.

However, surgery may not be applicable to the posterior fossa VMs, in which the disruption of the VM had been reported more often to be catastrophic\textsuperscript{17}. 


CONCLUSIONS

The venous malformations of the brain are congenital anomalies of the normal draining veins.

The most important clinical manifestations encountered in our patients had been: hemorrhage, epileptic seizures, hemiparesis, aphasia, trigeminal neuralgia, peripheral facial palsy, dizziness, balance disorders and headache.

The venous malformations had been located supratentorially, at the junction of the superficial and deep venous systems, in the proximity of the cortex or near the ependymal surface of the ventricles.

The venous malformations of the brain had been associated with cavernomas (5 cases) and with arteriovenous malformations (2 cases). They can be also associated with the Sturge-Weber syndrome, the Moyamoya disease, telangiectasias, gyral dismorphism and cerebral tumors.

The relevant imaging investigations had been the MRI and the angiography.

Most of the surgeons recommend the conservative treatment. For the patients with important hemorrhages and cavernous malformations it is recommended the surgical treatment with the conservation of the venous malformation. The occlusion of the venous malformations is followed by cerebral edema, venous hypertension and hemorrhagic infarction.

REFERENCES

The venous malformations of the brain


