MR Perfusion Imaging in a Case of a Vein of Galen Malformation with Secondary Capillary Angioectasia

Y.-C. WEON, D. DUCREUX, H. ALVAREZ, P. LASJAUNIAS

Department of Neuroradiology, C.H.U. de Bicêtre, Paris XI University, Le Kremlin-Bicêtre; France

Key words: magnetic resonance imaging, vein of Galen malformation, perfusion

Summary

Vein of Galen Aneurysmal Malformations (VAGMs) are uncommon vascular malformations associated with dilatation of the vein of Galen embryonic forerunner with single or multiple direct arteriovenous fistulas within its wall without direct reflux into normal cerebral veins. We describe a patient with a late neurological onset presenting a classic VGAM complicated by secondary thalamic capillary angioectasia imaged with MR perfusion. In our patient, abnormal MR perfusion parameters were not seen on conventional MRI; they probably reflect underlying venous hypertension. They were located in areas involved in motor neurological deficit.

Introduction

Vein of Galen malformations (VAGMs) are uncommon vascular malformations thought to develop between six and 11 weeks of intrauterine life and due to persistence of the embryonic median vein of Markowski, consisting of an aneurysmal dilatation of the draining vein with single or multiple arteriovenous fistulas within its wall or adjacent choroid fissure without reflux into the cerebral veins^{2,8}. Clinical manifestations of VAGMs generally occur in the neonatal period due to congestive heart failure.

In early childhood, macrocrania, developmental retardation, facial vein enlargement, hydrocephalus, visual deterioration, seizures, hemiparesis, epistaxis can also be found³. Venous hypertension and anomalous venous anatomy with decreased tissue perfusion phenomena are the preferred suggested mechanisms for most of these neurological manifestations^{2,3}. During infancy, frequent skull base venous dural sinus dysmaturation with jugular bulb obstruction increases this venous hypertension and could explain the early appearance of symptoms in this disease.

Secondary changes include intracerebral or subependymal capillary angioectasia, a particular kind of microcapillary network which may be associated with seizures², without obvious physiological relationships with the cortex. Many hypotheses were proposed^{4,6,12}, one of them implicating the local or regional haemodynamic disturbances induced by the arteriovenous shunt⁴.

We describe a patient with a vein of Galen malformation and late onset neurological deficits in whom MR quantitative perfusion parameters including time to peak (TTP), decrease ratio of signal (DR), cerebral blood volume (CBV) and cerebral blood flow (CBF) were abnormal reflecting the effect of venous hypertension on the arterial system.

Figure 1 FLAIR (axial, A), EE T1 (sagittal, B) and SE T2 (frontal, C) images show multiple foci of signal loss (arrowheads) in the thalami and moderately enlarged vein of Galen (arrow) and falcine (Dot) sinus. There is no dilatation of lateral ventricles or cerebral oedema.

Case Report

An eight-year-old girl with a VAGM diagnosed in utero was admitted to our hospital for progressive amyotrophy of the inferior limbs, right side paresis and clonus that appeared simultaneously. She had cardiac insufficiency at birth, well controlled medically, and developmental retardation. The malformation was em-

bolized twice during the first year of life (six and ten months). She developed hydrocephalus at 15 months of age and was treated with ventriculo-peritoneal shunt.

MRI (figure 1) showed multiple foci of flow-void in the thalami associated with a moderately enlarged vein of Galen and falcine sinus. There was no dilatation of the lateral ventricles. Carotid angiography (figure 2) confirmed

Figure 2 Right internal carotid angiogram, early arterial phase, (lateral view, A); early arterial (frontal, B) and mid-arterial (lateral, C) phases show prominent choroidal, subependymal and thalamo-perforating arteries (arrowhead) feeding the moderately enlarged vein of Galen (arrow). Note presence of a large falcine sinus (Dot). The venous phase (lateral, D) view shows patent jugular bulb, cavernous capture and no pial venous reflux.

bilateral prominent choroidal, subependymal and thalamo-perforating arteries feeding the moderately enlarged vein of Galen. Full opacification of posterior dural sinuses is seen without cortical venous reflux. The jugular bulbs are narrowed but patent. Cavernous capture is present but cavernous sinus drainage is poor. Epsilon veins are not seen. Quantitative MR Perfusion was performed on a 1.5 t General

Electric Signa EchoPlus system with implementation of the indicators dilution theory (central volume theorem of Stewart-Hamilton, and relation between endovascular gadolinium concentration and MRI signal variation⁵). After fifteen T1-weighted sagittal slices (5 mm, 256 x 256, 240 mm FOV, TR = 450, TE = 12 ms), twenty FLAIR axial slices (5 mm, 256 x 256, 240 mm FOV, TR = 9900, TE = 105, TI = 2200

ms), and twenty T2-weighted coronal slices (5 mm, 256 x 256, 240 mm FOV, TR = 3500, TE = 96 ms) were positioned on the whole brain covering the whole temporal lobes. We performed a magnetic susceptibility sensitive echo planar T2-weighted gradient echo MR sequence which has the deepest signal decrease when the gadolinium bolus arrives¹¹ as follows: eighteen echo planar imaging T2-weighted gradient echo axial slices (5 mm thickness, 0.5 mm gap, 96 x 64 matrix, 240 mm FOV; TR = 2340, TE = 38 ms; flip angle: 90°, single shot, bandwidth = 62.50 MHz; 20 phases, interleaved, minimum delay). There were no macro visible motion artefacts because of a Velcro band keeping the patient's head inside the head coil. The injection protocol was of eighteen slices per volume with gadolinium injection begun three seconds after starting the image acquisition. Twenty milliliters of Gd-DTPA (0.2 mmol/kg) were manually injected into a left antecubital vein during three seconds (6 ml/s flow), immediately followed by a saline flush (identical quantity and flow)¹⁰.

The whole brain was imaged in 47 seconds every 2.34 seconds (20 volumes). The perfusion images were processed with a home made software developed in Delphi® (*Inprise*, Scotts Valley, CA) using Microsoft Windows 2000® (*DP-Tools*, <http://www.neuronet-software.org>). In brief, the first volume was used for display purposes. Other volumes were interpolated with a 3 x 3 matrix. To implement indicators dilution theory, MRI signal intensity was converted to gadolinium concentration using the following equation: $C_m(t) = -K \cdot \ln[S(t)/S_0]$ ^{5,9} where $C_m(t)$ is the Gd-DTPA concentration versus time, K is a constant dependent on the magnetic field, contrast medium, TE and MR sequence (here gradient echo, simplified constant¹⁰), $S(t)$ is the MR signal intensity versus time, and S_0 is the basal MR signal before the gadolinium arrival and after a steady state magnetization was achieved. Three images were averaged to compute S_0 (2nd, 3rd et 4th volumes). Perfusion parameters were then calculated voxel by voxel. The time to peak (TTP) was the time of the maximum gadolinium concentration $C_m(t)$ in the tissue; it can be negative if the arterial peak is set as the temporal reference. The decrease ratio (DR) was calculated using: $DR = S_{TTP}/S_0$ where S_{TTP} is the signal value when $t = TTP$, and S_0 is the basal signal reference. To obtain

quantitative measurements, we computed the arterial input function with a small nine voxels (32 mm³) region-of-interest (ROI) positioned on the left middle cerebral artery. Small AIF ROI size was intended to avoid partial volume effect in further AIF computations. The AIF was located on the left MCA because we routinely used this particular AIF location to compare MR perfusion results between different subjects of our database.

A gamma variate function was used to eliminate recirculation using a least square algorithm such as: $G(t; G_{peak}, a, \tau) = G_{peak} (t/\tau)^a e^{-(a(t/\tau)+a)^1}$, where G_{peak} is the maximum of the model curve, τ is the time of this maximum, a is an adjustment parameter and t is time.

Using the images (AIF voxels superimposed on the selected artery, AIF(t) time curve and its gamma fit), the user checked and corrected the AIF location. When the AIF peak was the highest and the sharpest one, other parameters were calculated in a voxel by voxel fashion (CBV, CBF) with these equations^{7,10}: $CBV = (\kappa/\rho) \cdot \int C_m(t)dt / \int AIF(t)dt$ where $\kappa = (1-HCT_{LV})/(1-HCT_{SV})$ which corrects for the hematocrit (HCT) in large blood vessels ($HCT_{LV} = 0.45$) is superior to small vessels ($HCT_{SV} = 0.25$), and ρ is the brain parenchyma density (1.04 g/ml)¹⁰. In one slice, mean and standard deviation CBV values were calculated; each value out of ± 3 DS range from the mean value was set to 0 and values above 100% were set to 100.

$CBF = CBV \times C_{max} / \int C(t)dt$ with $C(t) = C_m(t) \otimes^{-1} AIF(t)$ where $C(t)$ is the residual tissue function of gadolinium concentration in the brain parenchyma when the arterial bolus is a dirach (delta function), C_{max} is the maximum of this curve, $\otimes^{-1}$ is the deconvolution operation with Fourier transform: $C(t) = TF^{-1} \{TF[C_m(t)]/TF[AIF(t)]\}$. AIF(t) and $C_m(t)$ FFT sampling (*Optivec*, Dr Martin Sander) were interpolated by 2 (with zero filling of the last values to obtain a multiple of 2) then filtered with low pass $< 3 >$ interpolating filter:

$$y_n = x_n + 1/3 \cdot (x_{n+1} - x_n).$$

Twelve mirror ROIs of 49 voxels (172 mm³) were placed on both internal capsulae (4 ROIs), thalami (2 ROIs), centra semi-ovale (2 ROIs), central sulcus (2 ROIs) and nidus area (2 ROIs).

Figure 3 MR Perfusion Imaging in the nidal area (1) at the level of the central semiovale (2) and at the level of the central sulci (3). From left to right, T2-weighted (A), TTP (B), CBV (C) and CBF (D) parametric perfusion images. The color scale shows high values in red, mean values in green and low values in blue. Note the high CBV and CBF values in the nidal zone (white arrow). Note increased perfusion in the left corona radiata (yellow arrow), and the bilaterally increased TTP values remote from the nidus in the white matter (white arrowhead). Truncation of the images in the right posterior region is due to artefact from the shunt valve.

Results and Discussion

Our results are summarized in table 1. Capillary angioectasia involved the thalami and showed surrounding MR signal abnormalities (figure 1). There were also bilateral MR perfusion abnormalities (figure 3). Brain perfusion was asymmetrical: the left hemisphere had higher CBF values compared to the right. The intra-nidal areas showed hyperperfusion with slightly higher values in the left hemisphere. Early TTP was seen surrounding the nidus and in the left internal capsule when compared to the AIF reference. The left internal capsule showed high perfusion values with increased

CBF and CBV when compared to the right. The centra semi-ovale also showed abnormal but symmetrical areas of increased blood flow. Significantly delayed TTP values were found in the white matter near the right central sulcus compared to the left one, highlighting the hyperperfusion of the left hemisphere.

Capillary angioectasia (CA) complicating brain AVMs² is thought to be a secondary phenomenon induced by the AVMs haemodynamic stresses on the brain with ischemic triggers or by haemorrhage with clot resorption. It appears on angiography similar to proliferative angiopathy (PA), which is a primary disease: PA is thought to be an uncommon arteriove-

nous shunt with an extensive capillary network occurring in young adults mostly on the cortex. The natural history of PA is not well known, but it is often associated with progressive occlusion of proximal cerebral arteries. Angiogenesis and diffuse transdural supply are dominant features. CA occurs as a secondary angioarchitectural change during the history of pre-existing brain AVM. CA consists of both angiogenesis and angio-ectasias, where angioectasia seems dominant. In our patient, the angiogenesis may have affected the normal regulation capabilities of the adjacent normal brain parenchyma, with venous hypertension and asymmetric tissue perfusion being part of the suggested mechanisms for the neurological sequelae in patients with VGAM². The negative TTP values found around the left side of the nidus may suggest a physiological haemodynamic adaptation of the local vascular network in response to a chronic brain stress phenomenon. Our patient had progressive atrophy of the right lower limbs and paresis and clonus on the right side. Conventional MRI findings (multiple foci of flow void in the thalami and a moderately enlarged vein of Galen and falcine sinus) failed to show parenchymal abnormalities that correlated with the motor sequela of

the disease, but the asymmetrical abnormal hyperperfusion pattern (normal expected values range from 6 to 10% for CBV, and from 40 to 80 ml/min/100 g for CBF in the grey matter, from 2 to 6% for CBV and from 20 to 40 ml/min/100 g for CBF in the white matter) surrounding the left thalamic nidus and the posterior limb of the left internal capsule might be anatomically correlated to the neurological deficits of this patient. Internal capsule vasculature is *stricto sensu* anatomically independent of VGAM vasculature patterns. Perfusion abnormalities found in these areas may help to differentiate between true Galen vein malformations and aneurysmal dilatation of the Galen Vein secondary to thalamic or diencephalic AVMs. Chronic haemodynamic disturbances may result in overwhelmed regulation capabilities in these particular areas, and progressive neurological deficit may have resulted from chronic or acute venous ischemic onsets (no evidence in this patient). The fact that the angioectasia could be seen on angio and MRI does not make it the cause of the phenomenon demonstrated; it can be part of a group of changes responsible for the PWI abnormalities as an indicator of a local response to chronic venous ischemia similar to that leading to diencephalic

Table 1 ROI locations in the three images of figure 3. Measurements estimated with TTP in seconds, DR and CBV in %, CBF in ml/min/100g. Negative TTP values in the left thalamus and posterior internal capsule reflect earlier bolus peaks compared to the arterial reference peak (AIF)

Image	ROI	Location	TTP	DR	CBV	CBF
1	1	Right Anterior Internal Capsule	0.33	9.77	10.59	61.15
	2	Left Anterior Internal Capsule	0.10	11.12	11.39	72.82
	3	Right Thalamus	-0.10	23.92	39.63	135.02
	4	Left Thalamus	-1.19	33.02	40.57	299.87
	5	Right Posterior Internal Capsule	0.00	12.38	11.91	85.21
	6	Left Posterior Internal Capsule	-1.43	34.44	42.59	313.59
	7	Right Nidus Area	0.00	58.73	64.15	491.52
	8	Left Nidus Area	0.00	62.59	74.15	568.39
2	9	Right Centrum Semiovale	0.91	8.19	8.98	46.51
	10	Left Centrum Semiovale	1.82	8.85	9.40	44.47
3	11	White Matter, Right Central Sulcus	14.33	7.17	11.12	42.01
	12	White Matter, Left Central Sulcus	9.03	7.71	11.72	44.27

cephalic calcifications in children of the same age with VGAM. The natural incompetence of such capillaries may also induce neighbouring dysbalances in the haemodynamics. Areas with earliest TTP, increased CBF and CBV values around the nidus coexisted with relatively less perfused zones also showing later TTP (see table 1). It is difficult to interpret these abnormal time values because of the relatively poor time resolution used (repetition time of 2.3 s) in such high flow diseases. In that case, DR and CBV and CBF values were increased inside the nidus probably because of the partial volume effect due to the presence of microcapillaries intermingled with brain parenchyma^{2,3}, but surrounding or remote from the nidus they may suggest attempts at haemodynamic regulation adaptations to preserve regular brain

functions¹³. Unfortunately, our timely restricted vision of PA is unable to describe all the processes implied in this brain hemodynamic regulation which might quickly change from one state to another.

Conclusions

We have documented altered brain MR perfusion parameters in a patient with secondary capillary proliferation in a VGAM. The involved anatomical areas matched the clinical manifestations. The haemodynamically abnormal regions were normal on MRI. Thus, it is possible that perfusion MRI may play a role in classifying and evaluating patients with VGAM when clinical deficits are not explained or demonstrated by other imaging techniques.

References

- 1 Fisel CR, Ackerman JL et Al: MR contrast due to microscopically heterogeneous magnetic susceptibility: numerical simulations and applications to cerebral physiology. *Magn Res Med* 17: 336-347, 1991.
- 2 Lasjaunias P, Berenstein L, ter Brugge K.G: *Surgical Neuroangiography*. Springer Verlag, Heidelberg Berlin, vol 1: 14-22, 2002.
- 3 Lasjaunias P: *Vascular Diseases in Neonates, Infants and Children: Interventional Neuroradiology Management*. Springer-Verlag, New York 1996.
- 4 Kader A, Young WL: The effects of intracranial arteriovenous malformations on cerebral haemodynamics. *Neurosurg Clin N Am* 7 (4): 767-781, 1996.
- 5 Meier P, Zierler LL: On the theory of the indicator-dilution method for measurement of blood flow and volume. *J of Applied Physiology* 6: 731-744, 1954.
- 6 Meyer B, Schaller C et Al: Physiological steal around AVMs of the brain is not equivalent to cortical ischemia. *Neurol Res* 20 (suppl 1): S13-17, 1988.
- 7 Ostergaard L, Weisskoff RM et Al: High resolution measurement of cerebral blood flow using intravascular bolus passages. Part I: Mathematical approach and statistical analysis. *Magn Res Med* 36(5): 715-725, 1996.
- 8 Raybaud CA, Strother CM, Hald JK: Aneurysms of Vein of Galen: embryonic considerations anatomical structures relating to the pathogenesis of the malformation. *Neuroradiology* 31: 109-128, 1985.
- 9 Rosen BR, Belliveau JW et Al: Contrast agent and cerebral haemodynamics. *Magn Res Med* 19: 285-292, 1991.
- 10 Smith AM, Grandin CB et Al: Whole brain quantitative CBF, CBV, and MTT measurements using MRI bolus tracking: implementation and application to data acquired from hyperacute stroke patients. *J Magn Reson Imaging* 12 (3): 400-410, 2000.
- 11 Villringer A, Rosen BR et Al: Dynamic imaging with lanthanide chelates in normal brain: contrast due to magnetic susceptibility effect. *Magn Res Med* 6: 164-174, 1988.
- 12 Willinsky R, ter Brugge K et Al: Venous congestion: an MR finding in dural arteriovenous malformations with cortical venous drainage. *Am J Neuroradiol* 15 (8): 1501-1507, 1994.
- 13 Young WL, Pile-Spellman J et Al: Evidence for adaptive autoregulatory displacement in hypotensive cortical territories adjacent to arteriovenous malformations. Columbia University AVM Study Project. *Neurosurgery* 34(4): 601-610, discussion 610-611, 1994.

Denis Ducreux, M.D.
Department of Neuroradiology
C.H.U. de Bicêtre, Paris XI University
78 rue du Général Leclerc,
94270 Le Kremlin-Bicêtre, France
E-mail: denis.ducreux@bct.ap-hop-paris.fr