Brain and Spine AVMs, Vein of Galen Malformation Treatments and Embryological Considerations

P. L. LASJAUNIAS

Neuroradiologie vasculaire diagnostique et thérapeutique, Hôpital de Bicêtre; Le Kremlin Bicêtre; France

On the Congenital Nature of Brain AVMs

The concept of cerebral arteriovenous malformation has significantly evolved the last 10 years.

As an heritage for the anatomo-clinical conditions, diagnostic neuroradiology has developed high quality non invasive imaging and thus brought AVM from clinically eloquent diseases to that of potentially incidentally discovered ones. In addition the convergence of patient's flow to few center has increased the exposure to brain AVM management. Both early diagnosis, large population profiles, natural history and partial or radical treatment could be observed and followed up. The distance taken to the technical challenge related to the elimination of the brain AVM has finally opened the discussion on their congenital nature.

"Malformation" means constitution of the morphology out of the range of the normal variation (anomaly). In addition to this "malformed shape" (abnormality) the word introduces the idea that it is detectable by vision, or visible.

The term "congenital" introduces the complementary idea that the process occurs "during the in utero phase" of the development.

Congenital malformation therefore expresses a detectable lesion that appears in utero. Such postulates imply that the lesion being at the latest present at birth can be detected before, and that the so-called natural history starts at birth. All implications that turned to be erroneous.

The experience gained over the last 20 years has shown that in fact 1% of the brain AVM (cerebral sub-pial) and 40 to 50% of the vein of Galen aneurysmal malformations (VGAM) and of the dural sinus malformation (DSM) are diagnosed in utero. Obviously not all the AVM diagnosed post nally have benefited of pre-natal ultrasound, however these numbers point to the rarity of the in utero diagnosis of intracranial arteriovenous shunts (AVS).

When one looks to large single center series the amount of clinically eloquent AVMs in neonates are rare. In addition the lesion that are diagnosed in neonates or infants are significantly different (angioarchitecturally) from those of adults: single hole arteriovenous fistulas and not nidus arranged. These are in 40% multifocal and in 30% suggestive of hereditary haemorrhagic telangiectasia (HHT or Rendu Osler Weber). Actually the intra cranial, intra dural AVF in children are a specific phenotype of that age group. These features are found supra and infratentorially or at the spinal cord level; nidus AVMs aspect becomes the main architecture after 6 years and is current in adults.

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Scheme:CAVM embryological aspects

CAVM

Clonal mutation is likely to produce "Clonal" phenotypic expression:
 Specificity of the timing (window of exposure) and aspecific trigger; a mutation involves a clone of cells;
 specificity of the substrate and selective recognition by the trigger; a phenotype of functional phenotype is shared by a group of cells
 at a certain moment creating an identity; thus a recognizable target group

CAVM Development

Several additional facts are in favor of late appearance of AVM. The specific vulnerability of the brain tissue in infants point to the rarity of associated regional brain damage in adults patients with brain AVM. Conversely brain AVMs present during infancy produce rapidly focal melting brain syndrome and if the drainage involves more of the midline intracranial venous structure, bilateral melting brain syndrome. These early active brain AVM (at the post-natal period) soon interfere with the maturation processes of the hydrovenous system at the skull base and the superior sagittal sinus and actually illustrate the dominant role played by macrocrania as a revealing symptom at that age. These post-natal maturation events do not seem to be disturbed in the adult diagnosed brain AVM patients. In older children and adults, cerebral function is often preserved in the immediate vicinity of the nidus, suggesting the poor interference with the maturing brain, or the absence of AVM when function takes place.

Since the large lesion do not result from the growth and the small ones, one can reasonably postulate that shared cellular malformation

(within a clone or closely related cells) will be fired and revealed during one triggering phase in a given tissue or organ. In cerebro-facial syndromes (CAMS), an early stage abnormal development involve various tissue environment which confer more or less susceptibility, therefore although lesions are embryologically related, they will reveal at different ages.

Finally it has to be stressed that brain AVM like all arteriovenous shunts are diseases of the venous side of the vasculature and not of the

CAVM: Vascular vulnerability and phenotypic expression

CAVM: metamereric syndromes

arterial one. Most of the biological knowledge acquired from aortic or coronary vessels, fails to provide sufficient biological insight to understand this group of diseases. Such approach to AVM should encourage specialists to leave the mechanistic discussions on AVMs as they preserve erroneous concepts, promote heterogeneous collection of diseases, and thus hamper the development of true therapeutic innovation in that field.

It is therefore necessary to change the concept of "congenital malformation" from a detectable morphological alteration to an intracellular, eventually clonal malformation, quiescent at birth, revealed (or recognized) by various (unknown) exogenic or endogenic triggers. The earlier, the causative trigger, the larger the population of cells involved, the higher the chances for large and multi-focal AVMs and AVFs. The later the higher the chances to face a focal and small size AVM.

Spinal Cord AVMs Endovascular Treatment

Spinal cord arteriovenous shunts (SCAVSs) are currently classified according to their mor-

phology. Certain shunts are however beyond the predetermined categories usually described and cannot be fully integrated into them. These classifications were reappraised according to recent anatomical, biological and genetical advances.

We have reviewed the clinical and radiological files of 200 consecutive SCAVSs seen in Bicêtre.

They were examined according to their number (single or multiple), their primary architecture (nidus or fistula), their possible links with associated metameric lesions. All SCAVSs were either AVMs or fistulas, the latter being either micro or macro lesions. All SCAVSs corresponded to 3 categories: genetic hereditary (macrofistulas and HHT1), genetic non hereditary (all of them being multiple with metameric or myelomeric ties), and single lesions (that could represent an incomplete spectrum of one of the previous groups).

81% of SCAVSs of our series were single. 19% were multiple: among these 59% were having a metameric disposition (SAMS). (Cobb, Klippel Trenaunay and Parkes Weber syndromes), all with associated cord lesions.

19% of SCAVSs were fistulas : 23% of them were macrofistulas, of whom 83% were related to HHT (Rendu-Osler-Weber). Recognition of factors originally responsible for the shunt (genetic hereditary, genetic non hereditary) allows a different classification of SCAVSs.

A population of 155 patients seen between 1981 and 1999 were retrospectively reviewed for the purpose of therapeutic decisions.

- 25% consulted our group but were not referred for further management.
- 14% were surgically treated as they were felt to be poor candidates for embolization.
- 16% were considered non treatable by either surgery or embolization; follow up was proposed but only 8 of them were appropriately followed and are stable since then.
- 69 patients (45%) (20 children and 49 adults) were submitted to endovascular approach under general anaesthesia without provocative tests, mainly with acrylic glue (in 98,5%).

The mean number of diagnostic and therapeutic sessions was 3.5 per patient, and the mean number of pure therapeutic sessions was 1,5 per patient. Follow up ranged between 4 years and 18 years (mean 7,5 years). In 16% of patients anatomical exclusion of SCAVSs was obtained. Embolization reduced more than 50% of the SCAVS in 86% of cases. No recanalization was noted on follow up angiograms. Good clinical outcomes were obtained in 83% of patients : 15% of them are asymptomatic, 43% are improved and 25% are stable. In 4% of patients embolization failed to stabilise the disease. Transient deficits were seen after embolization in 14% of cases; per-

manent severe complications occurred in 4% of patients (Karnovski score below or equal to 70); mild worsening was seen in 9% (Karnovski score 80). No bleed or rebleed was seen after endovascular treatment was felt completed. Careful analysis of the SCAVM populations is mandatory before comparing therapeutic offers and follow up results.

Clinical result is important to assess the value of morphological end points. Embolization with acrylic glue proves to be a therapeutic option that favourably compares to surgery or embolization with other agents (particles, coils or balloons). It offers long term stable clinical results.

Objectives and Methods of Treatment in Vein of Galen Aneurysmal Malformation (VGAM)

Our primary therapeutic objective is to preserve a normal development without neurological deficit. To achieve this normal cerebral development does not require, in all cases or at all times, a complete morphological disappearance of the AV shunt or even a rapid shrinkage of the ectasia. To reach these clinical objectives, since 1981, we have chosen *transarterial embolization* using the femoral approach with glue (NBCA) as the embolic agent.

In Neonates (140 cases referred including antenatal)

The idea that a neonate in severe multiorgan failure would benefit from emergent VGAM has never been demonstrated; on the opposite

VGAM

NATURAL HISTORY OF VEIN OF GALEN ANEURYSMAL MALFORMATIONS

Bicêtre Neonatal Evaluation Score

VGAM

Points	Cardiac function	Cerebral function	Respiratory function	Hepatic function	Renal function
5	Normal	Normal	Normal	-	-
4	Overload, no med tt.	Subclinical isolated EEG Abn's	Tachypnea, finishes bottle	-	-
3	Failure - stable with med tt.	Non-convulsive intermittent neurologic signs	Tachypnea, does not finish bottle	No hepatomegaly, normal function	Normal
2	Failure - not stable with med Tt.	Isolated convulsion	Assisted ventilation, normal saturation FIO ₂ < 25%	Hepatomegaly, normal function	Transient anuria
1	Ventilation necessary	Seizures	Assisted ventilation, normal saturation FIO ₂ > 25%	Moderate or transient hepatic insufficiency	Unstable diuresis with treatment
0	Resistant to med Tt.	Permanent neurological signs	Assisted ventilation, desaturation	Abn coagulation, elevated enzymes	Anuria

Maximal score = 5 (cardiac) + 5 (cerebral) + 5 (respiratory) + 3 (hepatic) + 3 (renal) = 21

VGAM

there is evidence that in these neonates, following properly performed emergent embolization, showed disastrous neurological outcome even despite some apparently normal pretherapeutic brain imaging (ultrasound or CT). We are very aware of the difficulty of making the appropriate decisions and this actually represents the basis and purpose of our neonatal score. Evidence of severe cerebral damage (25/140) or severe multiorgan failure (score < 8, 17/140), in whom embolization would only be a technical challenge without hope of acceptable

clinical benefit, are beyond therapeutic possibilities according to the goals pursued. Such decision must be based on proper clinical assessment and highly specialized pediatric intensive care management.

Such decision represented 17% of our referral in VGAM, but 30% of the neonates referred. Failure to observe a response to the ICU management (or stagnation) will lead to early embolisation at neonatal age (24%). The end point of partial embolisation is usually the reduction of 1/3 of the shunt in order to obtain

VGAM Material
1981-2002

	Age at diagnosis	Age at 1 st consultation	Lost of follow up	Patients embolised elsewhere
Fetus	93	18	7	
Neonates	119	122		5
Infants	82	125	6	8
Children	23	52	4	4
Total	317	317	18	17

VGAM
Therapeutic Decision
1981-2002

Proposed treatment

	Embolisation	Abstention	Total
Neonates	95	45	140
Infants	109	16	125
Children	46	6	52
Total	250	67	317

VGAM
Therapeutic results
1981-2002

Neurological outcome

	BOS 5	BOS 4	BOS 3	BOS 2	BOS 1	BOS 0	Total
neonates	1	1	2	6	1	12*	23 *
Infants	74	28	10	16	14	11	153 **
children	9	15	3	8	5	-	40
Total	84	44	15	30	20	23*	216

*1 technical failure, 3 A° without E. = 4 deaths

** 2 A° without = BOS 1 and 2

5 spontaneous occlusions = BOS 2 / 4 / 5 / 5 / 5

a significant change. Lack of response to drugs must lead to careful search for an associated cardiac malformation. We always try to wait for the 5th month to perform the first diagnostic and therapeutic angiography.

In Infants (125 cases referred) and Children (52 cases referred)

Our concern at that age is to anticipate the natural history to avoid ventricular shunting. Premature attempts to exclude an asymptomatic

VGAM
Therapeutic results
1981-2002

Clinical results in the embolised group

	Neonates	Infants	Child.	Total
Neurol. normal BOS 3,4,5	<u>36,4%</u> 4/11	<u>78,9%</u> 112/142	<u>67,5%</u> 27/40	<u>74%</u> 143/193
Moderate retard. BOS 2	<u>54,5%</u> 6/11	<u>11,3%</u> 16/142	<u>20%</u> 8/40	<u>15,6%</u> 30/193
Severe retard. BOS 1	<u>9,1%</u> 1/11	<u>9,8%</u> 14/142	<u>12,5%</u> 5/40	<u>10,4%</u> 20/193
Death despite or because E°	<u>52%</u> 12/23	<u>7,2%</u> 11/153	<u>0%</u> 0/40	<u>10,8%</u> 23/216

BOS: Bicetre Outcome Score

matic lesion or taking significant technical risks to exclude in one session a VGAM that presents no immediate risks and can be eradicated in 2 or 3 sessions, should not be promoted. Conversely, to decide not to treat on the assumption that an asymptomatic lesion is a well tolerated lesion is certainly dangerous. At that age it is recommended to rely on the clinical parameters, MRI and pediatric scores. The dysmaturation of the jugular bulb are present in about a third of the untreated infants. It will reroute the flow of a given VGAM into pial veins necessitating the complete exclusion, as a formal goal, in order to eliminate the risk of haemorrhage. Prognostic factors and anticipation is dependent on the venous remodeling and should be carefully monitored.

Results: In the embolised group of cases (216 cases) we observed 10% mortality because or despite embolization. In the surviving group (193 cases): 2% permanent neurological deficits from erratic emboli or haemorrhage; 2% transient deficits and 10% non neurological incidents. At present half of the patients have at least 90% of their lesion excluded, and 40% of the remaining children between 50-90% exclusion. 74% of children are neurologically nor-

mal, 15,6% have a mild deficit or a moderate delay, 10,4% a significant delay or deficit. Many of these delays were fixed when the children were referred.

At the presented time patient selection still remain key in the management of these lesions. Clinical assessment and results are of paramount importance to compare managements. Loyal information to the parents is indispensable to obtain full understanding and support.

References

- 1 A Berenstein, P Lasjaunias, K terBrugge: Surgical Neuroangiography. Vol 2, 2nd Edition Springer Verlag 2003.
- 2 P Lasjaunias, K terBrugge, A Berenstein: Surgical Neuroangiography. Vol 3, 2nd Edition Springer Verlag, Heidelberg 2004.

Pierre L. Lasjaunias, M.D. PhD
Hôpital de Bicêtre
Neuroradiologie vasculaire
diagnostique et thérapeutique
78 rue du Général Leclerc
94275 Le Kremlin Bicêtre Cedex, France
mailto:pierre.lasjaunias@bct.ap-hop-paris.fr
web site: neuroradio.ap-hop-paris.fr