Congress report

4th World AVM Congress 2018

Montreal, October 14-16

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welcome

From 14th-16th October 2018 the 4th edition of the AVM World Congress was held. After Edinburgh, Nancy, and San Francisco, Montreal welcomed this major event. The aim of this congress is to involve the actors responsible for the daily treatment of AVM and to share opinions, data and innovations in this area. More than 400 people from 47 different countries participated in this event.

During the welcoming talk, Jean Raymond discussed this disease which remains for him a poorly understood pathology. He talked about the passion about this pathology, the importance of the knowledge of the anatomy, the science and the technical aspects mandatory to progress toward a better management of these patients. He finished his talk with a short video showing a consultation, highlighting the difficulties in the management of these patients in the context of the post-ARUBA period, and the lack of evidence of the benefits of intervention especially in unruptured AVMs.

To embrace the pedagogic purposes of the congress, attendees can attend "breakfast anatomy refresher courses" on spinal cord AVMs and on posterior fossa AVMs with great and experienced animators as Dr Spetzler, Dr Rodesch, Dr Lawton and Dr Darsaut.

During the congress, participants can also attend case discussions in two sessions of "Dodi-morbidity-Dodi-Mortality rounds" with complications of the AVM treatments, technical, and strategy difficulties in difficult cases. Discussions were led by Dr Januel and Dr Boccardi.

Here is the report day by day.

Dr AC Januel (PH Toulouse)

Pr JC Gentric (CCA Brest)

Day 1

Plenary Session: science and brain AVMs

Dr Radovanovic presented "the Genetics and Biology of Human BAVMs" and raised the point that they are likely caused by germ line or somatic mutations in specific genes disrupting signaling network involved in AVM specification and maintenances. He highlighted the discovery of an activating mutation in KRAS protooncogene in 63% of the patients in 72 patients harbouring an AVM. This work has been published in the NEJM in January 2018. Following this idea, pharmacological approaches could in the future be an option to treat AVMs. Dr Hua presented "Best Science of Brain AVMs 2016-2018" and started by citing the previous article. She focused her talk on the new genes and expanded signaling pathways, and described the other somatic variants reported recently in the literature for intracranial and extracranial AVMs. After, she presented a work by Winkler et al. (published in JNS in 2018) suggesting that reductions in brain pericytes are associated with AVM ruptures and micro-hemorrhages. She cited a work on the effects of thalidomide which can increase the pericytes coverage and potentially reduce the risk of haemorrhage in an AVM mouse model (Zu et al. Stroke 2018). She finished by the identification of potential therapeutic targets for systemic treatment of focal AVMs. Dr Berenstein illustrated the two previous talks by showing pediatric cases and the ability of an AVM to change over time and/or after endovascular treatment (EVT). He showed cases of proliferative angiogenesis of angioarchitectural major modification over years, and especially of evolution of fistulous lesions toward more nidal lesions.

Workshop: the venous route to AVMs

Venous route is the hot topic of the moment concerning EVT and AVMs. Two great speakers presented their experience during 30 minutes alternatively: Dr Mounayer & Dr Chapot. Dr Mounayer started with this first question concerning the venous route: should we go for venous route first or should we begin by an arterial reduction? He insisted on the fact that venous injection might lead to arterial occlusion and advocated for an injection on the arterial side to first reduce the nidus when possible. In any case, a microcatheter must be placed on the arterial side to complete or to stop the arterial flow if needed. Dr Chapot started talking with the paradox of AVM embolization: on one hand, occlusion of the vein of drainage induces haemorrhage, on the other hand, it is mandatory to occlude this vein to cure the AVM. So, occlusion of the vein requires occlusion of all shunts to avoid haemorrhage. But it can be hard to be sure, and the smaller the AVM is, the smaller the vein is, and the easier the retrograde injection can be, but the venous navigation can be harder. Dr Mounayer presented the concept of the porcelain vein: transvenous embolization does not induce acute haemorrhage because of the circumferential distribution of the embolic agent allowing to the vein to remain open until closure of most of the AVMs. On the other side, Dr Chapot advocated the retrograde pressure cooker technique using a plug of coils and NBCA prior to retrograde injection via a second microcatheter. The goal is the limitation of the length of venous occlusion. Dr Mounayer and Dr Chapot also presented the possibility to have a partial treatment of more complex nidus using one vein. They agreed on the need of an excellent comprehension of the nidus, and especially the venous part and the necessity to be able to isolate the main outflow vein and the primary veins. Dr Mounayer and Dr Chapot will be the PIs of a randomized trial on the venous route vs the arterial embolization (TATAM).

Then Dr Piotin presented the safety and the efficacy of the use of the venous route in his center in about 35 cases. He highlighted the possible navigation difficulties caused by angulation between sinus and cortical veins and reported 14% failed venous navigation. He also reported transient deterioration of clinical status in 6%, 9% of permanent deterioration, and a mortality of 9% all due to haemorrhages. Their total occlusion rate was 80%. He presented examples of how large venous ectasia can be trapped using the venous route.

Grand conference: "To see nor not to see the brain is the question!"

Dr Chokron from the Fondation Ophtalmologique of Rothschild, Paris, France presented this beautiful conference about vision. Vision is a cognitive function. It is a basis for cognitive, motor and social development, and is much more than visual acuity and contrast sensitivity. Vision is the basis for spatial navigation, spatial cognition and spatial orientation, the basis for reading, writing, calculating, for memory… vision is in fact a construction of our brain and we basically don't "see" the visual information our eyes receive. She showed examples of hidden images in larger images and insisted on the possibility to learn how to see a picture using an example from the painter Degas. Occipital AVM represents a pathological model of vision, a local cerebral dysfunction using the plasticity, the brain is able to reorganize cortical functions. And this pathological condition is true before and after embolization. A focal pathology as occipital AVM is able to move the function around the lesion and in the homologous area in the contra lateral hemisphere. She showed the possibility of visual restoration because we see with our brain and our brain is able to re-learn to see.

Day 2

Plenary session: advanced imaging in brain AVMs:

Dr Chandran opened the session and shared his experience of 4DCTA in AVMs. After a description of the technique, he presented the good sensitivity and specificity in the detection and the characterization of AVM and DAVF by citing a paper of Biswas et al. Neuroradiol J 2015. He presented his experience of using 4DCTA in cases of acute ruptured AVM to decide on EVT targeted on a risk factor if detected. He also talked about other potential applications as the follow up after treatment or the non-invasive screening tool for suspicion of vascular malformation on other non-dynamic exams. Dr Houdart gave the opinion of a "MR user" on MR sequences for AVM exploration, the importance of a large TOF, the interpretation difficulties of SWI sequences imaging. He highlighted the usefulness of the dynamic sequences (and the saturation of his PACS) which cannot replace a conventional angiography which remains mandatory in many situations as the exploration of lobars hematomas.

Dr Gentric presented his work on the reliability of the 4DDSA for AVM angioarchitectural study. We showed the feasibility of the use of 4DDSA in daily practice. We also demonstrated the reliability of 4DDSA especially on the arterial side to identify the potential risk factors of bleeding as prenidal aneurysms. The performance of 4DDSA on the venous side were not as good as on the arterial side, with especially the possibilities of veins false stenosis in case of flow competition. The 4DDSA related irradiation was responsible for 6% of the total dose of our angiographic exams.

Dr Blanc presented how to improve the safety and the efficacy during embolization using augmented images and registration even in cases of supraselective injections. The 2D vision, the partial vision of the AVM, the difficulties related to the vision near the cast, the absence of direct vision of the brain are some difficulties to face during embolization. He also highlighted that, because of flow competitions, we only have access to a partial visualization with supraselective injection. This image will not be representative of the whole LEA injection to come. He described the technical aspects of segmentation of the AVM using 3DRA and the possibility of fusion of the 3DRA and the MR. He also showed cases of AVM treatment using optimized 3D road maps using the arterial and also the venous route.

Dr Mendes Pereira closed the session by presenting some relevant articles of the place of non-invasive imaging in the detection of haemorrhage, in the detection of an AVM under a haemorrhage. He explained his strategy of using CTA first then MR and considering DSA after. He showed the ability of the MR to increase the detection of small haemorrhages. He also pays particular attention to the diagnostics of microavms and the facility to repeat the angiography in cases of unexplained and lobar hematoma especially in young patients.

Plenary Session: Spinal Cord AVMs

Dr Januel presented a few clinical situations for which it will be asked at the end of the sessions, the therapeutic options suggested among the panel. This, to introduce the different possible strategies and to emphasize our lack of evidence.

Dr Shigematsu and Dr Finitsis showed us literature is very poor talking about treatment of spinal cord AVMs. Few papers and few patients supported in a very inhomogeneous way. He emphazised the fact that series were old, technique has improved, since neuromonitoring and ICG video angiography, 3D fusion images and assisted use of endoscope. He raised the need to have a standard spinal AVM classification, to evaluate treatment, results and outcomes. He suggested a multi institutional prospective database.

Dr Houdart, reminded us of an old technique of embolization with particles. He shared his experience and beliefs with us: risk of bleeding and rebleeding is changed after partial or temporary embolization. He mentioned the work of his team published by Collin et al (J NeuroIntervent Surg, 2018;0:1-5), about their experience and results since 1990. He gave us tips and tricks for how he does it: particles are injected in free flow, selectively into the radiculo medullar artery, one by one, if possible with Embogold® because they are coloured and visible in the hub. In complex shunt and partial treatment, the rule is to re-embolize every two years. It is safe & efficient in many shunts; zero rebleeding, zero deterioration after particules embolization.

Dr Bernstein presented his team's work about the preventive effect of endovascular treatment for recurrent haemorrhage in patients with spinal cord AVMs (Niimi et al AJNR 36:1763-68 sep 2015). A retrospective study between 1980 & 2010 showed about 80 patients with haemorrhage presentations (55% SAH, and 45% hematomyelia). Among recurrent haemorrhage in 44% patients, 87.2% didn't have embolization and 2.4% had embolization. Haemorrhage is prone to recur within the first months in 31%. Related aneurysm is related to recurrent haemorrhage. The conclusion is endovascular treatment, even if partial, is effective to prevent haemorrhage instead of conservative management.

Dr Ling raised two questions: Should we completely obliterate spinal cord AVMs? The answer is: partial obliteration is not enough. Risk of rebleeding remains even if lower, and risk of clinical re-aggravation persists. She cited the Pooled analysis done by Gross and Du (Neurosurgery, 2013): after partial surgical treatment the annual risk of bleeding was 3%. In the paper of Krings's team (Stroke, 2014) rebleeding rate was 4.8% if not treated, 2.9% if partial treatment, and 0% if complete occlusion. Reasons for re-aggravation (25%) were new aneurysm formation, main drainage vein occlusion, and AVM regrowth.

Can we completely obliterate a SAVMs? Angioarchitecture under microscope is always more complicated than DSA images. An intra-operative triple angiography can help. Combination of ICG, Methylene Blue angiography, intra-op DSA to understand shunts assess complete resection. Experience in MEP and SEP monitoring are essential for neurological functional preservation. Her conclusion is that most spinal cord AVMs should be resected if at all possible; pre-operative embolization might be necessary.

Dr Rodesh emphasized the interest of a classification. Easy comprehension in order to recognize properly and objectively the disease, proper understanding and proper therapeutic orientation. He deplores "more classifications than lesions"… He raised questions and suggested to add to anatomical and architectural data introducing genetical data and metameric dispositions to better understand the natural history.

Dr Consoli shared the work of the Kremlin-Bicêtre team on spinal cord arterio-venous shunts in a pediatric population. This is a rare disease, difficult to detect (25% detected before 10 years). Haemorrhagic presentation is the most frequent; hematomyelia, mostly cervicothoracic, associated with syndrome in 50% (SAMS, HHT), and with scolisosis in 16.6%, multiple in 25%. After the first event, spontaneous improvement is frequent. There is no rush to treat; pre-treatment rebleeding occurs in late phase. Staged endovascular treatment is safe and feasible, but the goal is the cure whenever possible. Targeted partial treatment might be sufficient to improve or stabilize.

To end the session there was a round table discussion after all these literature considerations and previously presented cases, and… no real consensus.

It was then an honour to listen to Pr ROBERT SPETZLER 's lecture:

SPINAL CORD AVM'S: Lessons from a life time of surgical experience.

He highlighted his classification through case discussions and very nice schemas.

He first described Spinal arteriovenous fistula.

He then went on Spinal AVM. He explained how angioarchitecture and anatomical location of the shunt could explain natural history and clinical presentation.

He detailed on conus AVM, category he defined in 2002 (Spetzler and al J Neurosurg. 2002), for which he believes multimodal approach is the best option with encouraging results regarding ambulatory. He ended his lecture with observations and thoughts on management of Intramedullary AVMs.

Day 3

Plenary Session: Complications of AVM Treatments

Different techniques lead to different kind of complications, even if we are treating the same disease.

Dr Redekop, neurosurgeon, gave us keys to lead a high performing surgical team. He emphasized being a team member; he encouraged discussing cases with colleagues from different backgrounds to take advantage of their experience. "Your recommendations to patients must rely on your results honestly tracked and on your personal experience. You should present your results as well as the results of alternative approaches in your institution. Be humble and remember each procedure has a risk."

Dr Bracard, Interventional Neuroradiologist, listed the potential type of complications. He focused first on intra-operative complications which are mainly ischemic and haemorrhagic. Ischemia because of crioric embolism, proximal glue or onyx embolism (catheter rupture), reflux or transnidal passage. Haemorrhage because of an arterial or venous rupture. They can result from technical errors (dissection during catheterisation) or technical defect (catheter rupture or undetachable). He then commented on post-operative haemorrhage being the most frequent and serious complication, which can occur immediately or some time after the intervention. Whatever the access route or the embolic agent, the bleeding mostly comes from the venous side – possibly due to premature venous occlusion. He advised to be very thorough in the evaluation of the angioarchitecture of the AVM, to have glue at hand in case of vascular rupture, carefully and meticulously visualize the progression of the embolic agent (biplan++ fluoro 3D mapping), use intra-operative hypotension. He opened the discussion on the use of anticoagulation. His take home message was "carefully analyse your complications to try to understand and share them during morbimortality meetings. Learn from them".

Dr Zadeh, for radiation therapy complications, started with the article of Flickinger et al., (Int. J. Rad Oncolo Biol.Phy2000) about a model to predict post radiosurgery permanent deficit; location and 12Gy volume matters. The background for her retrospective analysis is based on T2 signal changes; which are frequent, delayed, a function of dose and volume; and presented variable associations with complications. From their series, they developed a prediction model of adverse radiation effects, based on vascular parameters and volume of T2 signal changes; about 125 AVMs with previous haemorrhage in 56.5%, and a median ttt volume of 2.21cc. T2 changes occurred in 49.3%, mostly at 12 months from onset/treatment. Complications occurred in 27%: transient in 16.5%, permanent in 10.6% (hemiparesis and visual field defect). A Target volume of more than 4 cm^3 without previous haemorrhage predicts higher risk of symptomatic T2 signal change. Location is a poor predictor. Vascular parameters such as dose/volume effects were not significant. High rates of fixed visual field deficits suggest the optic radiation is a critical radisosensitive structure (role of DT in GK planning?).

Dr Mast ended the session with legal and insurance aspects of living with an unruptured brain AVM, after ARUBA.

Plenary Session: Posterior Fossa AVMs

Dr Magro had the difficult task of working on a systematic review of Posterior fossa AVMs. She suggested that, despite posterior fossa AVMs being very rare, there is an abundance of literature with a lot of information and a great heterogeneity in reporting. It prevents a meta-analysis. She extracted some "crude" information: Posterior fossa AVMs comprise 13% of all AVM, 4% in brainstem and 9% cerebellar. Clinical presentation is mostly haemorrhagic (74%) with high risk of rebleeding; 23% mortalitys with low risk of seizures and highly associated with aneurysms (29%). She suggested agreeing on standardized reporting: SM grading and Radiosurgery based in AVM description, mRS at admission & at follow-up. The results should be stratified by grade, presentation, & treatment modality, using a multi-institutional database such as the TOBAS study.

Dr Krings discussed anatomical features and clinical presentation of posterior fossa AVMs, showing us cases. He started with a Posterior fossa pial AV fistulae. These kinds are mostly seen in neonates or young adults, often associated with HHT/RASA1 mutations, and often multiples. They are mostly symptomatic, because of Arterial steal (hypoxemia), leading sometimes to a melting brain. Haemorrhage is common. Ruptured or not they need to be treated. He then discussed cases of nidus type AVM: if ruptured, identify cause of haemorrhage (intranidal outpouchings, aneurysm, foci of contrast

stagnation, venous stenosis, etc) and treat. If unruptured but symptomatic because of venous rerouting or congestion, understand symptoms and venous anatomy to treat; if unruptured but asymptomatic, understand the AVM, and treat or watch.

Dr Steinberg focussed his presentation on brainstem AVMs, starting from the Standford surgical experience. Among 1312 treated AVMs, only 58 were located in the brainstem. Presentation is most often haemorrhage (92%) with a high morbidity/mortality rate. Majority are located in the midbrain, pial, and unilateral. They are small (82% ≤ 3cm, half ∠15 mm) with a deep venous drainage (80%). Surgery offers the best chance of cure (90%, alone or in combination).

Dr Radatz fixed the background for STRS (Stereotactic Radiosurgery): Obliteration rate is dose dependent, complications are dose and size dependent, location matters. Then he shared the results of the Sheffield experience of radiosurgery for AVMs in deep critical regions (Nagy et al Neurosurgery. 2012), about 160 brainstem lesions over 4350 AVMs since 1986: Size and location are major determinants of outcome. STRS is safe and effective even in non-microsurgical deep & eloquent places in AVMs smaller than 4cc; (obliteration rate 65% for medulla/pons location). Obliteration rate is low in the midbrain but as morbidity is mild and low, it allows repeated STRS to achieve effective results. Over 4cc brainstem lesions have poor obliteration and high complication rates, and should not be treated with single stage. Cerebellar lesions larger than 10cc need volume staging. He ended his presentation thinking toward the future; volume staged STRS will have an increasing role.

Dr Saatci shared the endovascular Ankara experience of over 20 years: 31 posterior fossa AVMs among 504 have been treated (6.2%), mostly ruptured (23), 55% cured by embolization alone. Mortality is 6.5% (bleeding) and post op morbidity 16.1%. For brainstem location, targeted embolization may be the choice followed by STRS. TV approach is considered when arterial access is not possible or deemed more risky.

Dr Lawton emphasized supra and infratentorial AVMs are different anatomically (smaller, deeper, less eloquent), in presentations (no seizure, more haemorrhage), with different tolerance to clot volume and different outcomes. These differences reduce the accuracy of the SM grading system. Lawton et al proposed a new grading scale: The Supplemented Spetzler-Martin grade (Supp-SM). It adds patient age, (1 if <20, 2 if between 20-40, 3 if >40) history of haemorrhage, (0 if ruptured, 1 if unruptured) and nidus type (0 if compact, 1 if diffuse) in addition to the classical SMS factors. Lawton & Young grading increases the accuracy of surgical risk prediction in general, and in the posterior fossa in particular, and provides a valuable tool for surgical selection.

Plenary Session: Clinical Trials

Dr Kim warned us about strengths and limitations of registries. She demonstrated how to detect bias: selection bias, information bias and especially from missing data - giving a very interesting example from a meta-analysis of haemorrhage predictor of untreated brain AVMs (Kim, Neurology 2014). If you want to learn more about the "prognostic modelling assumption" concept, read this article from J.Raymond, AJNR 2011). Her conclusion was: best remedy for bias is prevention.

Dr Parides assessed RCT as gold standard, providing the best evidence for evaluating therapeutic effectiveness and safety of treatments. But they are not always feasible because of ethical reasons (lack of equipoise), because of practical reasons (cost and rare disease), and because of clinician and patient resistance to randomisation. He showed us that even if there are no good alternatives to the RCT we can do it differently. Observational studies: prospective (cohort study), retrospective (case control study), registry-based, require adjustment for bias, in analysis or design (matching). But the keys are: study design must be tailored to the question with a rigorous protocol; reproductible, with pre-specified eligibility criteria, representative sample, & clear endpoint definitions.

Dr Raymond continued the discussion from the clinician point of view. He thinks observational studies can't replace RCT of their own practice. Instead he suggested making a bridge between clinical care and research: the clinical care research. For example where clinical care can offer the validated treatment, the care research can offer 50% chance of getting a new experimental treatment and 50% chance of getting standard treatment. He ended his presentation with these sentences to consider, "A true science of practice must be within the practice; research integrated to care means using science as a norm to guide clinical interventions in real time one patient at a time. Science should guide clinical interventions in a real time feedback to reality".

After the theory, practice: Dr Magro convinced us that pragmatic trials integrated to care are feasible for the treatment of brain AVMs. She presented TOBAS, launched by the Canadian team from Montreal CHUM. This study is composed of two independent randomizations: (1st) observation versus treatment, (2nd) embolization or not prior to surgery. And two registries: observation registry or stratified treatment registry (surgery, radiosurgery, embolization). 364 patients have so far been included (218 in France!). A few results: Observation registry includes mainly unruptured AVMs (half large, half small grade); treatment registry includes mainly small grade ruptured AVMs. The first Randomization is proposed in most of the cases for small grade unruptured AVMs. Those results are very encouraging. Don't hesitate to join the trial!

Dr Darsaut presented a multicentric randomized trial about the venous route to brain AVMs: TATAM. A way to safely introduce innovative treatment. The hypothesis is that transvenous embolization (+/- arterial embolization) leads to a higher rate of AVM angiographic occlusion than classical trans-arterial embolization alone. Failure of catheterization and incomplete embolization at the end of the final procedure are considered as failure to reach primary endpoint. Standard safety outcomes are adjudicated as secondary outcomes. TATAM will start soon; Montreal already has IRB approval!

Grand Conference: The future radiation therapy of brain AVMs - Recent advances and future perspective

Dr Shih gave us an interesting lecture about radiation therapy SRS. SRS is an effective AVM treatment but latency of years to obliteration make it secondary, or deserved for ineligible lesion to surgery or embolization. Recent advances in SRS have been made to improve efficacy, especially for high grade AVMs, and safety. Dose-staged SRS (hypofractionated: giving multiple moderate high doses of radiation in a few fractions), Volume staged SRS (dividing the nidus volume and SRS given in different sections per session separated by few months), Repeat SRS, Proton radiation can be considered for less normal brain exposure and toxicity (she cited the paper of Hattangadi et al, IJROBP 2014). And she ended her presentation with this new developing concept: non uniform hypofractionation or spatiotemporal SRS to increase the biological effect to AVM and decrease dose to brain; each fraction weighted to a unique subvolume with the same total physical dose.

Plenary session: the future

Two very different points of view presented by our peers… or a clash of titans!

Dr Lawton: Primacy of surgery. He emphasized his 20 years of experience managing surgery of brain AVMs; 49x more relative to ARUBA. He insisted despite the backlash of ARUBA, surgical indications and results remain strong for low grade AVMs and should be the primary first line AVM treatment. Is it time for a new RCT? BARBADOS Beyond Aruba, resection of unruptured Brain AVM

Dr Chapot demonstrated with wonderful cases how embolization can cure complex AVMs with combined arterial and venous approach; (transanastomostic, transnidal navigation, staged venous sessions, etc) and how embolization can solve difficult AVMs which may be unreachable surgically (too deep).

Dr Raymond closed this remarkable meeting passing the torch to Dr Berenstein who will bear the responsibility to organize the Fifth Edition of the World AVM Congress, that will be held in New York in October 2020. We want to thank Dr Raymond and the whole CHUM team for these three days of intense work, rich in teaching and sharing. You have allowed all of us, participants from all over the world from different backgrounds and specialities, to share lively discussions and debates that will improve our knowledge and daily practice.

‘L’expérience de chacun est le trésor de tous’

‘The experience of each becomes the wealth of all’’

Gérard De Nerval