THE ANGIOARCHITECTURE OF BRAIN ARTERIOVENOUS MALFORMATIONS AND ITS' ASSOCIATION WITH INTRACRANIAL HAEMORRHAGE: An analysis

By

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Dedication

To My beloved mother, My late father, sweet grand mother

My caring husband and My cute brothers

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Abbreviations

ACA	Anterior cerebral artery
BAVM	Brain arteriovenous malformation
CT	Computed Tomography
3D-CTA	3D Computed Tomography Angiography
DAVF	Dural arteriovenous fistula
FGF	Fibroblast growth factor
HUSM	Hospital Universiti Sains Malaysia
IADSA/DSA	Intra-arterial Digital Substraction Angiography
ICA	Internal carotid artery
ICD	International Statistical Classification of Diseases and Related Health problems
ICH	Intracranial haemorrhage
IVH	Intraventricular haemorrhage
MCA	Middle cerebral artery
MRI	Magnetic Resonance Imaging
SAH	Subarachnoid haemorrhage
SPSS	Statistical Package for Social Sciences
VEGF	Vascular endothelial growth factor
WHO	World Health Organization

Abstrak

Tajuk: Hubungan reka bentuk saluran darah dalam otak dan risiko pendarahan dalam otak: satu analisa

Pendahuluan dan objektif: Malformasi arteri-vena system saraf pusat (AVM) adalah sejenis malformasi salur darah di dalam otak yang terdiri daripada salur darah vena dan arteri yang berpintal, dan tidak mempunyai kapilari darah sebagai penghubung antara kedua-duanya. Golongan lelaki lebih terdedah kepada penyakit ini dan mereka menunjukkan gejala klinikal yang berbeza seperti sakit kepala, sawan, kecacatan saraf dan pendarahan otak. Pesakit yang mengalami pendarahan otak secara tiba-tiba mempunyai kadar morbiditi dan mortaliti yang signifikan. Oleh itu, kajian ini adalah bertujuan untuk mengenalpasti faktor yang berkaitan dengan pendarahan otak dan seterusnya membantu pakar perubatan untuk merawat pesakit dengan lebih baik. Kajian ini juga membolehkan kami menentukan hubungan di antara isipadu pendarahan AVM ditengkorak dengan faktor rekabentuk 'BAVM'. Hubunagn antara faktor-faktor ini dan risiko pendarahan otak adalah penting bagi meramalkan perkembangan 'BAVM'.

Kaedah: Kajian ini dijalankan secara retrospektif di mana pesakit yang melakukan pemeriksaan radiologi di jabatan di radiologi telah diambil dari tahun 2000. Sejumlah 58 pesakit telah dimasukkan di dalam kajian ini setelah tidak diambilkira fistula arteri dan vena dura dan hemangioma otak ('brain haemangioma'). Saiz nidus telah diukur berdasarkan pemeriksaan angiogram otak. Pengaliran keluar darah melalui saluran

vena, kemasukan bekalan darah melalui arteri, pembengkakan salur darah dan lokasi 'DAVM' telah dianalisa dengan lebih lanjut melalui pemeriksaan angiogram dan skan CT/MRI. Hubungan antara faktor reka bentuk saluran darah dan pendarahan otak telah dianalisa dengan menggunakan analisa multivaria. Objektif tentang hubungan antara faktor dan isipadu pendarahan juga telah ditentukan dengan model univaria.

Keputusan: Di HUSM, malformasi salur darah otak ('BAVM') didapati lebih ramai di kalangan lelaki muda dengan purata umur mereka adalah 26.67(SD±12.96). Saiz nidus yang kecil (p-value=0.000) dan kedudukan nidus yang dalam (p-value=0.000) telah dikesan sebagai faktor untuk meramal pendarahan otak. Pengaliran keluar darah melalui vena yang dalam pula hanya signifikan pada analisa univaria kerana saiz sampel yang kecil. 100% daripada pesakit yang mempunyai 'DAVM' dan mengalami pendarahan otak juga didapati mempunyai pembengkakan salur darah. Faktor-faktor reka bentuk saluran darah dalam otak dalam menentukan isipadu pendarahan otak didapati tidak signifikan dari segi statistik, tetapi dalam pemerhatian klinikal sebanyak dari faktor kedalaman nidus, 63% dari saiz nidus yang kecil, 66.7% dari pengaliran keluar darah vena yang dalam 70% dari pengaliran berkalan darah arteri yang dalam dan kehadiran kebengkakan salur darah didapati mempunyai pendarahan yang menyeluruh.

Kesimpulan: Kesimpulannya, faktor reka bentuk saluran darah dalam otak boleh meramalkan risiko pendarahan otak dan ini boleh membantu dalam perawatan pesakit

berisiko tinggi. Kami juga telah mendapati 'BAVM' yang kecil dan kedudukan yang dalam mempunyai pendarahan otak yang menyeluruh, di mana ianya memerlukan lebih perhatian daripada kumpulan doktor yang merawat kerana pendarahan yang menyeluruh menunjukkan kerosakan yang lebih teruk kepada otak.

Abstract

Title: The angioarchitecture of brain arteriovenous malformations and its' association with intracranial haemorrhage: an analysis

Introduction and objectives: Central nervous system arteriovenous malformation (AVM) is a vascular malformation of the brain and consists of a tangle of veins and arteries without an intervening capillary bed. It predominantly affects young male patients and presents with different clinical manifestations namely headache, seizures, neurological deficit and intracranial haemorrhage. The patients who present acutely with intracranial bleed have a significant morbidity and mortality. Thus, the aim is to study the angioarchitecture of BAVM and determine intracranial bleed.

This study also enabled us to look for the association between the volume of haematoma and the architecture of the brain arteriovenous malformation.

The correlation between the features and risk of intracranial bleed is invaluable in predicting the behaviour of BAVM.

Methodology: This was a cross sectional study where patients who attended the Department of Radiology were retrospectively collected from the year 2000. A total of 58 patients were included after excluding dural arteriovenous fistula and brain haemangiomas. The nidal size of the lesion and its maximum diameter were measured

on cerebral angiogram. Venous drainage, feeding arteries aneurysms and location were further evaluated on cerebral angiogram and CT scan/MRI.

The association between the angioarchitecture of BAVM and intracranial haemorrhage were analysed using multivariate analysis. The other objective to evaluate the association between angioarchitecture and volume of haematoma was determined using univariate model.

Results: In HUSM, BAVM was seen predominantly in a young male patient with a mean age of 26.67 (SD ±12.96). Small nidal size (p-value = 0.000), deep location (p-value = 0.000) was found to be predictors of intracranial bleed. And deep venous drainage was significant at a univariate level only due to a small sample size. All patients with brain arteriovenous malformation and coexisting intracranial aneurysms presented with intracranial bleed.

The angioarchitecture of BAVM determining the volume of haematoma was not found to be significant statistically, but on clinical interpretation diffuse bleed was seen in 69 % deeply located, 63 % small sized and 66.7 % deep draining vein, 70 % deep arterial feeders and presence of coexisting aneurysms.

Conclusion: The angioarchitecture of BAVM like nidal size, deep location and deep venous drainage can predict the risk of intracranial bleeding and can help in the management of high risk patients without any delay. Small sized and deep seated

lesions have a diffuse type of intracranial bleed which eventually need more attention to the managing team as diffuse haematoma indicates more insult to brain.

INTRODUCTION AND LITERATURE REVIEW

1.0 Introduction

Brain arteriovenous malformation (BAVM) is a congenital vascular malformation in the supratentorial and infratentorial compartments of the brain. The term arteriovenous malformation of the brain was described by H. Troupp in 1965 (Troupp, 1965). Subsequently, in 2001, the Joint Writing Group of the Technology Assessment Committee American Society of Interventional and Therapeutic Neuroradiology which helped to provide guidelines and uniformity in definitions preferred the term BAVM to cerebral AVM as it is more precise term than cerebral, which excludes more caudal structures, and imprecise terminology such as "true" AVM or "pial" AVM. Further, "cerebral" AVM is usually abbreviated as CAVM, which might lead to confusion with cavernous malformation (Joint writing group., 2001)

BAVM represents one of the most challenging neurovascular lesions in the field of endovascular interventional neuroradiology and is one of the causes of stroke in young patient. Whereby, stroke is defined as per WHO stroke registers "as rapidly developed clinical signs of focal (or global) disturbance of cerebral function lasting more than 24 hours (unless interrupted by surgery or death), with no apparent cause other than a vascular origin: it includes patients presenting with clinical signs and symptoms suggestive of subarachnoid haemorrhage, intracerebral haemorrhage or cerebral ischaemic necrosis. It does not include transient cerebral ischaemia or stroke events in cases of blood disease (e.g. leukemia, polycythaemia vera), brain tumour or brain metastases. Secondary stroke caused by trauma should also be excluded."

Stroke in young patients have a significant morbidity and mortality (Al Shahi et al.,2001) In this regard, the risk of death and permanent neurological deficits are present. This has prompted and kept the clinicians to be alert and investigate patients fully. In so doing, BAVM was found to be the culprit where stroke in young patients were concerned. BAVM is a complex lesion and a poorly understood one. Many studies (Brown *et al.*, 1988, Duong *et al.*, 1998) have been carried out to understand the lesion in terms of its angioarchitecture, anatomy and haemodynamics and also which factors can lead to cerebral haemorrhages and seizures. The angioarchitecture in this study implies the location of the lesion, size of the nidus, arterial feeders, aneurysm and venous drainage. These factors are thought to be responsible for intracranial bleed, and thus by studying these factors we will be able to predict the risk of haemorrhages and at the same time help clinicians to manage the patients and help in follow up.

In this 21st century many advances have taken place regarding the in vivo visualization, clinical behaviour and above all the characterization of these brain vascular lesions, namely BAVM. In addition to this, the technology to approach the lesion endovascularly has been explored in all its avenues. But despite all the efforts to understand and characterize the lesion, BAVM still remains an enigmatic lesion in many aspects. They maintain uniqueness in themselves.

This study was carried out in order to further understand the angioarchitecture, risk of haemorrhage, clinical manifestations and type of bleed of BAVM presenting to HUSM, a referral center for interventional neuroradiology cases. So far, no studies of the natural history, prevalence, clinical manifestations and the angioarchitecture of BAVM have been done in Malaysia. Therefore this study is highly beneficial as it will give preliminary

information about BAVM. Nowadays, BAVM have increasingly gained recognition as awareness about the lesion has spread in the continent. At the same time, with the availability and advent of new and improved imaging tools in this 21st century, it is easier to identify the patients with BAVM and characterize the lesion.

2.0 Literature Review

2.1 Definitions of Brain Arteriovenous Malformation

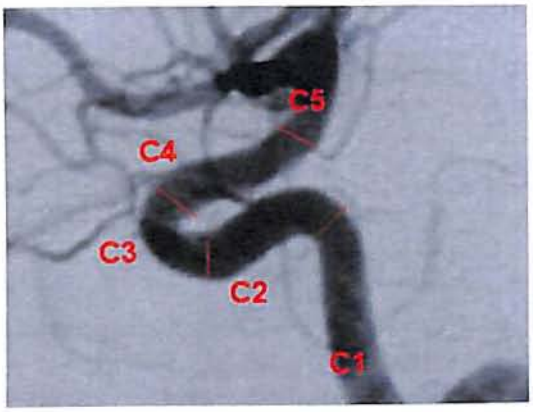
Brain arteriovenous malformation (AVM) is a congenital disorder of blood vessels within the brain characterized by tangles of veins and arteries without an intervening capillary bed. World Health Organization classifies brain arteriovenous malformation by ICD-10 Chapter XVII: Congenital malformations, deformations and chromosomal abnormalities in Block Q28.2 (revised version 2006) here ICD (International Statistical Classification of Diseases and Related Health Problems) is the international standard diagnostic classification for all general epidemiological and many health management purposes. It is used to classify diseases and other health problems recorded on many types of health and vital records including death certificates and hospital records. Unfortunately, this international classification of diseases codes are ambiguous, making it impossible to use such codes (C.Staph and J.P.Mohr, 2000)

Brain arteriovenous malformations are also described as pathobiologically, angioarchitecturally and haemodynamically complex system of arteriovenous shunts with specific neurovascular relationships, a variable and mostly unpredictable clinical presentation and a dynamic, for certain features age-dependent but only partially understood natural history, associated with an annual bleeding rate of 4 % and an annual rate of mortality of 1% and severe morbidity of 1.7% (Mansmann *et al.*, 2000, Valavanis *et al.*, 2004).

2.2 Vascular anatomy

2.2.1 Anterior Circulation

The internal carotid artery (ICA) supplies the anterior cerebral circulation and basilar arteries supply posterior circulation. ICA lies on the dorso lateral aspect of external carotid artery in the neck. It is commonly divided into the cervical, petrous, cavernous, supraclinoid and intracranial (Fig 1). The cervical segment (C1) of internal carotid artery has no branches. Petrous segment (C2) is intraoseous. Two small branches arise from the cavernous part (C3) of internal carotid artery namely the meningohypophyseal artery and inferolateral trunk. Once the internal carotid artery pierces the dura mater that is the supraclinoid portion (C4), it gives off ophthalmic artery (Fig 3) as the first branch. Posterior communicating and anterior choroidal arteries are the deep branches of the distal ICA(Grainger and Allison, 2001, Meschan, 1976).



Adapted from internet, Authors: Niriko Salamon MD, Daniel Valentino, Ph.d, Pattanasak Mongokolwat Ph.d, William Chou B.S, Georges Salamon M.D
The Department of Radiological Sciences at U.C.L.A. INSERM U6 (Neuroradiology) and Northwestern University

Figure 1: Classification of ICA branches into segments

2.2.1.1 Anterior Cerebral Artery

Anterior cerebral artery is divided into three anatomical segments: the horizontal/pre-communicating (A1), vertical/ post communicating segment (A2) and distal ACA /cortical branches of ACA (A3) (Fig 2)

The A1 segment gives rise to a number of perforating branches, the medial lenticulostriate and recurrent artery of Heubner. Recurrent artery of Heubner is the largest of the perforators and may arise from the A1 or A2 segment. A1 segment may be hypoplastic or aplastic. Other variations can include the fusion of A2 segment in the midline to give a single azygous anterior cerebral artery. The A2 segment gives off a frontopolar branch and then divides at the level of genu of corpus callosum into callosomarginal and pericallosal arteries (Fig 3) which is A3 segment. Cortical branches of the callosal marginal artery supply the medial frontal lobe where as cortical branches of pericallosal artery supply medial parietal lobe (Grainger and Allison, 2001)

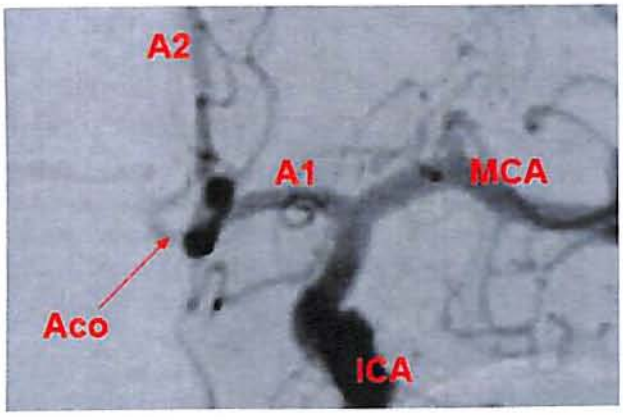


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Figure 2: Classification of ACA branches into segments