Craniofacial Vascular Malformations in Wyburn-Mason Syndrome

Chao-Bao Luo[1]*, Pierre Lasjaunias[2], Jo Bhattacharya[2]

[1]Department of Radiology, Taipei Veterans General Hospital and National Yang-Ming University School of Medicine, Taipei, Taiwan, R.O.C., and [2]Department of Diagnostic and Interventional Neuroradiology, Bicetre Hospital, Paris, France.

Background: Wyburn-Mason syndrome (WMS) is a rare syndrome associated with multiple arteriovenous malformations (AVMs) involving the orbit, brain and/or face. The purpose of this study was to analyze the imaging spectrums of craniofacial vascular malformations in 14 patients with WMS.

Methods: The medical records of 14 patients with the diagnosis of WMS who underwent neuroimaging studies (computed tomography [CT], 8; magnetic resonance imaging [MRI], 12; conventional angiography, 14) were reviewed, emphasizing the location, extension and type of facial, orbital and brain vascular malformations. Complete WMS was defined as vascular malformations involving all the 3 zones of the face, orbit and brain, while partial WMS was considered as vascular malformation distributed in 2 zones.

Results: The craniofacial vascular malformations were confined on the left side in 7 patients, 2 were found on the right side, while the remaining other 5 patients had midline brain AVMs involving both sides. All but 1 of these 14 patients had orbital and/or brain AVMs; facial vascular malformations were documented in 5 patients. The most common site of involvement was the optic nerve ($n=12$), followed by the retina ($n=10$), optic chiasma/hypothalamus ($n=9$), thalamus ($n=7$), basal ganglion ($n=5$), midbrain ($n=2$), occipital lobe ($n=1$), temporo-occipital lobe ($n=1$) and fronto-temporo-parieto-occipital lobe ($n=1$). The complete form of WMS was found in 2 patients and the partial form in 12. CT, MRI and conventional angiography have the capacity to demonstrate the extent of intracranial AVMs. However, MRI is superior to both CT and angiography for detecting the size, extent of AVMs and the effects of AVMs on adjacent brain. Conventional angiography is superior to both CT and MRI in determining the detailed angioarchitecture of AVMs.

Conclusion: WMS has a wide spectrum of multiple AVMs involving unilateral or bilateral craniofacial regions. The most common involved site is the orbit, followed by the brain. WMS should be considered in patients with ocular AVMs associated with brain AVMs. [*J Chin Med Assoc* 2006;69(12):575–580]

Key Words: arteriovenous abnormalities, brain, face, orbit

Introduction

The simultaneous occurrence of multiple vascular malformations involving the orbit, brain and face is extremely rare. A review of the literature indicates that the first case of retinal vascular malformation associated with ipsilateral cerebral arteriovenous malformation (AVM) was documented by Bonnet et al[1] in 1937, then it was further reviewed in detail by Wyburn-Mason in 1943.[2] Since then, the Wyburn-Mason syndrome (WMS) has been the nomenclature designated for a distinct clinical entity comprising: (1) AVM of the midbrain; (2) congenital vascular abnormality of the ipsilateral retina; (3) facial nervi; and (4) mental change. Subsequent reports described single cases or small series of patients associated with different locations and extensions of AVMs in the craniofacial regions.[3–5] The purposes of this study are to report the imaging spectrum of craniofacial vascular malformations in 14 patients with WMS and to review the literature with emphasis on the locations and distributions as well as types of these vascular malformations.

*Correspondence to: Dr Chao-Bao Luo, Department of Radiology, Taipei Veterans General Hospital, 201, Section 2, Shih-Pai Road, Taipei 112, Taiwan, R.O.C.
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Methods

From 1982 to 2001, there were 1,826 patients with brain AVMs who were referred for assessment or treatment to the Department of Diagnostic and Interventional Neuroradiology, Bicetre Hospital, Paris. Of these, 14 patients (9 men, 5 women; mean age, 19 years) were found to meet the criteria for WMS. We retrospectively reviewed the case records and imaging studies of these patients. Initial neuroimaging studies consisted of computed tomography (CT) in 8 patients and magnetic resonance imaging (MRI) in 12 patients to determine the size, type and location of vascular malformations. Conventional 4-vessel angiographic studies were performed in all 14 patients to delineate the spectrums of vascular malformations in terms of angioarchitectures (e.g. feeding artery and venous drains). All images were reviewed by 2 neuroradiologists with experience in cerebrovascular anatomy and angioarchitectures of vascular malformation with emphasis placed on the locations and types of vascular malformations. In addition, the management and outcome of these 14 patients were retrospectively analyzed. As an aid to diagnosis, we divided the involved areas into 3 zones: face, orbit and brain, and employed the criteria that lesions must be present in at least 2 of these zones for the diagnosis to be made. In addition, the complete form of WMS was defined as vascular malformations involving all 3 zones, while the partial form of WMS was defined as vascular malformations involving 2 zones only.

Results

The findings of individual cases with the locations and types of vascular malformations are summarized in Table 1. The age of these patients when they presented with symptoms (mean age, 19 years) was younger than the age of patients with sporadic brain AVMs (mean age, 40 years).[6] The most common clinical manifestation in these 14 patients was decreased visual acuity ($n=10$), followed by neurologic deficit ($n=6$), headache ($n=4$), oronasal bleeding ($n=3$), intracranial hemorrhage ($n=3$), and seizure ($n=2$) (Table 1). Complete WMS was found in 2 patients (Figure 1), while the other 12 patients were grouped as having the partial form of WMS (Figure 2). In terms of facial vascular malformations, 5 patients had facial cutaneous lesions, and 4 of them were verified to have underlying facial vascular malformation (Figure 1E).

Table 1. Demographic characteristics of 14 patients with Wyburn-Mason syndrome

No/sex/age (yr)	Clinical manifestation	Lesion side	Location of vascular malformation		
			Face	Eye	Brain
1/F/9	Decreased visual acuity, oronasal bleeding	LT	Yes	Retina, optic nerve	Optic chiasma, hypothalamus, thalamus, basal ganglion, midbrain
2/M/4	Headache, seizure, hemiparesis, ICH	LT	No	Optic nerve	Optic chiasma, hypothalamus, thalamus, occipital lobe
3/M/13	Decreased visual acuity, epistaxis, headache	LT	No	Retina, optic nerve	Thalamus, basal ganglion
4/M/34	Hemiparesis, ICH	LT	No	Retina, optic nerve	Optic chiasma, hypothalamus
5/F/11	Hemiparesis	LT	Yes	Retina	Optic chiasma, hypothalamus, thalamus, basal ganglion
6/F/13	Decreased visual acuity	LT	No	Retina, optic nerve	Optic chiasma, hypothalamus
7/M/49	Decreased visual acuity, ICH	LT	No	Retina, optic nerve	Optic chiasma, hypothalamus
8/M/7	Decreased visual acuity, headache, hemiparesis	RT	No	Retina, optic nerve	Thalamus, basal ganglion, fronto-temporo-parieto-occipital lobe
9/F/14	Decreased visual acuity, hemiparesis, seizure	RT	No	Retina, optic nerve	Thalamus, basal ganglion, temporo-occipital lobe
10/M/49	Epistaxis	Midline	Yes	None	Optic chiasma, hypothalamus
11/M/28	Decreased visual acuity, headache	Midline	Yes	Retina, optic nerve	Optic chiasma, hypothalamus, occipital lobe
12/M/8	Decreased visual acuity, hemiparesis	Midline	No	Optic nerve	Thalamus
13/M/16	Decreased visual acuity	Midline	No	Optic nerve	Optic chiasma, hypothalamus, thalamus, midbrain
14/F/10	Decreased visual acuity	Midline	Yes	Retina, optic nerve	Nil

LT = left; RT = right; ICH = intracerebral hemorrhage.

All 14 patients had intracranial AVMs. The most common site of intracranial AVM was the optic nerve ($n=12$), followed by the retina ($n=10$), optic chiasma and hypothalamus ($n=9$), thalamus ($n=7$), basal ganglion ($n=5$), midbrain ($n=2$), occipital lobe ($n=1$), temporo-occipital lobe ($n=1$) and fronto-temporo-parieto-occipital lobe ($n=1$). Unilateral lesions were found in 9 patients (right = 2, left = 7; Figure 2), while

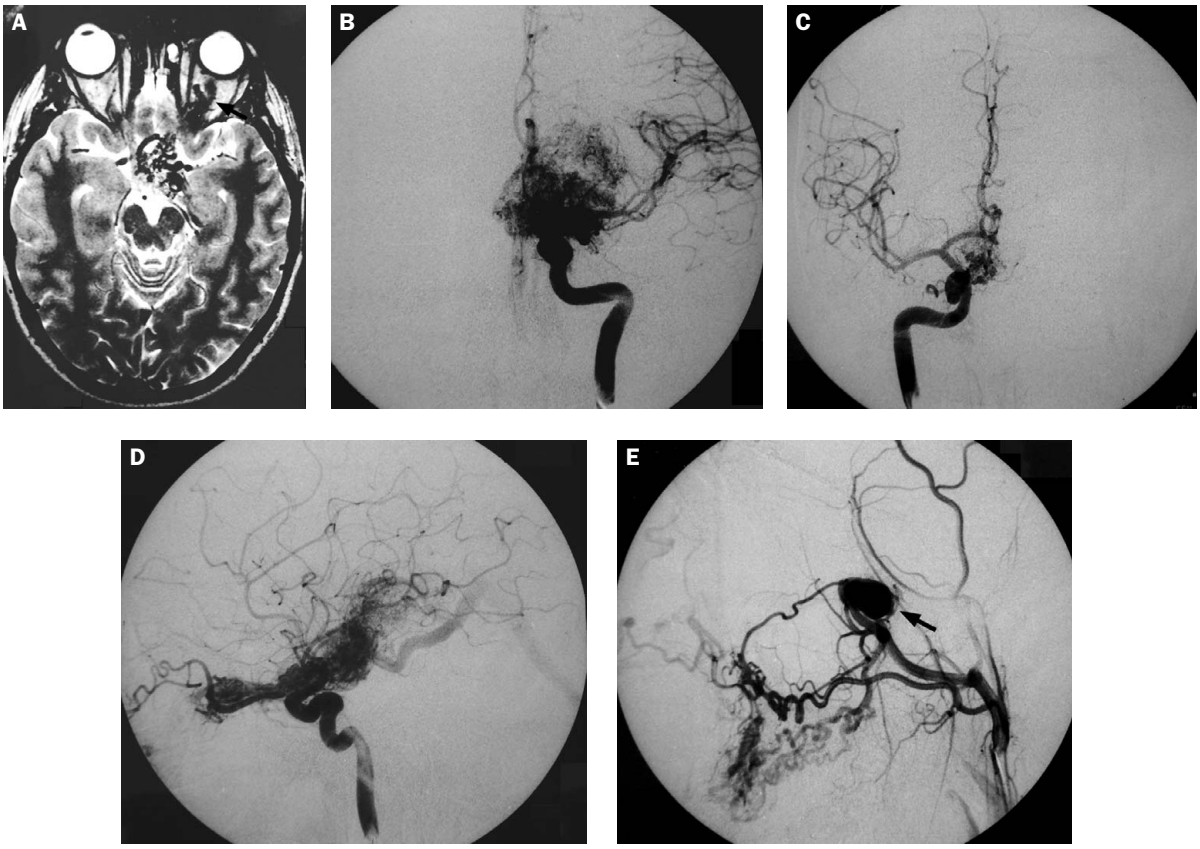

Figure 1. Images of a 28-year-old man with the complete form of Wyburn-Mason syndrome, involving the face, orbit and brain. (A) Axial T2-weighted image shows arteriovenous malformations (AVMs) at the left orbit (arrow) and midline of the hypothalamus. (B, C, D) Bilateral internal carotid angiograms demonstrate AVMs involving the left orbit and midline of the hypothalamus and thalamus, which were supplied by the ophthalmic artery and perforating branches of the middle and anterior cerebral arteries, draining to the internal cerebellar vein to the straight sinus. (E) Left external carotid angiogram depicts maxillary AVMs associated with aneurysmal formation in the pterygopalatine segment of the internal maxillary artery (arrow).

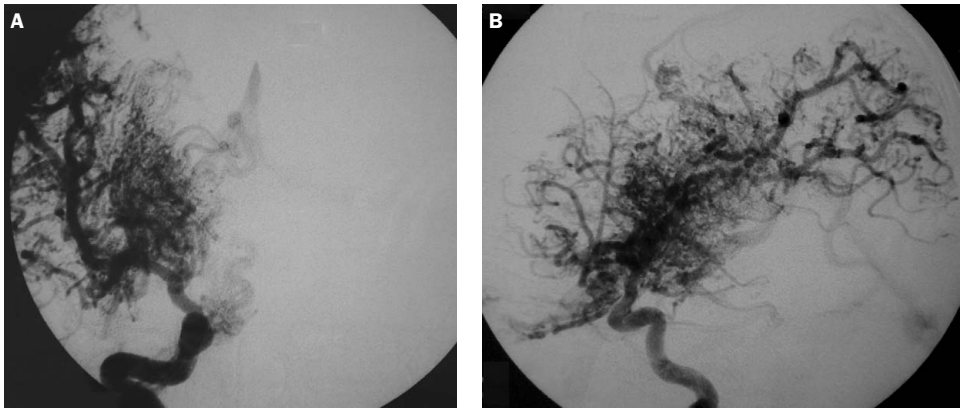

Figure 2. Images of a 7-year-old boy with the partial form of Wyburn-Mason syndrome, involving the right brain and orbit. (A, B) Right carotid angiograms reveal diffuse arteriovenous malformations involving the right orbit, thalamus, basal ganglion and fronto-temporo-parieto-occipital (FTPO) regions, supplied by the ophthalmic artery, perforating branches of the middle cerebral artery as well as its cortical branches of FTPO and draining to the superficial cortical veins and deep internal cerebral vein to the straight sinus.

midline lesions involving both sides were documented in the remaining 5 patients (Figure 1). Regarding the imaging studies, CT, MRI and conventional angiography had the capacity to detect the distribution of the vascular malformations. In general, CT and MRI were superior to conventional angiography for demonstrating the precise anatomic location of the AVM nidi. MRI proved especially valuable for defining the location of the AVM nidi with respect to the surface of the brain, the ventricular system, and the corpus callosum because of its capability of multiplanar images. Conventional angiography was superior to both CT and MRI for showing the exact feeding arteries and draining vein of the vascular anomalies, as well as risk factors of AVM such as flow-related or intranidal aneurysm.

Seven patients who were referred for imaging consultation were lost to follow-up after assessment. Seven patients had received endovascular embolization in an attempt to reduce the risk of bleeding or rebleeding of the cerebrum ($n=5$) and oronasal region ($n=2$); all of these 7 patients were stable in the mean follow-up period of 15 months (range, 5–37 months). Because all intracranial AVMs were multiple and large as well as deep-seated, no lesion was considered as morphologically curable by surgical removal, embolization or radiosurgery alone or by combined modalities.

Discussion

Multiple brain AVMs are rare; in a review of 203 patients with brain vascular malformations, 9% of patients could be included in the multiple AVMs category and only 1 (0.4%) of them was considered to have WMS.[7] The exact etiology of this rare syndrome is unknown. In its partial form, definite retinal involvement is absent, in contrast to the classic form of the syndrome as originally defined.[8] Tsuneoka et al[9] subsequently further advocated that the incomplete form of WMS be characterized as brain AVM, usually situated unilaterally in the thalamus, in association with either retinal or intraorbital AVM. On the contrary, in its extreme or complete form, intracranial AVMs can extend forward, continuously, from the occipital or parietal lobe and thalamus via the hypothalamus, optic chiasm and optic nerve to the retina, with midbrain and cerebellar involvement occasionally described. In our series, only 2 patients (14%) had the complete form, involving all 3 zones. Nevertheless, 44% of patients in Theron et al's review were considered to have the complete form;[3] this was presumably due to an overlooking of partial forms of WMS as sporadic AVMs.

The variable and broad spectrums of vascular malformation of WMS are best understood by addressing the embryologic relationship of the involved vessels. In recent years, under the control of hox genes, segmentation of the rhombencephalon into rhombomers and forebrain analog into prosomeres has been substantiated in birds, mice and other animals, and then in humans.[10,11] Hox gene-encoded positional information in the neural crest cells is known to be involved in patterning of the pharyngeal arches and is most likely involved in determining neural crest cell distribution among the arch-derived arteries such as brain, orbit and face. Any inherent defect in these primitive brains would likely affect their derivative tissues. Therefore, there is a potential spectrum of metameric craniofacial AVMs in those patients with dysgenesis of primitive brains.[12] The distribution of vascular malformation of partial or complete WMS depends largely on the involved primitive brains. In the past, the lesions were thought to be unilateral, being invariably ipsilateral to the intracranial lesions, therefore Theron et al[3] named the syndrome wrongly as "unilateral" retinocephalic vascular malformations. In fact, the AVMs are not confined unilaterally; they can involve both sides[4] in midline location, as was demonstrated in 5 cases in our series.

Patients with WMS exhibit a variety of clinical manifestations and various degrees of severity of vascular malformation. In general, there are 3 types of clinical manifestations: ocular, neurologic or facial. Ocular manifestations include decreased visual acuity, visual field defect, proptosis and conjunctival injection caused by spontaneous hemorrhage or ischemia or mass effect with compression of the optic tract, chiasm or nerve. Although retinal involvement is no longer considered essential for the diagnosis of WMS, ocular manifestations of AVMs in the retina and/or orbit remain important clues for the diagnosis of this condition. Among the 14 patients in our series, decreased visual acuity was the most common symptom and was found in 10 patients (71%); 93% of patients had orbital ($n=12$) and/or retina AVMs ($n=10$). The retinal and/or orbital lesions range from ophthalmoscopically barely visible vascular anomalies to large tangles of tortuous and dilated vessels covering a substantial portion of the retina. Therefore, when ocular AVMs are recognized initially, a systematic neuroimaging examination should be performed in search of a potential intracranial vascular lesion to exclude WMS.

A wide variety of neurologic manifestations of WMS differing in site and extent of the cerebral lesions are reported. The symptoms are related to the ruptured AVMs with intracranial hemorrhage and/or mass

effect of the AVMs. Headache, seizure and neurologic deficit are the usual indicators of central nervous system involvement, although the specific symptoms and signs depend on the location and extent of the brain AVM. The neurologic presentation of patients with WMS may differ from those of patients with sporadic brain AVMs. Mackenzie[13] found that epilepsy (32%) or hemorrhage (30%) was the most common presenting complaint in 50 patients with sporadic brain AVMs, whereas Theron et al[3] reported that hemiparesis (50%) was the most common presenting complaint in 27 patients with WMS; hemorrhage was only present in 12% and epilepsy appeared in 5%. In our series, the most common neurologic symptoms were hemiparesis (43%), followed by headache (31%), hemorrhage (21%) and seizure (14%). The decreased incidence of seizure probably reflects the deep location of the brain AVMs in WMS.

Maxillofacial cutaneous manifestations were found in a minority of patients in this series as compared to lesions of the orbit and brain. However, these facial lesions may be the first signs to be detected because of asymptomatic intracranial vascular malformations. When present, such facial lesions vary from a faint cutaneous discoloration to high-flow maxillofacial and/or mandibular AVMs, which may present with life-threatening hemorrhage in addition to severe cosmetic and psychologic problems. When lesions of the maxilla or mandible are found, angiographic studies should be obtained to define the nature of vascular malformation and extension of the lesion. In addition, the angiograms should include the brain to search for potential intracranial vascular malformations of WMS. In our series, only 5 patients were detected as having facial involvement, and this facial vascular anomaly may be overlooked or ignored, particularly in those patients with subtle change. In addition, facial vascular anomalies may be confused with neurocutaneous syndromes or phakomatoses associated with neurovascular anomalies such as PHACE syndrome, Sturge-Weber syndrome, tuberous sclerosis and neurofibromatosis. Unlike WMS, which is associated with craniofacial AVMs, PHACE syndrome is related to arterial anomaly of the extra- and intracranium.[14] Sturge-Weber syndrome is classified as a venous anomaly. Tuberous sclerosis and neurofibromatosis are associated with intracranial tumor growth.

CT, MRI, and the more recently developed high-resolution magnetic resonance angiography are non-invasive neuroradiologic screening tools for intra- and extracranial lesions. In the present series, CT and MRI provided useful information on the exact location and extent of the AVMs and their relation to adjacent vital structures such as the optic nerve and brain stem, and could help guide the aggressiveness of any subsequent therapy. Nonetheless, confirmation of the diagnosis needs conventional angiography. For all the intracranial or extracranial vascular lesions, 4-vessel cerebral angiography is the only means of providing accurate anatomic localization of the vascular malformations. Moreover, knowledge of the extent, pattern, and number of the vessels feeding and draining the malformation as well as potential risk angioarchitectures such as flow-related and/or intranidal aneurysms is needed in planning the most suitable mode of therapy.

The management of this particular syndrome remains controversial, and there are only a few reports in the literature because its long-term prognosis and natural history are unknown. In addition, most brain AVMs of WMS are diffuse and deep-seated and are not usually amenable to direct surgical intervention due to the significant postoperative neurologic sequelae. Therefore, many physicians prefer to treat patients conservatively. Surgical treatment of selecting suprasellar AVMs has been reported to be associated with severe unilateral vision loss.[15,16] By far, less invasive endovascular embolization with partial treatment targeting a weak-point angioarchitecture of AVMs, such as intranidal aneurysm, is chosen in most cases. In our series, 7 patients coming from abroad was lost to follow-up after image consultation; 5 patients underwent endovascular embolization of cerebral AVMs in an attempt to reduce the risk of rebleeding ($n=3$) or bleeding ($n=2$). Two patients with intractable oronasal bleeding were controlled by endovascular procedure by infusing embolic particles into the vascular malformation. In no case were the intracranial AVMs considered to be morphologically curable by surgical removal, embolization or radiosurgery alone or by combined modalities.

In conclusion, WMS is associated with a wide spectrum of multiple vascular malformations involving unilateral or bilateral orbits, brain and/or face. These spectrums of malformations can be determined by CT, MRI and conventional angiography. Most patients have the partial form of WMS that involves 2 zones of orbit, brain and/or face. The most common involved sites are the orbit and brain, followed by the face. WMS should be considered in patients with ocular AVM associated with brain or facial vascular malformations.

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