Int J Clin Exp Med 2015;8(11):21351-21357
www.ijcem.com /ISSN:1940-5901/IJCEM0009621

Original Article

Ischemic and hemorrhagic moyamoya disease in adults: CT findings

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Received April 26, 2015; Accepted November 2, 2015; Epub November 15, 2015; Published November 30, 2015

Abstract: Objective: To investigate the findings of adult moyamoya disease (MD) of different types on plain CT, brain perfusion CT (CTP) and brain CT angiography (CTA). Materials and methods: A total of 48 patients with ischemic MD and hemorrhagic MD were recruited into present study, and findings were collected from plain CT, CTP and CTA. Results: The incidence of watershed or cortex stroke in ischemic MD (55.6% and 38.9%) was higher than in hemorrhagic MD (0%). The incidence of ventricle or basal ganglia stroke in hemorrhagic MD (40.0%, 43.3%) was higher than in ischemic MD (0%, 5.6%). CTP showed hypoperfusion in 11 patients, hyperperfusion in 12 and normal perfusion in 25. Ischemic MD patients were more likely to present hypoperfusion (61.1%; normal perfusion: 22.2%; hyperperfusion: 16.7%). Hemorrhagic MD patients were more likely to present normal perfusion (70%; hyperperfusion: 30%; hypoperfusion: 0%). The incidence of grade II MD in ischemic MD (27.8%) was higher than in hemorrhagic MD (6.7%). The incidences of grade IV and V MD in hemorrhagic MD (33.3% and 16.7%) were higher than in ischemic MD (16.7% and 11.0%). Conclusion: Hemorrhagic MD is dominant in adults with MD and stroke of these patients mainly occurs at the intraventricular space and basal ganglia. Ischemic MD in adults is characterized by hypoperfusion and hemorrhagic MD by normal perfusion on CTP. MD in adults is usually classified as grade II, III or IV on CTA.

Keywords: Adults, moyamoya disease, computerized tomography

Introduction

Moyamoya disease (MD) was first reported in Japan in 1957 [1]. It refers to a chronic, progressive cerebrovascular occlusive disease of unknown cause and is characterized by the narrowing or occlusion of the unilateral or bilateral distal internal carotid artery, middle cerebral artery and proximal anterior cerebral artery, accompanied by formation of network ("puff of smoke") of small vessels at the base of the brain and pia mater [2]. In 1969, this disease was named MD due to network of vessels appearing as a "puff of smoke" on conventional angiography [2]. MD is frequently reported in East Asia where its incidence is more than 10 times that in western countries. Especially, the incidence of MD is as high as 3.16-10.5 per 100000 persons in Japan [3]. Women are more likely to develop MD as compared to men, and it is mainly found in children aged 0-10 years and adults aged 30-40 years. Clinically, symptoms of brain ischemia are usually found in MD children, while transient or permanent brain infarction and intracranial hemorrhage are noted in MD adults [4-6]. The diagnostic and evaluation techniques rely on magnetic resonance imaging (MRI), magnetic resonance angiography (MRA) conventional angiography, and cerebral hemodynamics measurements [7]. The diagnosis of MD is dependent on the narrowing of the distal portion of the intracranial arteries and the formation of newly generated blood vessels which reflects the progression of vascular stenosis. Accurate evaluation by imaging is crucial for the diagnosis and therapy of MD. Although MRA is helpful for the confirmed diagnosis of MD, computerized tomography (CT) angiography (CTA) is also indicative for the stenosis of intracranial vessels in MD. Thus, in the areas whether MRI is not available, CTA may

Table 1. Basic information of patients in two groups

	Hemorrhagic (n=30)	Ischemic (n=18)	*P* value
Age (years old)	42.23±8.78	35.17±5.82	0.002
Gender (Male, %)	14, 46.7	7,38.9	0.765
Stage			0.001
Early (n, %)	2, 6.7	9, 50	
Intermediate (n, %)	22, 73.3	9, 50	
Late (n, %)	6, 20	0, 0	

Table 2. Location of stroke in patients with ischemic and hemorrhagic MD

Location	Type		*P* value
	Ischemic (n=18)	Hemorrhagic (n=30)	
Cortex (n=18, %)	10, 55.6	0, 0	0.000
Watershed (n=7, %)	7, 38.9	0, 0	
Basal ganglia (n=14, %)	1, 5.6	13, 43.3	
Intraventricular space (n=12, %)	0, 0	12, 40.0	
Subarachnoid space (n=5, %)	0, 0	5, 16.7	

the median age of 41.6 years (range: 25-72 years) (**Table 1**).

Clinical manifestations

Patients with ischemic MD presented repeated headache and dizziness, intermittent headache, intermittent limb weakness, blurred vision, slurred speech, and incidental convulsions, of whom 2 had acute brain infarction. Patients with hemorrhagic MD mainly manifested abrupt headache and vomiting, abrupt coma and unconsciousness, and abrupt hemiplegia, of whom 3 had recurrent hemorrhage.

Methods

be employed as an alternative for the diagnosis of MD [8]. Perfusion CT has a high popularity and can be used to rapidly quantify the lesions. Thus, perfusion CT has been widely used in the diagnosis of acute ischemic events. In the present study, the locations of stroke, features of brain perfusion, and patterns of vascular compensation were investigated in adults with MD, aiming to provide imaging findings for the rationale and timely therapy of MD.

Materials and methods

General information

A total of 48 adult patients were recruited into present study. They were diagnosed with MD by CTA, MRA or DSA. MD was diagnosed according to the radiological diagnostic criteria developed by the Moyamoya Disease Research Committee of Ministry of Health in Japan [9]: (1) stenosis or occlusion of distal portion of the internal carotid artery and possibly also of proximal portion of middle cerebral artery, and anterior cerebral artery; (2) combined with extensive arterial collateralization around the base of the brain; (3) bilateral abnormalities. The above 3 items should be present simultaneously and other systemic diseases be excluded before the diagnosis of MD. Of 48 patients, 18 were diagnosed with ischemic MD and 30 with hemorrhagic MD. There were 21 males and 27 females with

Light-speed 64-slice VCT (GE, USA) was used for the plain CT, CTP and CTA in 48 MD patients. In the brain perfusion scanning, bolus injection of nonionic iopromide 370 (50 ml) was performed via the cubital vein at 5 ml/s at a high pressure, and 5 s later, dynamic scanning was done for 45 s with an movie mode at 8 layers with basal ganglia as a center, the detector covered 40 mm, the rotation time was 1 s, the slice thickness was 5.0/8i, the tube voltage was 80 kV and the tube current was 200 mA. All the images captured were transferred to a workstation and ADW4.6 Perfusion software affiliated to the Light-Speed VCT (GE, USA) was used for the image processing. Cerebral blood flow (CBF), cerebral blood volume (CBV), mean transit time (MTT), and time to peak (TTP) were measured. In CTA, patients were placed in a supine position, and the head was fixed. Bolus injection of nonionic iopromide 370 (1.0 ml/kg) was done at 4.8 ml/s, and the delayed time of scanning was determined with Smart-Prep software. Monitoring of the internal carotid artery was done at the level of fourth cervical vertebra, and the patient was scanned from the bifurcation of common carotid artery to the top of the skull. The trigger threshold was 180 HU. The tube voltage was 140 kV, the tube current was 350 mA, the slice thickness was 0.625 mm, the slice interval was 0.625 mm, the pitch was 0.984:1, the tube rotation time was 0.5 s,

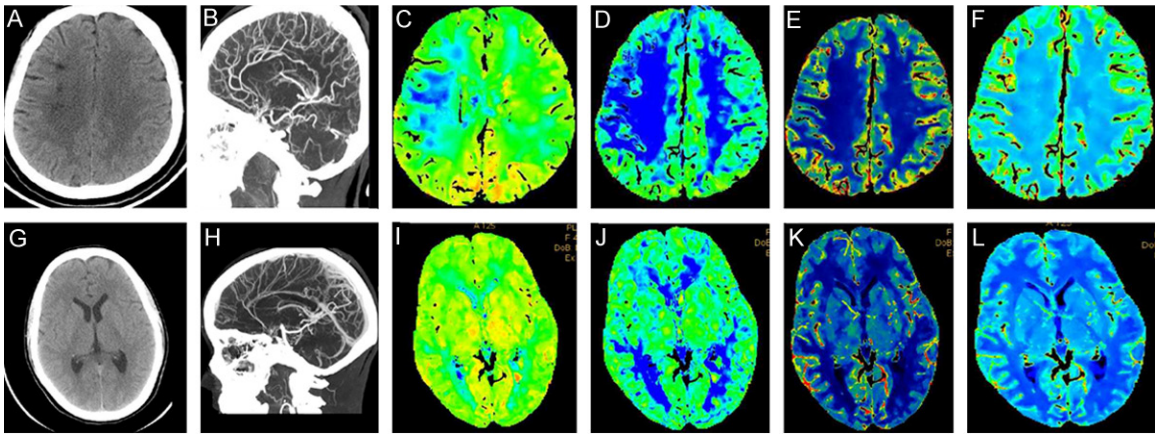

Figure 1. A-F were from the same patient with ischemic MD. G-L were from the same patient with hemorrhagic MD. A: Plain CT. a few patchy hypoperfusions were found at the right prefrontal cortex; B: MIP. Opening of posterior choroidal artery and dorsal pericallosal artery; C: TTP. TTP increased at the right prefrontal lobe; D: MTT. MTT increased at the right prefrontal lobe; E: CBF. Blood flow reduced at the right prefrontal lobe; F: CBV. Blood volume slightly reduced at the right prefrontal lobe. G: Plain CT one year after hemorrhage and the hemorrhagic focus was completely absorbed; H: MIP. Opening of posterior choroidal artery and dorsal pericallosal artery; I: TTP. TTP decreased at the left basal ganglia region; J: MTT. MTT decreased at the left basal ganglia region; K: CBF. Blood flow increased at the left temporal lobe; L: CBV. Blood volume slightly increased at the left temporal lobe.

and the matrix was 512×512. The raw images were processed with ADW4.6 workstation, and volume rendering (VR), maximum intensity projection (MIP) and multi-planar reconstruction (MPR) were employed for the post-processing of images.

Angiographic grades of MD according to Suzuki classification system

According to the Suzuki classification system [10], the angiographic grades of MD were determined: grade I: narrowing of internal carotid artery apex; grade II: dilation of anterior and middle cerebral artery and formation of several newly generated vessels at the internal carotid artery apex; grade III: partial involvement of anterior and middle cerebral artery and formation of a lot of newly generated vessels at the internal carotid artery apex; grade IV: further deteriorated narrowing or occlusion of internal carotid artery apex, obvious involvement of anterior and middle cerebral artery, newly generated vessels reducing at the internal carotid artery apex; grade V: undeveloped anterior and middle cerebral artery, and newly generated vessels further reducing at the internal carotid artery apex; grade VI: anterior circulation supplied via external carotid artery and complete disappearance of newly generated vessels. Grade I or II, grade II or IV and grade V or VI were grouped as early, intermediate and late stage.

Statistical analysis

Quantitative data were compared with t test, and categorical data with Mann-Whitney U test. A value of $P<0.05$ was considered statistically significant. The effects of age and clinic stageson CT outcomes were investigated by using multivariate logistic analyses. Statistical analysis was performed with SPSS version 13.0.

Results

Plain CT scanning

Among patients with ischemic MD, cortical stroke was found in 10 patients, and characterized by gyrus-like hypointensity at the frontal and parietal lobes with focal brain atrophy; watershed stroke was found in 7 patients and characterized by patchy hypointensity at the subcortical white matter with a clear boundary; basal ganglia stroke was found in 1 patient and characterized by patchy hypointensity at the basal ganglia with a clear boundary. Among patients with hemorrhagic MD, basal ganglia hemorrhage with or without ventricular involvement was found in 13 patients and characterized by patchy hyperintensity at the basal ganglia with or without ventricular involvement;

Table 3. Brain perfusion on CTP and CTA in patients with ischemic and hemorrhagic MD

Type	n	CTP			CTA					
		Normal	Hypo	Hyper	I	II	III	IV	V	VI
Ischemic	18	4	11	3	1	5	7	3	2	0
Hemorrhagic	30	21	0	9	0	2	12	10	5	1
P value			0.000				0.213			

simple ventricular hemorrhage was found in 12 patients and characterized by mould-like hyperintensity at the ventricle; subarachnoid hemorrhage was found in 5 patients and characterized by hyperintensity at the suprasellar cistern, ambient cistern, lateral and interhemispheric fissure cistern (**Table 2**).

CT perfusion

Of patients with ischemic MD, hypoperfusion was noted in 11 patients (**Figure 1A-F**), focal hyperperfusion in 3 patients and normal perfusion in 4. Of patients with hemorrhagic MD, hyperperfusion was observed in 9 patients, normal perfusion in 21 and none had hypoperfusion (**Table 3**). In ischemic MD, the incidence of hypoperfusion was higher than that of normal perfusion and hyperperfusion; in hemorrhagic MD, the incidence of normal perfusion was higher than that of hyperperfusion, and hypoperfusion was absent.

CTA

Of 48 adult patients with MD, grade I-VI MD was found in 1, 5, 7, 3, 2 and 0 patients, respectively, in MD and 0, 2, 12, 10, 5 and 1 patients, respectively, in hemorrhagic MD (**Table 3**). The proportion of grade II and III MD in ischemic MD was higher than in hemorrhagic MD; the proportion of grade IV and V MD in hemorrhagic MD was higher than in ischemic MD. Results multivariate logistic regression showed that age (OR: 1.01; 95% CI: 1.00-1.04; P=0.06) and clinical stages (OR: 1.05; 95% CI: 1.00-1.10; P=0.09) were not significant associated with CT outcomes.

Discussion

MD is a group of diseases related to chronic, progressive cerebrovascular stenosis and mainly involves the distal portion of the internal carotid artery, the proximal portion of the anterior cerebral artery and middle cerebral artery, and occasionally the posterior cerebral artery. Cerebral angiography shows a collateral network of vessels at the base of the brain, appearing as a "puff of smoke" ("moyamoya" in Japanese). It was first reported by Japanese investigators [11] and its cause is still unclear. It has been reported familial MD and genetic factors are found to be involved in the pathogenesis of MD in some patients [10]. When used alone, the term "moyamoya phenomenon" refers to this cerebral angiopathy regardless of its cause, although this angiographic pattern can have multiple causes. Moyamoya syndrome (MS) corresponds to moyamoya angiopathy with unilateral vascular involvement or associated with other causes (such as arteritis, leptospirosis infection, radiation injury, trauma, cocaine abuse, arteriosclerosis and others) [12]. MS is not necessary the MD, but may develop into MD. In the present study, MD with unilateral vascular involvement and MS were excluded. The cerebral hemodynamic changes over the progression of MD in adults, and the blood flow also changes dynamically. Infarction, hemorrhage and change in the blood flow may be present in the brain. The compensatory development of a collateral network of vessels also varies at different stages of MD.

Locations of stroke in MD

The initial symptoms of MD in adults are those related to brain ischemia or hemorrhage. When the brain ischemia is severe and the collateral vessels become decompensatory, the brain tissues may present morphological changes, causing ischemic brain infarction and atrophy, and then producing corresponding symptoms. The brain infarction is closely related to the progression of intracranial arterial lesions [13]. Findings in early studies indicated that brain infarction in MD patients usually occurred at the regions susceptible to hypoperfusion (such as anterior and posterior watershed) [14]. In clinical practice, brain infarction is often found at the watershed and cortex (especially the frontal lobe and parietal lobe), and less observed at the basal ganglia and thalamus. In the present study, the incidence of brain infarction at the cortex and watershed (55.6% and 38.9%, respectively) was significantly higher

than that at the basal ganglia (5.5%). Infarction may be single or multifocal, and be unilateral or bilateral. The number and location of brain infarction are related to the extent of ICA stenosis, the extent of vascular compensation and the severity of posterior cerebral arterial lesions [15]. However, hemorrhagic MD is usually found at the basal ganglia, intraventricular space and subarachnoid space, especially the thalamus and intraventricular space. In the present study, the incidence of hemorrhage at the basal ganglia and intraventricular space was 43.3% and 40%, respectively, which were significantly higher than that at other sites. The causes of hemorrhage in MD include [16]: (1) Aneurysm rupture of collateral vessels or other vessels, and recurrent hemorrhage occurring in a short time; the vascular network with abnormal dilation developing small aneurysm rupture; (3) choroidal artery ruptures: the choroidal artery and medullary artery in MD patients enlarging, which suggests that the vascular load increases at the posterior and lateral ventricle. This is a major cause of intraventricular hemorrhage and simple parenchymal hemorrhage. We speculate that the presence and location of hemorrhage are closely related to the extent and location of vascular compensation, the concomitant aneurysm and the focal pressure load of compensatory vessels.

Blood flow in MD patients

The evaluation of brain perfusion is crucial for the diagnosis and therapy of MD and the follow up of moyamoya angiopathy [17]. The hemodynamic change may be found in the whole course of MD. According to the compensation patterns of blood flow and brain metabolism [18], the hemodynamic can be classified as stage 0 (blood flow reduces slightly, the cerebral perfusion pressure is nearly normal, but the blood volume increases and the cerebrovascular reserve remains normal), stage I (blood flow reduces moderately, the cerebral perfusion pressure reduces slightly, the blood volume increases and the cerebrovascular reserve is damaged. Collateral circulation forms for compensation to maintain the requirements); stage II (blood flow reduces significantly, the cerebral perfusion pressure reduces markedly, the cerebrovascular autoregulation becomes abnormal, the cerebrovascular reserve exhausts and the blood volume reduces. Network of collateral vessels forms abnormally for compensation). In ischemic MD, the decompensation of collateral vessels causes uneven brain perfusion, and the regions with obvious hypoperfusion are susceptible to infarction. In hemorrhagic MD, the network of collateral vessels is sufficient for compensation, which maintains the cerebral perfusion pressure. Thus, patients are usually asymptomatic before hemorrhage, but abrupt aneurysm rupture of the compensatory vessels or small vessels may cause hemorrhage. In the present study, the incidence of hypoperfusion (61.1%) was significantly higher than that of normal perfusion and hyperperfusion in ischemic MD. We postulate that the presence of normal perfusion is ascribed to the sufficient brain perfusion, but the presence of focal hyperperfusion is attributed to the sufficient focal vascular compensation. In hemorrhagic MD, the proportion of normal perfusion (70%) was higher than that of focal hyperperfusion (30%), suggesting that the vascular compensation is sufficient in hemorrhagic MD. In both ischemic MD and hemorrhagic MD, the whole brain perfusion showed uneven, regions with hypoperfusion were mainly found at the frontal and temporal lobes of anterior circulation, and those with hyperperfusion at the bilateral thalamus and brain lobes besides midline, which is ascribed to the vascular compensation.

Angiographic grades and vascular compensation

More collateral vessels form for compensation in adult MD, which is different from MD in children. However, this may cause the formation of small aneurysms and even the vascular rupture. The vascular compensation and its extent are directly related to the presence of ischemia and hemorrhage [15]. There is evidence showing that, in adult MD, the incidence of vascular compensation in the hemorrhagic hemisphere was higher than in the ischemic hemisphere; regardless the presence of concomitant occlusion of middle cerebral artery, the occlusion of anterior cerebral artery and intracranial aneurysm are major causes of hemorrhagic stroke in adult MD [5]. The severity of MD and the vascular compensation and its extent may be associated with the findings on CTA. According to the Suzuki classification system, MD was graded as I to VI [2]. Moreover, grade I and II was defined as early stage, grade III and IV as intermediate stage and V and VI as late stage.

In the present study, grade I-VI MD was found in 5.6%, 27.8%, 38.9%, 16.7%, 11.0% and 0% of ischemic MD patients, respectively, and 0%, 6.7%, 40%, 33.3%, 16.7% and 3.3% of hemorrhagic MD patients, respectively. The incidence of grade II MD in ischemic MD was higher than in hemorrhagic MD, but the incidence of grade IV and V MD in hemorrhagic MD was higher than in ischemic MD. The patterns of vascular compensation in adult MD include [19]: anterior cerebral artery or middle cerebral artery compensates for contralateral middle cerebral artery or anterior cerebral artery via the cortical of the pial artery; (2) tortuous expansion of anterior choroidal artery, or opening and dilation of posterior communicating artery-posterior cerebral artery-pial artery-anterior cerebral artery or middle cerebral artery, or posterior pial artery-posterior pericallosal artery-anterior cerebral artery; (3) compensation of deep perforating branches mainly forms network of vessels at the base of the brain; (4) the external carotid artery compensates, in which the ophthalmic artery, superficial temporal artery, middle meningeal artery and occipital artery may communicate with terminal branches of cortical vessels. The patterns 2 and 3 are mainly found in the hemorrhagic MD, but there is no specific pattern for vascular compensation in ischemic MD. The compensation of external carotid artery mainly involves the ophthalmic artery and middle meningeal artery. In Japan, epidemiological survey showed the formation of network vessels was related to hypoperfusion in the brain [4]. Cohort study with a large sample size also showed the formation of collateral circulation at the base was the most obvious in grade III and IV MD, and the cortical microvascularity mainly occurred at early stage of MD [20].

Taken together, the CT findings of adult MD are characteristic, and the compensation of collateral vessels and brain perfusion are also complex. The formation of collateral vessels plays an important role in the development of MD. CT perfusion and CTA are helpful for the evaluation of brain hemodynamic, angiographic grading and assessment of collateral compensation in MD patients, which are important for the selection of therapeutic regimens and the timing of therapy of MD.

Disclosure of conflict of interest

None.

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