Disease Progression

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Miki Fujimura and Teiji Tominaga

Abstract

Moyamoya disease (MMD) is a chronic occlusive cerebrovascular disease with unknown etiology characterized by progressive stenosis/occlusion at the terminal portion of the internal carotid artery and an abnormal vascular network formation at the base of the brain. MMD has an intrinsic characteristic to represent a gradual conversion of the cortical vascular supply from intra-cranial/internal carotid (*IC*) system to extra-cranial/external carotid (*EC*) system, so-called *IC-EC conversion*. MMD is known to represent bimodal age distribution with a peak each in childhood and young adulthood, and the disease progression in adult patients has been considered to be relatively rare. But recent advances in neuroradiology reveal that MMD patients, either pediatric or adult, have substantial risk for disease progression, although the exact mechanism underlying the progression of MMD is undetermined. The aim of this chapter is to introduce the basic pathology and neuro-radiological characteristic of MMD, especially focusing on its disease progression in adulthood.

Keywords

Moyamoya vasculopathy · Moyamoya disease · Progression · Suzuki's angiographic stage · Basic pathology

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15.1 Introduction

Moyamoya disease (MMD) is characterized by progressive stenosis/occlusion at the terminal portion of the internal carotid artery (ICA) and an abnormal vascular network formation at the base of the brain [1, 2]. The disease progression in adult patients has been considered to be relatively rare [3, 4], but recent advances in neuroradiology reveal that MMD patients, either pediatric or adult, have substantial risk for disease progression [5, 6]. In this chapter, we sought to summarize current understanding of the basic pathology and neuro-radiological characteristic of MMD, focusing on its disease progression in adulthood.

15.2 Suzuki's Angiographic Staging as an Intrinsic Temporal Nature of Physiological Compensatory Reorganization in MMD

MMD has an intrinsic temporal nature to attempt a gradual conversion of the cortical vascular supply from intra-cranial/internal carotid (*IC*) system to extra-cranial/external carotid (*EC*) system, so-called *IC-EC conversion* [7, 8], as initially illustrated by Suzuki's angiographic staging in 1969 [1]. This staging does not represent the severity of patients' clinical condition, but may indicate the natural pathophysiological course of MMD. Insufficiency of this physiological reorganization system occurs at stage 3 or 4 in most patients, when the abnormal vascular networks at the base of the brain are most prominent.

Stage 1: Narrowing of carotid fork.
Stage 2: Initiation of the "moyamoya vessels"; dilatation of the intracerebral main arteries.
Stage 3: Intensification of the "moyamoya vessels"; nonfilling of the anterior and middle cerebral arteries.
Stage 4: Minimization of the "moyamoya vessels"; disappearance of the posterior cerebral artery.
Stage 5: Reduction of the "moyamoya vessels"; the main arteries arising from the internal carotid artery disappear.
Stage 6: Disappearance of the "moyamoya vessels"; the original moyamoya vessels at the base of the brain are completely missing and only the collateral circulation from the external carotid artery is seen.

Malfunction of the "*IC-EC conversion*" system is considered to result in cerebral ischemia and/or hemorrhage from inadequate collateral vascular networks. On the other hand, substantial numbers of MMD patients accomplish "favorable" conversion process without manifesting as deleterious cerebrovascular events [8]. This 47-year-old woman experienced only slight numbness in her left hand while playing woodwind instrument, though her angio-architecture represents stage 6 MMD on the right hemisphere, where all the cortical blood supply is exclusively derived from EC system (Fig. 15.1).

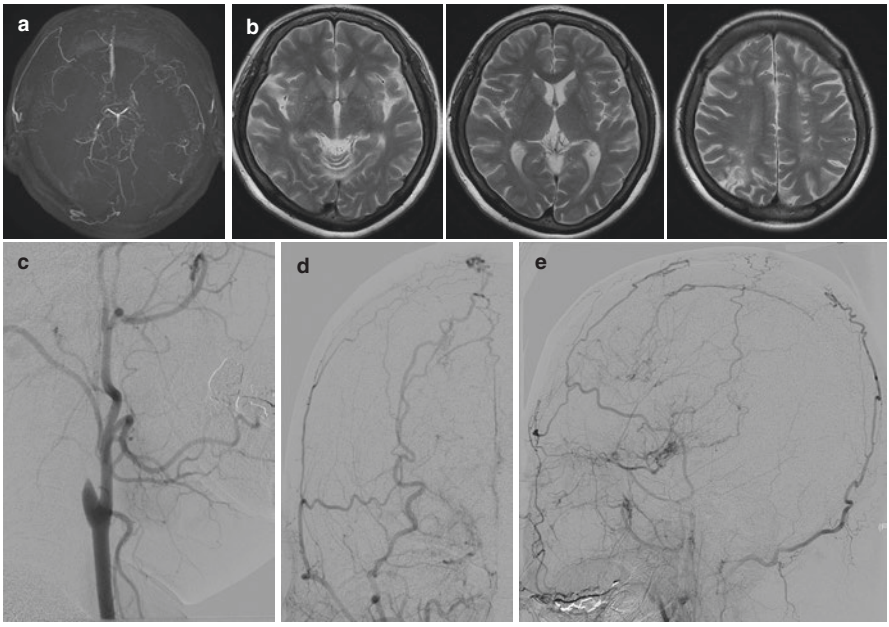

Fig. 15.1 **A:** Representative findings of stage-6 moyamoya disease (MMD). Magnetic resonance (MR) angiography (**a**), T2-weighted MR imaging (**b**), and right carotid angiogram (**c-e**) of a 47-year-old woman indicating that all the cortical blood supply is derived from external carotid system

15.3 Disease Progression in Adult MMD

The disease progression of MMD had generally been considered to occur exclusively in childhood with angiographic characteristics being completed before adulthood [3, 4]. In contrast to this classic observation, Kuroda et al. first reported in a multicenter observational study on adult MMD that the incidence of disease progression in adult patients was not as rare as previously considered [5] and similar result was reported also by Narisawa and colleagues [6]. In accordance with this observation, there were several reported cases of the de novo development of MMD in adulthood [9–11]. Interestingly, most of them were middle-aged females who generally lacked particular risk factors for atherosclerosis [9–11]. The mechanisms underlying the development and progression of adult MMD are undetermined, but physiological balance between female hormones is considered to be one of the major candidate environmental factors related to the development/progression of adult MMD patients [12]. This 47-year-old woman suffered mild weakness on her left hand and visited neurological service. Initial magnetic resonance (MR) angiography revealed only mild stenosis at the bilateral ICA terminus (Fig. 15.2a), but apparent progression of the steno-occlusive changes was found 1 year later, when she suffered crescendo transient ischemic attack (TIA) (Fig. 15.2b, d, e). In light of the presence of hemodynamic compromise on the

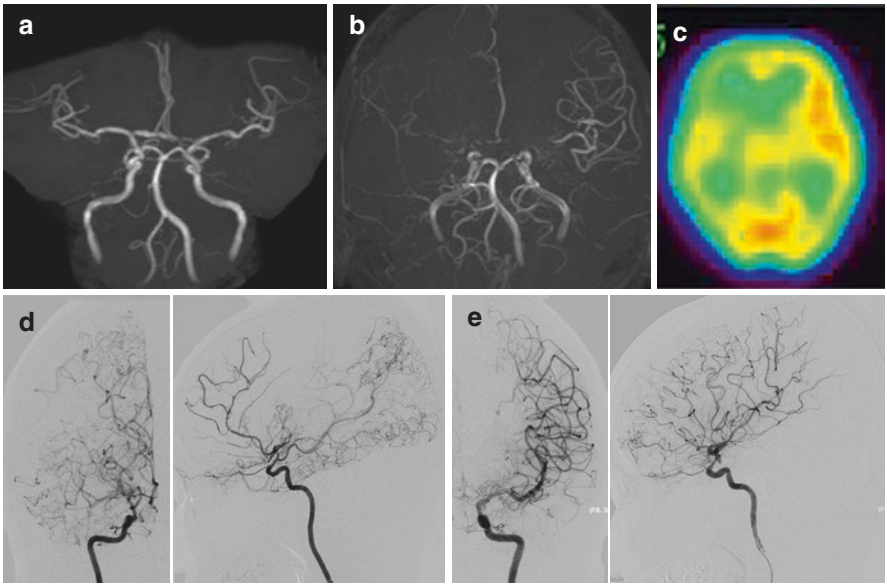

Fig. 15.2 Temporal profile of MR angiography before (**a**) and after the progression (**b**). ^{123}I-IMP SPECT (**c**) and catheter angiography (**d, e**) of this 47-year-old woman after progression demonstrating MMD with hemodynamic compromise on the right hemisphere

symptomatic hemisphere (Fig. 15.2c), she underwent right superficial temporal artery (STA)-middle cerebral artery (MCA) bypass combined with indirect pial synangiosis without complication (Fig. 15.3a-d). The ischemic attack disappeared completely after surgery, and flow study indicated the apparent hemodynamic improvement on the right hemisphere (Fig. 15.3e). Alternatively, possible involvement of the genetic variant of ring finger protein 213 (RNF213), a susceptibility gene for MMD, in the disease progression of MMD has been speculated [13]. In fact, Tashiro and colleagues reported de novo development of MMD in an adult female with a genetic variant of the RNF213 gene [11].

15.4 Significance of Progressive Stenosis in Posterior Cerebral Artery (PCA)

While following up the patients with MMD, it is clinically important not to overlook the progression of PCA stenosis, because the involvement of PCA stenosis has been reported to be significantly associated with the hemodynamic decline and the deterioration of the ischemic condition [14]. This 44-year-old woman was found to have the progression of the steno-occlusive change at the right PCA during her yearly follow-up by MR angiography (Fig. 15.4a, b). One month later, she suffered temporal weakness on her left hand, and catheter angiography confirmed the apparent progression of the right PCA stenosis (asterisk in Fig. 15.4e). Then she underwent right flow augmentation bypass, which resulted in the complete disappearance

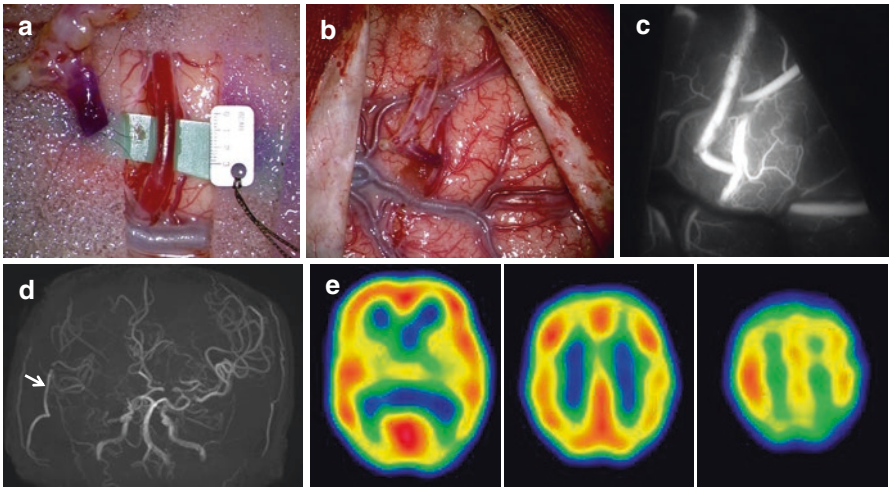

Fig. 15.3 Intra-operative view of direct/indirect combined revascularization. Surgical view before (**a**) and after left superficial temporal artery (STA)-middle cerebral artery (MCA) bypass (**b, c**). Indocyanine green video-angiography demonstrated apparently patent bypass (**c**). Post-operative MR angiography showing patent STA-MCA bypass (arrow in **d**), and hemodynamic improvement by ^{123}I-IMP SPECT (**e**)

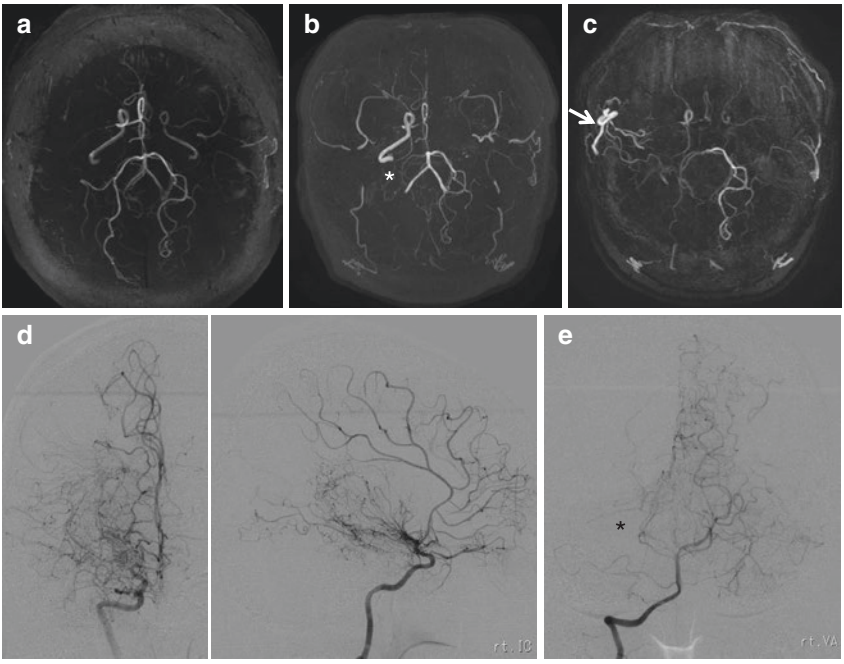

Fig. 15.4 Temporal profile of MR angiography before (**a**) and after the progression of right PCA stenosis (asterisk in **b**). Right carotid (**d**) and vertebral artery angiograms of this 44-year-old woman after progression demonstrating MMD with apparent PCA stenosis (asterisk in **e**). Post-operative MR angiography showing patent STA-MCA bypass (arrow in **c**)

of her TIA. Post-operative MRA indicated the apparently patent bypass (arrow in Fig. 15.4c). PCA involvement is also known to be an independent risk factor of posterior hemorrhage with high risk of re-bleeding [15, 16], thus identification of progressive PCA stenosis/occlusion is clinically important while following up the MMD patients neuro-radiologically at the outpatient service.

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