

Endoscope-integrated indocyanine green video angiography and the detection of the fragile periventricular collaterals associated with moyamoya disease: illustrative cases

Hiroyuki Koizumi, MD, PhD,^{1,2} Takuichiro Hide, MD, PhD,¹ Daisuke Yamamoto, MD, PhD,¹ Yuri Hyakutake, MD,¹ Hajime Handa, MD,¹ Hideto Komai, MD,¹ Yasushi Asari, MD, PhD,² and Toshihiro Kumabe, MD, PhD¹

Departments of ¹Neurosurgery and ²Emergency and Critical Care Medicine, Kitasato University School of Medicine, Sagamihara, Kanagawa, Japan

BACKGROUND Hemorrhagic moyamoya disease (MMD) and the fragile periventricular collaterals are known to have a causal relationship. Digital subtraction angiography and magnetic resonance angiography have shown the presence of fragile periventricular moyamoya vessels. However, dynamic fragile periventricular moyamoya vessels have never been observed under direct vision.

OBSERVATIONS The authors treated two patients with hemorrhagic MMD: a 42-year-old man with intraventricular hemorrhage and a 47-year-old woman with intracerebral hemorrhage. Endoscope-integrated indocyanine green video angiography (EICG angiography) could visualize the dynamic fragile periventricular collaterals. In particular, EICG angiography enabled visualization of invisible moyamoya vessels buried in the subependyma and characterization of the blood flow in the moyamoya vessels located inside the lateral ventricles and hematoma cavity.

LESSONS EICG angiography can confirm the fragile periventricular collaterals associated with MMD by direct visualization. The high spatial resolution and real-time imaging can help to avoid accidental hemorrhage in and after evacuation of hemorrhage in patients with MMD.

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KEYWORDS hemorrhagic moyamoya disease; indocyanine green; endoscopic surgery; periventricular collateral

Moyamoya disease (MMD) is a progressive disease of unknown origin characterized by stenosis or occlusion at the terminal portions of the internal carotid artery and the development of an abnormal vascular network at the base of the brain.¹ MMD usually manifests as ischemic events in childhood and as more severe hemorrhagic events in adults. The randomized, controlled Japan Adult Moyamoya (JAM) Trial demonstrated the effectiveness of direct bypass surgery for hemorrhagic MMD.^{2,3} Subgroup analysis of the trial results also demonstrated that direct bypass surgery is effective for preventing recurrences of posterior dominant initial hemorrhage.³ Recent radiographic analysis of patients with MMD presenting with intracranial hematomas revealed three fragile collaterals: lenticulostriate arteries, thalamic perforators, and choroidal arteries.⁴ The periventricular anastomosis formed by the bypass surgery is characterized by the connection formed between the medullary artery and the perforating or choroidal artery, which

consequently supplies the cortex. These findings are gradually clarifying a causal relationship between hemorrhagic MMD and these fragile collaterals.

Many studies have demonstrated the efficacy of endoscopic evacuation of spontaneous intracerebral hemorrhage (ICH).^{5,6} Neuroendoscopic surgery is just beginning to be applied to different types of intracranial hemorrhage, such as traumatic ICH, or hematoma caused by ruptured brain arteriovenous malformation.^{7,8} However, only a few cases of adult hemorrhagic type MMD were treated by neuroendoscopic surgery.^{9,10} Indocyanine green (ICG) endoscopy is useful for identifying the fine edge of the internal carotid artery and checking the patency of the intercavernous sinus and the cavernous sinus behind the dura mater in endonasal transsphenoidal surgery.¹¹ However, dynamic fragile periventricular moyamoya vessels have not been observed under direct vision.

ABBREVIATIONS CT = computed tomography; EICG = endoscope-integrated indocyanine green; GCS = Glasgow Coma Scale; ICG = indocyanine green; ICH = intracerebral hemorrhage; IVH = intraventricular hematoma; JAM = Japan Adult Moyamoya; MMD = moyamoya disease.

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This study applied endoscope-integrated ICG video angiography (EICG angiography) to explore the fragile periventricular collaterals with hemorrhagic MMD.

Illustrative Cases

ICG Fluorescence

The ICG compound (25 mg, Diagnogreen, Daiichi-Sankyo) was dissolved in sterile water (10 ml), and 2.5 ml of the solution containing 12.5 mg of ICG was injected into a peripheral vein as a bolus and then flushed with saline (10 ml).

Neuroendoscopy

ICG fluorescence was visualized with an ICG endoscope system consisting of TL400 (Power LED Rubina, OPAL1 NIR/ICG) as a light source, TH121 (IMAGE1 S 4U RUBINA, OPAL1 NIR/ICG) as a camera, and 28164AC (HOPKINS Telescope 0°, IC, Karl Storz). The ICG endoscope had 4-mm diameter and 18-cm length.

The ICG endoscope was positioned in a suitable position under white light and then switched to near-infrared light so the fluorescent signals from ICG flow in the periventricular moyamoya vessels became visible.

Case 1

A 42-year-old man experienced sudden onset of headache and deterioration of consciousness while driving and was arrived at our hospital by ambulance. On admission, the patient had decreased level of consciousness with Glasgow Coma Scale (GCS) score of 6. Computed tomography (CT) of the head revealed cast-formation intraventricular hematoma (IVH) and acute obstructive hydrocephalus. The bleeding point was suspected at the periphery of right trigone and posterior horn of the lateral ventricle based on the hemorrhage (Fig. 1A). CT angiography failed to show the intracranial arteries because of increased intracranial pressure.

Neuroendoscopic surgery to remove the IVH and decrease intracranial pressure was immediately performed. Neuroendoscopy used a rigid-rod neuroendoscope and a Neuroport transparent sheath of regular size with outer diameter of 10 mm (Olympus Corp.), which were introduced into the right lateral frontal burr holes. After removal of the hematoma from the right lateral ventricle, the right lateral ventricle was examined. The ICG endoscope provided real-time visualization of the site of the unexposed abnormal subependymal vessels at the slightly raised ventricle wall of the frontal horn of the lateral ventricle (Fig. 1B). ICG solution 2.5 ml was then injected into a peripheral vein, and the right lateral ventricle was again observed (Video 1). The endoscope demonstrated the abnormal vessels, but they immediately became invisible a few seconds after detection, indicating that the blood flow was comparatively fast (Fig. 1C). Observation of the body of the right lateral ventricle wall found fluorescence signals remaining in vessels (Fig. 1D). Finally, intraventricular lavage was used to check for residual bleeding, and the intraventricular catheter was placed inside the lateral ventricles.

VIDEO 1. Case 1. Clip showing that observation in the right lateral ventricle by EICG angiography could visualize invisible moyamoya vessels buried in the subependyma. [Click here to view.](#)

The diagnosis was IVH caused by MMD based on postoperative digital subtraction angiography. Right hemiparesis and aphasia persisted, but level of consciousness improved to GCS 15, and the

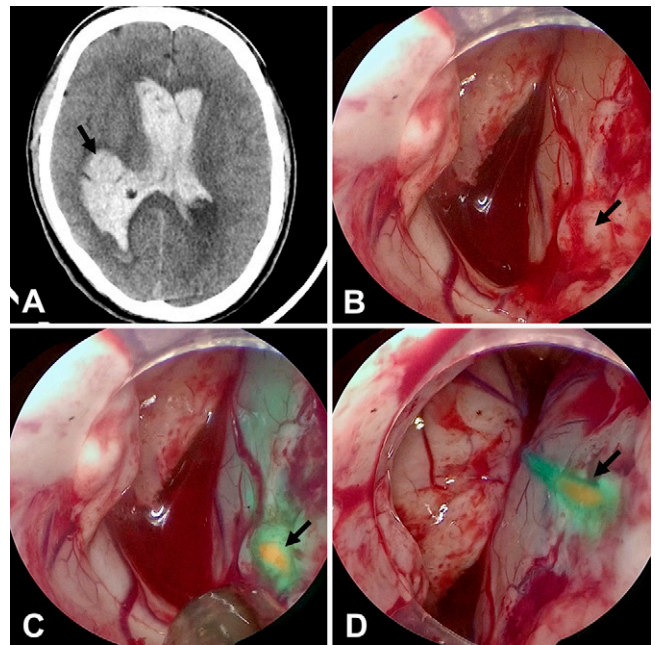


FIG. 1. Case 1. **A:** CT scan of the head showing cast-formation IVH and acute obstructive hydrocephalus. The bleeding point was suspected at the periphery of the right trigone and posterior horn of the lateral ventricle (black arrow). **B:** Neuroendoscopic image before intravenous injection of ICG showing no moyamoya vessels on the lateral ventricle wall (black arrow). **C:** Neuroendoscopic image after intravenous injection of ICG showing the invisible moyamoya vessels hiding in the subependyma on the lateral ventricle wall (black arrow). These vessels immediately became invisible a few seconds after detection, indicating that the blood flow was comparatively fast. **D:** Neuroendoscopic image after intravenous injection of ICG showing the fluorescence signals persisting in vessels in the subependyma of the body of the right lateral ventricle wall (black arrow).

patient was discharged to a rehabilitation hospital within 2 months. Eighteen months later, his modified Rankin Scale score was 2.

Case 2

A 47-year-old woman with MMD and a history of subcortical hemorrhage was referred to our institution. Magnetic resonance angiography revealed multiple collateral vessels branching from the basal arteries and connecting to the medullary arteries in the periventricular area (Fig. 2A). The patient was asymptomatic but requested bypass surgery for prevention of hemorrhagic events. However, she suffered a second ICH and arrived at our hospital by ambulance just before bypass surgery was planned. On admission, she had decreased level of consciousness, with GCS score of 7. CT of the head revealed subcortical hemorrhage in the right parietal lobe with IVH (Fig. 2B).

Neuroendoscopic surgery to remove the IVH and decrease intracranial pressure was immediately performed using a similar procedure to case 1. After removal of hematoma from the right parietal lobe, the hematoma cavity was examined, and one of the collateral vessels into the hematoma cavity was identified (Fig. 2C). EICG angiography visualized the tortuous collateral vessel very slowly (Fig. 2D); approximately 50 seconds after ICG injection, the overall appearance of the collateral vessel was clarified (Fig. 2E; Video 2). Postoperative CT depicted partial but adequate removal of the hematoma (Fig. 2F).

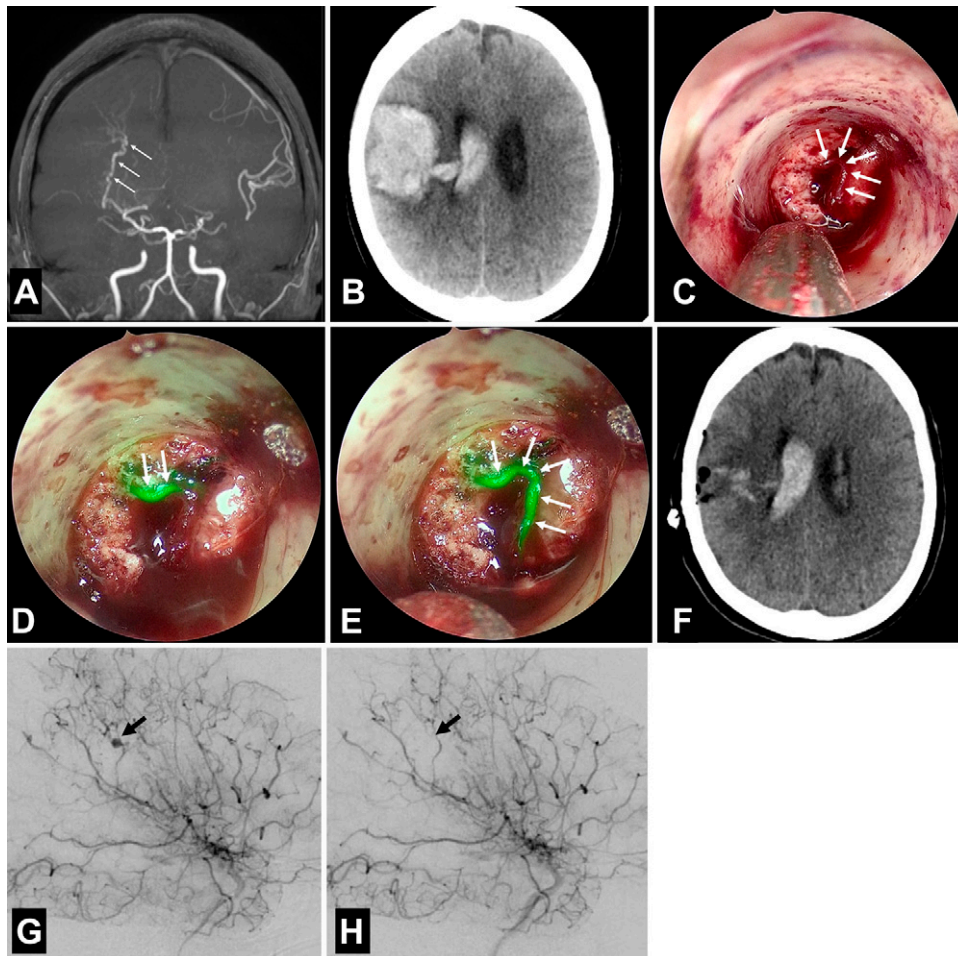


FIG. 2. Case 2. **A:** Coronal, thin-slab maximum intensity projection magnetic resonance angiogram showing multiple collateral vessels branching from the basal arteries and connecting to the medullary arteries in the periventricular area (*white arrows*). **B:** CT scan of the head revealing subcortical hemorrhage in the right parietal lobe with IVH. **C:** Neuroendoscopic image before intravenous injection of ICG showing one of the collateral vessels into the hematoma cavity (*white arrows*). **D:** Neuroendoscopic image about 30 seconds after intravenous injection of ICG showing the tortuous collateral vessel into the hematoma cavity visualized slowly (*white arrows*). **E:** Neuroendoscopic image over approximately 50 seconds clarifying the overall appearance of the collateral vessel being visualized slowly (*white arrows*). **F:** Axial CT scan obtained immediately after the emergent endoscopic surgery showing evacuation of the hematoma and no postoperative bleeding. **G:** Digital subtraction angiogram showing moyamoya vessels and an aneurysm (*black arrow*) at the distal segment of the right anterior choroidal artery that was postulated to be the cause of bleeding. **H:** Digital subtraction angiogram after embolization with N-butyl cyanoacrylate showing disappearance of the aneurysm (*black arrow*) at the distal segment of the right anterior choroidal artery.

Digital subtraction angiography demonstrated moyamoya vessels and an aneurysm at the distal segment of the right anterior choroidal artery that was postulated to be the cause of bleeding (Fig. 2G). The aneurysm was embolized effectively with N-butyl cyanoacrylate under general anesthesia with neuromonitoring (motor evoked potential; Fig. 2H).

VIDEO 2. Case 2. Clip showing one of the tortuous collateral vessels into the hematoma cavity by EICG angiography. Click here to view.

Left hemiparesis persisted, but level of consciousness improved to GCS score 15, and the patient was transferred to a rehabilitation

hospital within 2 months. Her modified Rankin Scale score was 4 on discharge from the hospital.

Discussion

Observations

The present study identified two previously unrecognized but important clinical issues. EICG angiography can visualize invisible moyamoya vessels buried in the subependyma. Therefore, EICG angiography is useful for the characterization of blood flow in moyamoya vessels.

EICG angiography during endoscopic evacuation of IVH in adult MMD has demonstrated some specific findings, including dilated

and tortuous vessels, intersecting vessels, black-brown macules in the subependyma, and rattan blind like bleeding vessels.¹⁰ Dilated vessels with thin walls were most frequently observed in the brain, mainly in the subependyma, subarachnoid spaces, and basal ganglia, with hemorrhagic lesions in 20 autopsy cases.¹² Therefore, the dilated vessels in the subependyma were especially likely to have a causal relationship with hemorrhage.¹² Our findings of EICG angiography neuroendoscopically confirmed the previous postmortem findings. ICG endoscopy is useful for discerning the fine edge of the internal carotid artery and checking the patency of the intercavernous sinus and the cavernous sinus behind the dura mater.¹¹ Similarly, EICG angiography could identify previously invisible hidden moyamoya vessels.

Previous radiological and pathological studies have determined the presence of fragile periventricular moyamoya vessels. Endoscopic procedures were performed in some reported patients with MMD with severe IVH, but the observation and description of ependymal tissue did not describe blood flow in the moyamoya vessels.¹⁰ In our cases, EICG angiography could observe the blood flow in the moyamoya vessels and found increased blood velocity and stagnation of periventricular moyamoya vessels.

Two different histological changes occur in MMD vessels: dilatation with thin vessel walls and obstruction by thrombi or mural thickening with or without elastosis or fibrosis.¹³ Therefore, such histopathological changes may be closely associated with the endoscopic changes seen in blood flow. Differences in development of the fragile collaterals connecting to the medullary artery and perforating the choroidal artery and supplying the cortex observed by the JAM Trial may cause the difference in blood velocity.⁴ In other words, the presence or absence of outflow pathway may affect blood velocity. If fragile collaterals communicate with the medullary artery, blood velocity may increase; if not, the blood flow may grow stagnant.

Digital subtraction angiography can provide superior performance as diagnostic imaging but may not reveal periventricular moyamoya vessels in detail. Consequently, the present finding of EICG angiography, that the blood flow in the dilated fragile collateral vessels was stagnant compared to other vessels, is extremely interesting. Local stress of blood flow in the dilated abnormal vessels induces rupture directly, or obstruction of blood flow with microthrombus may cause hemorrhage. Therefore, more EICG angiographic data may help determine the causes of hemorrhagic MMD.

The occurrence of IVH involves two distinct mechanisms: subependymal hemorrhage rupturing into the ventricle and rupture of intraventricular aneurysms.¹⁴ The former mechanism may have occurred in our case 1, based on the finding of hidden moyamoya vessels in the subependyma. These hidden fragile periventricular collaterals may have been the origin of the IVH. In this case, selection of direct bypass may make sense based on data presented in a paper for the JAM Trial.² The latter mechanism may have occurred in our case 2 because the IVH was caused by the rupture of intraventricular aneurysms. In this case, endovascular embolization or endoscopic clipping may be a therapeutic choice for the rupture of intraventricular aneurysms.¹⁵ Therefore, EICG angiography may become one of the solutions to determine mechanisms of the occurrence of IVH and choose a treatment option.

Lessons

In conclusion, EICG angiography was useful for real-time imaging, and its high spatial resolution facilitated detection of the fragile periven-

tricular collaterals in patients with MMD, especially invisible moyamoya vessels hiding in the periventricular subependyma. Consequently, EICG angiography was valuable for characterization of blood flow in moyamoya vessels.

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Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Koizumi, Hide. Acquisition of data: Koizumi, Hide, Yamamoto, Handa, Komai. Analysis and interpretation of data: Koizumi. Drafting the article: Koizumi, Hide, Kumabe. Critically revising the article: Kumabe. Reviewed submitted version of manuscript: Kumabe. Administrative/technical/material support: Hide, Yamamoto, Hyakutake, Komai, Kumabe. Study supervision: Asari.

Supplemental Information

Videos

Video 1. <https://vimeo.com/722576780>.

Video 2. <https://vimeo.com/722578903>.

Correspondence

Hiroyuki Koizumi: Kitasato University School of Medicine, Kanagawa, Japan. koizumi-h@cl.cilas.net.