IN 1957, Takeuchi and Shimizu29 in Japan published the first description of moyamoya disease in the medical literature, using the term “hypogenesis of bilateral internal carotid arteries.”27 The authors did not classify the findings as a new disease entity. The suggestion that moyamoya was a new disease was proposed to the Japanese medical community in 1963 by Suzuki, et al.28 The first report of moyamoya in the English literature was published by Kudo18 in 1968. In 1965, Krayenbuhl and Yaşargil’s17 textbook of cerebral angiography contained an illustration of moyamoya disease, but the authors referred to it as “capillary telangiectasia.”

Abbreviations used in this paper: ACA = anterior cerebral artery; EC–IC = extracranial–intracranial; EDAS = encephaloduroarteriosynangiosis; EMS = encephalomyosynangiosis; ICA = internal carotid artery; OA = occipital artery; MCA = middle cerebral artery; STA = superficial temporal artery.

Naming of Moyamoya Disease

The term “moyamoya” was introduced by Suzuki and Takaku27 in 1969 to characterize the angiographic appearance of the condition, which shows a collateral network of blood vessels at the base of the brain. As is described in the text, the Japanese word moyamoya means “something hazy just like a puff of cigarette smoke drifting in the air.” Although the official name of the disease is “spontaneous occlusion of the circle of Willis,” moyamoya disease is the term most commonly used. Based on 20 cases, Suzuki and Takaku described the angiographic patterns of moyamoya and related them to the clinical picture of the disease, although its pathophysiological features were still unknown.

From the clinical standpoint, the disease affects mostly children; however, an adult form also occurs. The findings in children include stroke, recurrent transient ischemic attacks, muscular weakness or paralysis, and seizures. Hemorrhagic presentation is more common in adults. Although the Japanese Research Committee on Spontaneous Occlusion of the Circle of Willis of the Ministry of Health and Welfare started research into moyamoya in 1977, the origin of the disease is still unknown. In 1999 Ikeda, et al.,8 mapped the gene loci for the familial type of the disorder to 3p (MYMY1), 17q25 (MYMY2; 607151), and 8q23.
(MYMY3; 608796). As mentioned by Yabumoto,\(^\text{12}\) in 1967 Pool, et al., reported that moyamoya disease is often associated with intracranial aneurysms.

**Treatments for Moyamoya Disease**

**Common Surgical Options**

Several surgical procedures, which can be classified as direct and indirect bypass methods, have been proposed for the treatment of this disease. The direct bypass techniques that have been proposed are vein grafts\(^\text{9}\) and EC–IC arterial anastomoses (STA–MCA and OA–MCA anastomoses).\(^\text{2,23}\) The indirect techniques are as follows: 1) EDAS;\(^\text{22}\) 2) EMS;\(^\text{12}\) 3) encephaloarteriosynangiosis;\(^\text{20}\) 4) the use of cranial bur holes;\(^\text{3}\) and 5) transplantation of omentum.\(^\text{14}\) Other options such as cervical carotid sympathectomy and superior cervical perivascular ganglionectomy have also been proposed.\(^\text{28}\) In this paper we describe the history of the development of surgical techniques to treat moyamoya disease.

**Cervical Carotid Sympathectomy and Superior Cervical Ganglionectomy**

After describing the angiographic patterns of moyamoya and relating them to its clinical presentation, Suzuki and Takaku\(^\text{27}\) began to think about alternative treatments for these patients, because medical management had not been proven capable of controlling or improving the disease. They decided to perform cervical carotid sympathectomy and superior cervical perivascular ganglionectomy based on studies of adrenergic axons in the walls of arteries and arterioles. Research on superior cervical ganglionectomy in dogs had shown degeneration of adrenergic axons in the cerebral arterial walls after 48 hours, and the disappearance of those axons after 4 days. These authors believed that if they could promote dilation of cerebral arteries and improve the collateral channels, the vascular flow through the brain would increase. With this in mind, Suzuki and colleagues\(^\text{29}\) performed cervical carotid sympathectomy and superior cervical perivascular ganglionectomy in 23 patients (10 children and 13 adults) between 1968 and 1973. In their study they reported good results in improving clinical symptoms, but in most cases the procedure could not prevent the progression of the disease and the deterioration of the angiographic pattern. This series was the first attempt at the surgical treatment of moyamoya.

**Direct Bypass Techniques**

For many years, surgical treatment for occlusive disease of the extra- and intracranial arteries supplying the brain was considered impossible. An EC–IC anastomosis to revascularize the brain was suggested by Fisher\(^\text{1}\) in 1959, but due to inadequate instruments, the surgery was not possible at that time. The introduction of microsurgical techniques by Jacobson and Suaraz\(^\text{25}\) in 1966 permitted the application of those principles to neurosurgery by Yaşargil,\(^\text{23}\) Reichman,\(^\text{24}\) and Sundt, et al.\(^\text{26}\) As reported by Ishii, et al.,\(^\text{9}\) the first STA–MCA anastomosis was performed in 1967 by Donaghy and Yasargil. This newer surgical technique prompted surgeons to start thinking about using surgically created anastomotic channels between the brain and the extracranial vessels as a reasonable treatment to increase cerebral blood flow in patients with moyamoya disease.\(^\text{16}\)

**The EC–IC Bypass**

Until 1975, most of the 700 reported cases of ischemic moyamoya disease were treated conservatively. Some medications, such as steroid drugs, vasodilating agents, and low-molecular-weight dextran had been tried without success.\(^\text{14}\)

The use of EC–IC arterial bypass surgery to improve cerebral blood flow in patients with moyamoya disease was proposed for the first time in 1973 by Kikuchi and Karasawa\(^\text{13}\) in Japan and in 1975 by Krayenbühl\(^\text{16}\) in Europe. Neurovascular surgeons expressed their reservations about applying this surgery to moyamoya, due to the obscurity of the hemodynamic pattern of the disease and the increased chance of complications compared with other forms of occlusive cerebrovascular disease.

As reported by Donaghy,\(^\text{7}\) the first STA–MCA bypass for moyamoya disease was performed by Yaşargil in 1972. In this case, a 4-year-old boy who suffered right hemiplegia and anarthria after awakening from a coma was admitted to the author’s neurosurgery clinic in June 1972. In an attempt to improve the patient’s anarthria by increasing cerebral blood flow, Dr. Yaşargil performed an EC–IC arterial bypass. The procedure consisted of an end-to-end anastomosis between the STA and an insular branch of the MCA. The 2-year follow-up evaluation demonstrated improvement of the patient’s right-sided weakness and of his tongue and speech disturbance. The angiography studies demonstrated improvement in the vascularization of the hemisphere through the anastomosis.\(^\text{16}\) In subsequent years Karasawa, et al.,\(^\text{13}\) obtained good results with the procedure in 23 patients.

In patients with a small STA, an OA–MCA anastomosis has been used as an alternative to the STA–MCA anastomosis.\(^\text{25}\)

**Vein Graft Bypass**

In November 1981, a 30-year-old woman who was experiencing left hemiparesis and hemihypesthesia was admitted to the Suiharago Hospital in Japan. She exhibited several areas of infarction on head computerized tomography scans as well as multiple occlusive lesions of the cerebral arteries. Two months later she presented with a large infarct of the right ACA accompanied by complete occlusion of the ipsilateral ICA, and was transferred to the Niigata University Hospital in Japan.

The neurosurgical team of Ryoji Ishii decided to perform a revascularization procedure in an attempt to avoid additional infarction of the contralateral side.\(^\text{9}\) The surgical procedure consisted of an STA–MCA anastomosis plus an STA–ACA anastomosis, which were completed using an interposed cephalic vein graft. These surgeons’ decision was based on an account by Lougheed, et al.,\(^\text{39}\) of bypass surgery in which vein grafts were used, and on attempts to revascularize the distal portions of the ACA reported by Ito.\(^\text{40}\) In the procedure, which Ishii, et al., performed in March 1982, they interposed a segment of the cephalic vein between the parietal branch of the STA and the callosal-
marginal artery in an end-to-end anastomosis. Although the authors reported excellent filling of the left ACA through the vein graft, they provided no information about the post-operative or follow-up clinical status of the patient.

**Indirect Bypass Techniques**

Many authors have reported the technical difficulties of performing a direct bypass, especially in children. These obstacles include the size of the vessels and fear of damaging the transdural anastomoses between the distal STA and the cortical arteries. These concerns triggered research into alternative ways to perform cerebral revascularization. Grafts and transplants were attempted in which the soft tissues of the scalp (muscles and galea) or transplantation of omentum were used to reach new collateral channels on the cortical surface.

**Development of EMS Surgery**

The EC–IC bypass procedures depend on the patency and suitability of the STAs or OAs. Because direct anastomosis was the only treatment for moyamoya disease during the early 1970s, patients who lacked a good donor vessel for this procedure presented a challenge to surgeons. Therefore, the development of other methods of revascularization for moyamoya disease was investigated.

The clinical and experimental basis for using EMS in moyamoya was based on the reports of Henschen, Tsubokawa, et al., and Goldsmith, et al. Henschen described a cerebral arterial bypass in which the temporal muscle was used as a donor organ. This procedure was performed in a patient who had occlusion of both ICAs and who was suffering from seizures. The surgery reduced the frequency of the seizures and Henschen named it “encephalo-myo-synangiosis.” In 1964 Tsubokawa, et al., reported a surgery in which a dural graft containing branches of the meningeal artery was laid onto the surface of the brain of a patient with ischemia. In 1973 Goldsmith, et al., reported good results in experiments in which they transplanted omentum onto the brain surface.

Karasawa and colleagues were the first to attempt to produce indirect cerebral vascularization by using a graft to treat moyamoya disease. Their study was based on evidence obtained in two patients in whom STA–MCA anastomoses failed or could not be performed. In these patients, new collateral channels in the MCA territory developed from the external carotid artery. Karasawa, et al., chose the temporal muscle because of its rich blood supply. The procedure consisted of suturing the temporal muscle to the dura mater. It was performed in 10 patients between December 1975 and December 1976, with good results.

**Intracranial Transplantation of Omentum**

Attempts to improve the circulation of ischemic organs date back to 1936, when O’Shaughnessy used transplants of omentum to increase blood flow to the heart. Goldsmith and colleagues were the first to apply the omentum transplantation technique experimentally in the nervous system. They transposed omentum obtained from under the skin of a dog’s abdomen to the brain and spinal cord. A procedure based on microsurgical techniques was also developed by Yaşargil, et al., in 1974 and yielded good results.

Based on the previously described results, Karasawa, et al., performed the first intracranial transplantation of omentum for moyamoya disease in February 1978. The patient was a 56-year-old woman who presented with blindness, left hemiplegia, and right hemiparesis. An angiographic study demonstrated obstruction of the terminal portions of the ICA, ACA, and MCA bilaterally. Surgery was performed, and consisted of a frontolateral parietooccipital skin incision, preserving the STA and the associated superficial temporal vein, followed by craniotomy. A resection of the anteriorinferior border of the bone flap was included for insertion of the omentum. A midline laparotomy was performed and a 13 × 13–cm segment of omentum containing perforating vessels of the gastroepiploic artery and vein was removed. An end-to-end anastomosis between the gastroepiploic arteries and the STA was performed, followed by the same procedure between the superficial temporal and gastroepiploic veins. Dural opening and arachnoid incision permitted spreading of the transplanted omentum on the yellow cortical surface. The patient was able to walk with a cane after undergoing physical therapy, but her blindness did not improve. She was free of cerebrovascular events and used no medication in the subsequent 2 years.

**Development of EDAS Surgery**

In 1979, STA–MCA anastomosis and EMS were the best surgical options for the management of moyamoya, despite reports of neurological deterioration in pediatric patients after STA–MCA bypass and seizures following EMS. Surgical alternatives and complementary procedures were still being evaluated.

In 1979, Matsushima and colleagues developed EDAS to treat moyamoya disease. They based the development of this procedure on several reports. The first was an attempt in 1964 by Tsubokawa, et al., to revascularize the brain of a 6-year-old girl who suffered cerebral ischemia after intracranial arterial thrombosis. The surgery was performed by inserting a dural graft containing the middle meningeal artery into the ischemic cerebral tissue. Good results were achieved. Another factor that Matsushima considered was that Ausman, et al., reported the development of anastomotic channels between the scalp and cortical surface after STA–MCA anastomosis. Clinical data also supported the suggestion that in moyamoya disease the vasculature forms collateral channels more easily than in normal tissue. Another crucial factor was Matsushima’s experience with repeated cranial operations, which made him suppose that vascular anastomosis occurs naturally between the adhesions of the dura mater and the brain. These reports all supported the principle behind the development of EDAS as a method for affixing to the cerebral cortex a type of tissue with a rich blood supply.

Matsushima and colleagues planned the first EDAS procedure on September 18, 1979, at a small local hospital in Japan to treat a 9-year-old boy who suffered from moyamoya disease. The boy presented with attacks of weakness in his extremities, accompanied by loss of consciousness, seizures, and a history of immature behavior. After left hemiparesis developed, the patient underwent an angiographic study, which indicated moyamoya disease. A right-sided EDAS in which the parietal branch of the right STA was used as the donor vessel was performed, with no complica-
tions. The patient's cognitive skills and attacks of weakness improved during the subsequent months. The 6-month follow-up angiographic study showed remarkable revascularization of the brain.

The procedure was named “encephalo-duro-arterio-synangiosis” because of the assumption that the operation would cause the formation of spontaneous anastomoses between the arteries of the cerebral cortex, dura mater, and scalp. The procedure was awarded the prize for the best poster of the 10th annual meeting of the Japanese Society of Pediatric Neurosurgery and was published in the official journal of the society.21

Development of Multiple Cranial Bur Holes for Cerebral Revascularization

The EMS, EDAS, and STA–MCA anastomosis treatments induce vascularization of the cerebral surface, especially in the territory of the MCA, but the vascularization is poor in the territories of the anterior and posterior cerebral arteries.30 This problem was a concern to Masataka Endo and the surgical team of the Kitasato University School of Medicine in Kanagawa, Japan. An answer arose in 1984 based on the case of a 10-year-old boy who presented with intraventricular hemorrhage. Due to the child’s clinical circumstances, intraventricular drains were inserted bilaterally through the frontal region. Three months later, a marked neovascularization in the frontal cerebral cortex via the frontal bur holes was noted. An EMS was performed in June 1985, and the 6-month follow-up angiograms demonstrated good filling of the MCA and ACA territories and improvement of the child’s intelligence quotient.3

The aforementioned case provided support for the first planned surgery of this type, on January 21, 1986. In that case, a 12-year-old girl underwent bilateral EMS and additional frontal bur holes were drilled during the same operation. After using the Kocher point to make the bur holes and opening the dura mater in a cruciate manner, the arachnoid membrane was stripped from the brain. Follow-up angiographic studies obtained at 8 months demonstrated neovascularization through the EMS and frontal bur holes. The authors reported good results from the procedure in five other patients and suggested the placement of occipital bur holes to improve the vascular supply to the posterior cerebral artery territory.3

Conclusions

The incidence of moyamoya disease in Japan is one per million per year, and the incidence is believed to be one tenth of this value in Europe. Almost five decades after its discovery, the origin of moyamoya disease is still unknown; some reports indicate a genetic basis and others an acquired environmental exposure. Fifty years of research have provided a variety of surgical and medical options for the management of moyamoya in affected patients. Some of these procedures have been abandoned, others have served as the basis for the development of better ones, and many are still in use today. The efforts of many individuals have led to a number of options for treating patients with moyamoya disease. Decisions about which procedure to use should be made on a case-by-case basis, after studying the patient’s presenting symptoms and angiographic pattern.

References

The history of neurosurgical procedures for moyamoya disease


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