Radiological findings in Moya Moya

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Learning objectives

Moyamoya disease is a unique chronic progressive cerebrovascular disease characterized by bilateral stenosis or occlusion of the arteries around the circle of Willis with prominent arterial collateral circulation formation.

To learn more about this disease we propose the following objectives:

- Explain the **Moyamoya disease**, a rare disease in our territory for whom diagnosis is essential the imaging technics.
- Describe the clinical features of the disease.
- Assess the complications of the disease.
- Mention the diagnostic criteria of moyamoya disease and differentiate it from "the probable moyamoya disease" and "the moyamoya syndrome".
- Identify the imaging features that help differentiate the moyamoya disease from other vascular lesions and the methods of imaging we need to use to characterize the disease.
- Discuss the imaging findings that should be included in radiology reports in patients with moyamoya disease.
- Compare between the different diagnostic methods, from the most invasive ones like the conventional angiography to other less invasives like MRI.
- List the different therapeutic methods available.
Background

INTRODUCTION

Moyamoya disease is a unique chronic progressive cerebrovascular disease characterized by bilateral stenosis or occlusion of the arteries around the circle of Willis with prominent arterial collateral circulation. Fig. 1 on page 12.

"Moyamoya" is a Japanese word meaning puffy, obscure, or hazy like a puff of smoke in the air. Thus, the term was used to describe the smoky angiographic appearance of the vascular collateral network.

Moyamoya disease was first described in Japan in 1957. Many similar cases have subsequently been reported, mainly in Japan and other Asian countries. The disease is found less frequently in North America and Europe.

ETIOLOGY

The etiology of moyamoya disease is unknown. The high incidence among the Japanese and Asian population, together with a familial occurrence of approximately 10%, strongly suggests a genetic etiology.

• Accumulating evidence suggests that the RNF213 gene on chromosome 17q25.3 is an important susceptibility factor for moyamoya disease in East Asian populations.
• In other studies, although, have linked familial moyamoya disease to chromosomes 3p24.2-p26, 6q25, 8q23, and 12p12.

Although the mode of inheritance is not established, one study suggested that familial moyamoya is an autosomal dominant disease with incomplete penetrance.

EPIDEMIOLOGY AND AGE DISTRIBUTION

In epidemiologic surveys conducted in Japan, the following observations have been made

• The annual incidence of moyamoya is 0.35 to 0.94 per 100,000 population
• The prevalence of moyamoya is 3.2 to 10.5 per 100,000 population
• There is a female predominance, with a male-to-female ratio of 1:1.8 to 1:2.2
The incidence among all patients with moyamoya in Europe appears to be about 1/10th of that observed in Japan.

Moyamoya disease and moyamoya syndrome occur in children and adults of all ages, although presentation in childhood is rare.

- Some studies found a major peak in the 10 to 14 year old age group and a lesser peak in the 40 to 49 year old group.

ASSOCIATED CONDITIONS

Classic angiographic findings of moyamoya vessels have been demonstrated in patients with other medical conditions.

Patients with the angiographic appearance of moyamoya and no known risk factors are considered to have moyamoya disease, while those with one of the well-recognized associated conditions are classified as having "moyamoya phenomenon" or "moyamoya syndrome". Fig. 2 on page 12, Fig. 3 on page 13.

Some of the conditions associated with moyamoya are included in the Table 1 on page 14.

CLINICAL FEATURES

The clinical manifestations of moyamoya are variable and include transient ischemic attack (TIA), ischemic stroke, hemorrhagic stroke, and epilepsy.

The expression of disease may differ by age at the time of diagnosis Table 2 on page 15.

Among symptomatic patients with moyamoya disease, some have only one or a few events, while others have multiple recurrences.

In children, symptomatic episodes of ischemia may be triggered by exercise, crying, coughing, straining, fever, or hyperventilation.

There are case reports of patients with moyamoya who develop dystonia, chorea, or dyskinesia, but these appear to be uncommon manifestations of moyamoya.
PATHOLOGY

Brain tissue of patients with moyamoya disease usually reveals evidence of prior stroke. However, the cause of death in most autopsy cases is intracerebral hemorrhage.

Although large vessel stenosis and occlusion are the hallmark of this disease, extensive territorial infarction is uncommon.

Vascular stenosis

Pathologic vascular lesions appear in the large vessels of the circle of Willis and in the small collateral vessels. Bilateral concentric stenosis or occlusion is consistently found in the distal internal carotid arteries and the proximal anterior and middle cerebral arteries. [Fig. 1 on page 12, Fig. 4 on page 16]. Less frequently, the posterior circulation is affected, especially the posterior cerebral artery.

Collateral vessels

One of the hallmarks of moyamoya disease is the presence of a collateral meshwork of overgrown and dilated small arteries, the moyamoya vessels, that branch from the circle of Willis. [Fig. 1 on page 12, Fig. 4 on page 16].

Leptomeningeal vessels are another source of collaterals in moyamoya. As a result of intracranial internal carotid artery stenosis, leptomeningeal anastomoses may develop among the three main cerebral arteries (middle, anterior, and posterior).

Aneurysms

Cerebral aneurysms have been associated with moyamoya disease in a number of reports.

Large artery aneurysms can develop at vessel branching points in the circle of Willis and cause subarachnoid hemorrhage when they rupture.

- In patients with unilateral moyamoya, these aneurysms are found most commonly in the anterior communicating artery/anterior cerebral artery complex.
- In patients with bilateral moyamoya, aneurysms are more often located in the basilar artery.
Aneurysms can also arise from the small collateral moyamoya vessels. These small vessel aneurysms are the major cause of parenchymal (intracerebral) hemorrhage in moyamoya disease.

Extracranial involvement

In patients with moyamoya disease, stenosis may also affect the extracranial and systemic arteries, including the cervical carotid, renal, pulmonary, and coronary vessels. Involvement of the renal arteries has been the most frequently reported. Fig. 5 on page 16.

CLASSIFICATION

Suzuki stages

Suzuki and colleagues followed patients with moyamoya disease and classified the angiographic progression into six stages. Table 3 on page 17.

DIAGNOSIS

The diagnosis of moyamoya disease is based upon the characteristic angiographic appearance of bilateral stenoses affecting the distal internal carotid arteries and proximal circle of Willis vessels, along with the presence of prominent basal collateral vessels.

TCMD

CT studies demonstrate nonspecific findings resultant from ischemia, such as parenchymal low-density spots, brain atrophy and ventricular dilatation.

- In the acute phase the TCMD is important for the detection of brain infarction and hemorrhage in patients with moyamoya. Fig. 6 on page 18.

- In the chronic phase we can usually see the dilatation of the sulci accompanied by focal ventricular enlargement indicating volume loss and atrophy. Fig. 7 on page 18.

CT angiography (CTA) can also noninvasively demonstrate the abnormal vessels of moyamoya disease, including the collateral moyamoya vessels in the basal
ganglia. In moyamoya disease the stenotic or occlusive lesion occurs not only at the supraclinoid portion of the ICA but also at the proximal intracavernous portion.

The main advantages compared to the MRA is the greater accessibility and reduced scanning time, in addition to completing the initial assessment studies TSA and perfusion.

MRI

MR imaging findings of moyamoya disease are well known; MR imaging can reveal stenosis or occlusion of the distal internal carotid artery and moyamoya vessels with signal voids in the basal ganglia, as well as ischemia, infarction, atrophy, and ventriculomegaly.

A variety of pulse sequences are used for MR imaging, including FLAIR imaging, diffusion-weighted imaging, perfusion MR imaging, and contrast-enhanced MR imaging.

Diffusion and perfusion MR techniques, is superior to CT scan for detection of small and/or acute ischemic brain lesions. Fig. 8 on page 19.

T2 weighted images seem to be better for visualizing the stenotic arteries directly, Fig. 9 on page 20, Fig. 10 on page 21, but FLAIR images are better for showing subtle parenchymal changes.

In patients with moyamoya FLAIR images and post contrast T1 images may show a linear pattern of increased signal in the leptomeninges and perivascular spaces. This pattern has been termed the “ivy sign”, since it resembles the appearance of ivy creeping on stones. The probable cause is slow retrograde collateral flow through engorged pial vessels via leptomeningeal anastomosis. Observational data suggest the ivy sign is correlated with decreased cerebrovascular reserve.

Gradient echo (T2*) MRI sequences and susceptibility weighted images (SWI) can show prominent hypointense signals in the draining veins within areas of impaired perfusion and may detect asymptomatic cerebral microbleeds the collateral vessels formation.
Angio-MR imaging has a great advantage of demonstrating blood vessels without requiring the use of contrast medium. The stenosis or occlusion of the carotid fork is demonstrated with MR-angiography and characteristic moyamoya vessels are apparent in most patients. Fig. 11 on page 22, Fig. 12 on page 23.

Brain perfusion in MMD demonstrates impaired perfusion in ischemic areas and in areas irrigated by the collateral vessels. Fig. 13 on page 24.

Angiography

Angiography is still the reference scan for diagnosis of intracranial stenosis, providing direct information on the degree of collateral circulation.

Although now used less frequently than MRA and CTA, conventional cerebral angiography is the gold standard for the diagnosis of moyamoya disease.

Characteristic angiographic findings include occlusion or stenosis of the supraclinoid portion of the ICA and extensive parenchimal, transdural, and leptomeningeal collateral vessels suppling the ischemic brain. Fig. 1 on page 12, Fig. 4 on page 16.

Performance of conventional angiography is still considered necessary for a definitive diagnosis. Angiography however is risky for patients with suspected moyamoya disease, since the frequency of complications resulting from this procedure is high and can include death from brain ischemia. Therefore, a safer, easier method is needed for diagnosis of moyamoya disease.

AngioRM Vs Angiography

MR can reveal stenosis or occlusion of the distal internal carotid artery and MR angiography (MRA) can demonstrate stenotic or occlusive lesions in the distal internal carotid arteries and the arteries around the circle of Willis. In addition, MRA can visualize the collateral "moyamoya vessels" in the basal region, although it is less sensitive to smaller vessel occlusion than conventional cerebral angiography. Nevertheless, due to its high diagnostic yield and noninvasive nature, MRA has supplanted conventional angiography in most centers as the primary imaging modality to evaluate moyamoya syndrome.

MR imaging shares a disadvantage of all cross sectional imaging methods: Blood vessels are not depicted as continuous structures. In contrast, one of the stengths
of MR angiography is that blood-vessel images are a composite of many MR imaging planes and show each vessel in its entirety. The degree of stenosis may be overestimated with MR angiography. However it seems to be an alternative diagnostic method with which to assess steno-occlusive lesions in patients with moyamoya disease.

AngioRM should be performed first when moyamoya disease is suspected, and angiography should be reserved for further examination of if surgery is planned.

Hemodynamic studies

Transcranial Doppler ultrasonography (TCD) provides a noninvasive way to evaluate intracranial hemodynamics by measuring blood flow velocity in large intracranial vessels at the circle of Willis. A focal increase in velocity usually suggests large artery stenosis.

In patients with suspected moyamoya disease, TCD has been used in the initial evaluation.

Although supporting evidence is limited, additional methods that may be useful to determine the extent of inadequate resting brain perfusion and blood flow reserve in patients with moyamoya disease prior to and after treatment include the following:

- Perfusion CT
- Xenon-enhanced CT
- Perfusion-weighted MRI
- Positron emission tomography (PET)
- Single-photon emission CT (SPECT) with acetazolamide challenge

Diagnostic criteria

Diagnostic criteria for idiopathic moyamoya disease proposed by a Japanese research committee include the following major requirements:

- Stenosis or occlusion at the terminal portion of the internal carotid artery and at the proximal portion of the anterior and middle cerebral arteries on magnetic resonance angiography (MRA)
- Abnormal vascular networks in the vicinity of the occluded or stenosed areas on MRA; these networks can also be diagnosed by the presence of multiple flow voids on brain MRI
• Angiographic findings are present bilaterally; cases with unilateral angiographic findings are considered probable. Fig. 14 on page 25.
• The following conditions should be excluded. Table 4 on page 26.

The diagnostic criteria for conventional cerebral angiography are similar to those for MRA.

Screening studies

Indications for angiographic screening studies in family members of patients with moyamoya are not well defined.

In individuals with a strong family history of moyamoya disease or those with medical conditions that predispose to moyamoya syndrome, the utility of angiographic screening is unclear, particularly since available medical and surgical treatment of asymptomatic moyamoya disease is of uncertain benefit.

TREATMENT

Acute management

For children and adults with moyamoya and acute stroke, acute treatment is mainly symptomatic and directed towards reducing elevated intracranial pressure, improving cerebral blood flow, and controlling seizures. Ventricular drainage and/ or hematoma removal is often required for patients with intracerebral hemorrhage. Measures to minimize pain, crying, and hyperventilation in children may reduce the risk of worsening ischemia.

Unfortunately, there is no acute intervention that is known to improve stroke outcome in patients with moyamoya. Guidelines from the ACCP suggest aspirin over no treatment as initial therapy for children with acute arterial ischemic stroke secondary to moyamoya.

Secondary prevention

There is no curative treatment for moyamoya disease. Secondary prevention for patients with symptomatic moyamoya is largely centered on surgical revascularization techniques. In patients with moyamoya syndrome, it is also important to search for and treat the underlying condition. The main example is sickle cell disease, where transfusion therapy is effective in primary and secondary stroke prevention.
Antiplatelet agents, usually aspirin, have been used to treat some patients with moyamoya disease or moyamoya syndrome, particularly those who are asymptomatic or have mildly symptomatic ischemic disease, or those considered to have a high risk for poor surgical outcome.

Oral anticoagulants are seldom used in children with ischemic moyamoya disease because of the risk of hemorrhage after incidental trauma and because of the difficulty maintaining therapeutic levels. In adults, hemorrhage is the predominant manifestation of moyamoya, and anticoagulation is generally not indicated.

Endovascular embolization has been evaluated in small uncontrolled studies to obliterate ruptured intracranial aneurysms or pseudoaneurysms associated with moyamoya disease.

Revascularization surgery

The goal of surgical treatment for moyamoya disease is to reduce the risk of ischemic stroke by improving the cerebral circulation. Thus, surgical procedures are used most often for patients with ischemic-type moyamoya who have cognitive decline or progressive symptoms.

Surgical techniques can be divided into direct and indirect revascularization procedures and their combinations.

- Direct revascularization is thought to improve the angiographic and cerebral blood flow abnormalities. Superficial temporal artery to middle cerebral artery (MCA) bypass or middle meningeal artery to MCA bypass are the most common direct techniques.
- Indirect revascularization is preferred in cases where the cortical recipient artery is not available for anastomosis. Indirect techniques enhance the collateral system and include the following. Table 5 on page 27.
- Combinations of direct and indirect revascularization methods.

Limited evidence suggests that revascularization surgery is more effective in children than in adults, especially in children who present with ischemic symptoms.
Fig. 1: Angiographic findings in moyamoya disease in a 42 years old female

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Axial flair and sagittal T1 weighted images demonstrating an important dilatation of the third and the lateral ventricles with an enlargement of the cerebral aqueduct and stenosis at the superior medullary velum. The fourth ventricle is not dilated. It is a chronic hydrocephalus sequelae of childhood meningitis in an adult patient.

**Fig. 2:** Axial flair and sagittal T1 weighted images. A 57 years male with moyamoya syndrome and chronic hydrocephalus as a sequelae of childhood meningitis

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Fig. 3: Axial T1 weighted images with intravenous contrast. A 57 years male with moyamoya syndrome and chronic hydrocephalus as a sequelae of childhood meningitis.
Table 1: Moyamoya syndrome causes

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Table 2: The expression of the disease by age at the time of diagnosis

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Fig. 4: Angiographic findings in moyamoya disease in a 42 years old female

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**Fig. 5:** Renal angiography findings in a 42 years female with moyamoya disease

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<thead>
<tr>
<th>SUZUKI STAGES</th>
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<tr>
<td><strong>STAGE I</strong></td>
<td>&quot;Narrowing of the carotid fork&quot;</td>
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<td>• Narrow ICA bifurcation</td>
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<td><strong>STAGE II</strong></td>
<td>&quot;Initiation of the moyamoya&quot;</td>
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<tr>
<td></td>
<td>• Dilated ACA, MCA and narrowed ICA bifurcation with moyamoya change</td>
</tr>
<tr>
<td><strong>STAGE III</strong></td>
<td>&quot;Intensification of the moyamoya&quot;</td>
</tr>
<tr>
<td></td>
<td>• Further increase in moyamoya change of the ICA bifurcation and narrow ACA and MCA</td>
</tr>
<tr>
<td><strong>STAGE IV</strong></td>
<td>&quot;Minimization of the moyamoya&quot;</td>
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<td>• Moyamoya change reducing with occlusive changes in ICA and tenous ACA and MCA</td>
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<tr>
<td><strong>STAGE V</strong></td>
<td>&quot;Reduction of the moyamoya&quot;</td>
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<td>• Further decrease in moyamoya change with occlusion of ICA, ACA and MCA</td>
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<td><strong>STAGE VI</strong></td>
<td>&quot;Disappearance of the moyamoya&quot;</td>
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<td>• ICA essentially disappeared with supply of brain from ECA.</td>
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**Table 3:** Suzuky stages

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**Fig. 6:** Axial CT. 56 years male with acute intraparenchymal hemorrhage

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CT scan shows hemorrhage in the right frontotemporoparietal region exerting mass effect on the right lateral ventricle
Fig. 7: Axial CT. 45 years old female with chronic atrophy.

CT shows dilatation of the sulci accompanied by ventricular enlargement indicating volume loss and atrophy.

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Right CMA acute stroke: On the left FLAIR demonstrates a high signal in right frontal lobe. On the middle and right images a DWI and a ADC map showing a high intensity on DWI that loses signal on the ADC. That indicates restriction of the ability of water protons to diffuse extracellularly.

**Fig. 8:** Axial FLAIR, DWI and ADC map. 43 years old female with right CMA acute stroke © - Bilbao/ES
**Fig. 9:** T2 weighted image. A 57 years male with moyamoya syndrome and chronic hydrocephalus as a sequelae of childhood meningitis

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Fig. 10: Axial T2 weighted image. 15 years old male with moyamoya disease.

T2 weighted image shows the occlusion of left CMA and the collateral vessel formation in moyamoya disease.

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Fig. 11: MIP and 3D reconstructions of MR angiography. 15 years old male with moyamoya disease

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Fig. 12: MIP reconstructions of RM angiography. A 57 years male with moyamoya disease

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Fig. 13: MRI perfusion. 15 years old male with moyamoya disease

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Fig. 14: Angio-RM diagnostic criteria.

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Table 4: Conditions that exclude moyamoya disease

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Table 5: Indirect revascularization techniques

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CT: A multidetector CT.

A sequential acquisition technique with 3mm thick reconstructions completed according the results by axial CT after intravenous contrast administration.

Angio-RM: A 1.5 tesla MRI is used to perform exams. Protocol included systematically: A sagittal T1 spin echo acquisition, axial T2 spin echo acquisition, axial FLAIR, DWI, T1 3D pre and postgadolinium injection, TOF, T2 gradient echo or Susceptibility weighted images and brain perfusión.

Arteriography: An arteriography of supra-aortic vessels by puncturing right common femoral artery completed according the results by selective renal vessels arteriography.
Conclusion

- The "Moyamoya Disease" is an entity of low prevalence in Western countries, and is considered the leading cause of stroke in Japanese children (most often female).
- The etiology of moyamoya disease is still unknown, the typical presentation strongly suggests a genetic etiology.
- The diagnosis of moyamoya disease is based upon the characteristic angiographic appearance of bilateral stenoses affecting the distal internal carotid arteries and proximal circle of Willis vessels, along with the presence of prominent basal collateral vessels.
- Nowadays it can be diagnosed by noninvasive techniques like the angioRM; conventional angiography should be reserved for further examination if surgery is planned.
- It is diagnosed after ruling out other possible entities that can develop this angiographic pattern.
- Other techniques such as CT are reserved for the acute ischemic and hemorrhagic complications.
- The goal of surgical treatment for moyamoya disease is to reduce the risk of ischemic stroke by improving the cerebral circulation. Thus, surgical procedures are used.
References


