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A REVIEW ON MOYAMOYA DISEASE: A RARE CAUSE OF STROKE OR TRANSIENT ISCHEMIC ATTACK

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ABSTRACT:

Moyamoya disease(MMD) is a progressive cerebrovascular disorder, a rare cause of Stroke or Transient Ischemic Attack (TIA), characterized by stenosis or occlusion at the base of the brain in an area called the basal ganglia. In Japanese, “Moyamoya” means “puff of smoke” due to the appearance of tiny abnormal intracranial vessels forming a network and showing a small cigarette smoke-like appearance in angiography. Moyamoya disease was first reported in East Asia, especially in the Japanese population in the 1960s and occurs in 1 in per 3,00,000 people, the case was originally reported in Japan. RNF213 (Ring Finger Protein) is a protein-coding gene, which is a susceptible gene in Moyamoya disease and is thought to be involved in mediating protein-protein interactions. Moyamoya disease can occur at any age between ages 30-50 in adults and 5–10 years in children. The treatment includes the usage of Aspirin, Anticonvulsant, calcium channel blockers, etc.

KEYWORDS: Moyamoya disease (MMD), Stroke, Transient Ischemic Attack (TIA), RNF213 (Ring Finger Protein).

INTRODUCTION

Moyamoya disease(MMD) is a progressive cerebrovascular disorder, a rare cause of Stroke or Transient Ischemic Attack (TIA), characterized by stenosis or occlusion at the base of the brain in an area called the basal ganglia. It mainly blocks the terminal portion of the internal carotid artery and their branches sometimes show abnormal net-like vessels bilaterally in angiographic findings, then the inadequate blood supply to the brain leads to reduced oxygen supply to the brain and the reduced oxygen supply shows the sign of the Moyamoya disease. The incidence of this rare disease was reported in East Asia, especially Japan's peoples are most susceptible to this disease. In Japanese "Moyamoya" means "puff of smoke" due to the appearance of tiny abnormal intracranial vessels forming a network and showing a small cigarette smoke-like appearance in angiography. RNF213 (Ring Finger Protein) is a protein-coding gene, which is a susceptible gene in Moyamoya disease and is thought to be involved in mediating protein-protein interactions. The stages of Moyamoya were classified as Stage I-IV, Stage I: narrowing of the internal carotid artery, Stage II: Moyamoya vessels develop at the base of the brain, stage III: the worsening of the Moyamoya vessels, Stage IV: Increase in collateral vessels from the scalp and decreasing of Moyamoya vessels.

SIGNS AND SYMPTOMS:

Moyamoya illness can strike adults between the ages of 30 and 50 and Children between the ages of 5 and 10.

Children with Moyamoya disease may present with conditions related to, the reduced blood supply to the brain including,

- Transient ischemic attack (TIA),
- Stroke
- Headache
- Numbness or weakness in both limbs
- Difficulty in walking and
- Progressive delay in growth.

Adults show signs and symptoms of

- Brain ischemia
- Hemorrhage
- High blood pressure is also seen in adults
- Difficulty in speaking
- Paralysis that can affect one side of the body
- Headache is also a common symptom
- Cognitive impairments
- learning impairments
- Seizures
- Also have a greater tendency to develop intracranial hemorrhage than children.

EPIDEMIOLOGY:

Moyamoya disease was first reported in East Asia, especially in the Japanese population in the 1960s and occurs in 1 in per 3,00,000 people, the case was originally reported in Japan and then reported elsewhere in Asia, Europe, North, and South America, and also in Western countries. The highest incidence is in Japan (0.35/1 lakhs), and the incidence in Western countries is 1/10 that of Japan. The incidence in India is 2-3/1,00,00 per year. Female is more affected than Male and the Male: Female ratio is 2:1. The occurrence of this disease is larger in 1st decade (age 11-20) and have a smaller peak in the age 30-49years.10-15 % of this disease has a familial form.

ETIOLOGY:

The primary cause of Moyamoya disease was unknown. However, it is known that the disorder may appear as a primary disorder that may have genetic determinants, RNF213 (Ring Finger Protein) is a protein-coding, which is a susceptible gene in Moyamoya disease and is thought to be involved in mediating protein-protein interactions. Conditions like genetic predisposition and environmental stimuli. The associated conditions like Immunologic: Grave's disease/thyrotoxicosis, Infections like Leptospirosis and Tuberculosis, Hematologic disorders: Aplastic anemia, sickle cell anemia, and lupus anticoagulant, Congenital syndromes: Apert syndrome, Down syndrome, tuberous sclerosis, Turner syndrome, NF-1& Hirschsprung disease, Vascular diseases: Atherosclerosis, fibromuscular dysplasia & hypertension, Others: Head injury, Pituitary tumor, craniopharyngioma.

PATHOPHYSIOLOGY:

Progression of the disease: The Moyamoya disease causes the narrowing of the internal carotid artery, then the Moyamoya vessels origins at the base of the brain area called basal ganglia, due to these the increased collateral vessels from the scalp, and then it causes complete blockage of internal carotid arteries. The primary lesion in Moyamoya disease is progressive fibro cellular thickening of fibro cellular materials, but without lipid or calcification as seen in atherosclerosis. The internal elastic lamina becomes enfolded, redundant, and fragmented. The media is thinned, with a diminished number of smooth muscle cells, and no inflammatory changes occur. Sometimes temporal arteries may be affected. The genetic cause of this disease is due to the smooth muscle proliferation that is associated with ACTA2 mutation and is a key mechanism of vascular occlusion in familial Moyamoya disease.

The susceptible gene in Moyamoya Disease: RNF213 (Ring Finger Protein) the protein-coding gene, is a susceptible gene in Moyamoya disease. The variant form of RNF213, called p. R4810Kwas familial in patients with Moyamoya disease and the exact mechanism of this gene in this disease was unknown there are several in vivo experiments suggesting that the role of RNF213 in Moyamoya was the abnormal development of vascular networks in ischemic conditions. In addition to the preclinical data, clinical data has also shown that exposure to environmental factors, such as an autoimmune response and infection/inflammation, in MMD-susceptible subjects, may be associated with the angiographic features of MMD. For example, autoimmune thyroid disease has been reported in different MMD populations (i.e., pediatric and adult-onset MMD, East Asians, and Westerners). For example, autoimmune thyroid disease has been reported in different MMD populations (i.e., pediatric and adult-onset MMD, East Asians, and Westerners). However, further studies are needed to explain the pathological role of this gene in Moyamoya.

The polymorphisms of mRNAs: MicroRNAs (miRs), also called small noncoding RNAs, negatively alter gene expression by regulating the expression of many proteins through post-transcriptional repression or mRNA degradation. Regulation of proliferation is a key role of miRs in the differentiation, survival, and senescence of various tissues and cells, including stem cells. There is evidence that altered miRs after focal ischemia is functionally important in stroke recovery. Preclinical studies in ischemic stroke have shown that miRs protect against focal ischemia and reperfusion injury by inhibiting oxidants. It is also involved in inflammation, neurogenesis, and angiogenesis.

Cytokines and their polymorphisms: MMD includes (a) growth factors such as vascular endothelial growth factor (VEGF), fibroblast growth factor, platelet growth factor (PDGF), and hepatocyte growth factor; Angiogenesis, including proteinases (MMPs) and their inhibitors, hypoxia-inducible factor-1α and cellular retinoid acid-binding protein-1 (CRABP-1), and (c) cytokines associated with inflammation. Studies on the role of these factors are inconclusive.

DIAGNOSIS:

In most patients, a diagnosis of Moyamoya can be made based on careful evaluation of MRI. Cerebral angiography confirms a diagnosis, determines the exact degree of stenosis in blood vessels, shows existing patterns of blood flow to different areas of the brain, and allows treatment decisions. For these reasons, this is the standard diagnostic tool for this condition. In particular, catheter angiography helps identify important vessels called "transdural collaterals." This is present in some cases and can greatly affect surgical planning and prognosis.

Magnetic resonance imaging (MRI): This test uses magnetic fields and radio waves to make detailed pictures of the brain and brain stem.

Magnetic Resonance Angiography (MRA): This test uses magnetic fields and pulses of radio wave energy. It provides a detailed picture of blood vessels in the body.

Computed Tomography (CT): This procedure uses special X-ray equipment. Create detailed cross-sectional images of internal organs, bones, soft tissues, and blood vessels.

Cerebral angiography: This procedure uses a special contrast agent (contrast agent) and X-rays. This helps doctors check the blood flow in the brain.

Positron emission tomography (PET) scan or single-photon emission computerized tomography (SPECT): In these tests, you're injected with a small amount of safe radioactive material and placed emission detectors over your brain. PET provides visual images of brain activity. SPECT measures blood flow to various regions of your brain.

Electroencephalogram (EEG): An EEG uses several electrodes affixed to your scalp to track the electrical activity in your brain. On an EEG, Moyamoya illness in children frequently shows abnormalities.

Transcranial Doppler ultrasound: Sound waves are utilized in transcranial Doppler ultrasound surgery to produce images of your head and occasionally your neck. This test may be used by doctors to assess the blood flow through your neck's blood arteries.

TREATMENT:

STANDARD TREATMENT:

- **Aspirin**: Aspirin can aid in the prevention of blood clots in the smaller, auxiliary blood arteries.
- **Anticonvulsants**: These drugs can stop seizures induced by Moyamoya illness.
- **Anticoagulants** can thin your blood and stop blood clots. But these medications carry risks, such as the possibility of difficult-to-stop hemorrhage. They are only prescribed in specific circumstances.
- **Calcium channel blockers**: These medications may reduce headaches caused on by Moyamoya illness. But these medications may also decrease blood pressure, which could make stroke risk higher. They are only prescribed in specific circumstances.

TREATMENT IN ADULTS:

Medications such as: may be administered to treat symptoms, lower the risk of stroke, or help control seizures.

Blood thinners: Patients were prescribed aspirin or another blood thinner after being diagnosed with Moyamoya illness if they first had only a little or no symptoms.

Calcium Channels Blockers: This class of drug, often referred to as calcium antagonists, may be useful in treating headache symptoms and may even lessen symptoms associated with transient ischemic episodes. To prevent blood vessel damage in persons with Moyamoya illness, these medications can assist regulate blood pressure.

Anti-epileptic drugs: For those who have experienced seizures, these drugs may be beneficial.

TREATMENT IN CHILDREN:

The progression of Moyamoya illness cannot be slowed down or reversed by medication. But it remains essential to treat signs and symptoms of Moyamoya disease

Calcium channel blockers: The blood arteries are widened by these drugs. They help lower blood pressure. Because of this, severe headaches, strokes, and mini-strokes are less common.

Anti-clotting medications: These medications help to prevent the formation of blood clots by thinning the blood. As a result, the risk of stroke and mini-strokes is reduced. The most frequently prescribed anti-clotting drug by physicians is Aspirin. Many people who receive treatment for Moyamoya continue to take their aspirin prescription daily for the rest of their lives.

Children who experience a stroke and receive a Moyamoya diagnosis may need rehabilitation therapy. A personalized treatment approach may involve physical, occupational, or speech therapy.

SURGERY

Surgery is the only effective long-term treatment for moyamoya illness. The purpose of surgery is to restore normal blood flow to the areas of the brain that this disease has impacted.

Direct Revascularization: A blood vessel outside the skull, typically the temple artery, is joined to a blood vessel inside the skull via direct revascularization (middle cerebral artery). This immediately opens up new blood flow routes.

Indirect Revascularization: Through a procedure known as indirect revascularization, a brain surface artery, muscle, or other tissue is implanted. New arteries will eventually branch off and generate new blood vessels, boosting the blood supply to the brain.

CONCLUSION:

There is growing evidence that MMD is predominantly proliferative, with enhanced yet aberrant angiogenesis and the development of obstruction as a result of endothelial and smooth muscle proliferation, even thou the pathogenic processes of the disease are still unknown (i.e., Moyamoya vessels). Significant, nuanced roles may be played by circulating factor changes, genetic impacts, and environmental variables. Surgery for revascularization is currently the main MMD treatment. However, there is a chance that surgical procedures could result in cerebral hyper perfusion syndrome or perioperative ischemic problems. With a greater understanding of the pathophysiology of MMD, non-surgical methods that target the disease's pathogenesis may be able to halt or reduce its growth. The use of (a) specific trophic factors or chemicals that promote angiogenesis, (b) anti-cancer medications to reduce smooth muscle cell proliferation, (c) retinoids to attenuate growth factor-stimulated smooth muscle cell migration and proliferation, (d) various methods to increase caveolin-1 levels, and (e) stem cell therapy to replace or restore the function of impaired EPCs or SPCs are examples of non-surgical approaches.

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