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Clinical Presentation of Paediatric Endovascular Proliferative Angiopathy of Middle Cerebral Artery

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Abstract
A well-developed girl child presented with two generalised seizures at 4-years of her age. She had well developed brain parenchyma as seen on computerised tomography (CT). She presented again at 11years of her age with hemiparesis and hydrocephalus ex vacuo as seen on brain magnetic resonance imaging (MRI). MR-angiography showed endoluminal steno-occlusive angiopathy of the middle cerebral artery (MCA).
Clinical history probably indicates natural history of endoluminal proliferative-angiopathy where-in, well developed brain parenchyma becomes completely atrophic in 6-7 years. It also reflects significance of angiographic diagnostic neuroimaging and early-intervention. It's a rare case wherein angiopathy remained unilateral & without moyamoya formation. Phylogenetic and molecular anatomy of middle cerebral artery (MCA) explains underlying vascular etiopathological process.
Key to success is table-mapping neurocognitive functions and therapeutic window period for prevention of brain atrophy.

Keywords: Hydrocephalus ex vacuo, MCA-occlusive proliferative angiopathy, Cerebral diagnostic angiography: digital subtraction angiography (DSA), Diminutive neurocognitive functions.

Introduction

Hydrocephalus ex vacuo first described as increase in the volume of cerebrospinal fluid (CSF) caused by encephalic volume loss [1]. Radiologically described as enlargement of cerebral ventricles and subarachnoid spaces. First described in 1957 on angiographic studies as hypoplasia of the bilateral internal carotid arteries [2] (ICA)
Pathological process starts in the angiogenic phase either during a) foetal b) infantile c) neonatal d) early childhood or e) in the adolescent age groups. Proliferative angiopathy is progressive and irreversible; involves intracranial vessels at the skull base. It can result in aneurysmal, dolicho or endoluminal cellular proliferation. Endoluminal proliferation results in luminal stenosis or occlusion. Intra-arterial steno-occlusive process is non inflammatory and non atherosclerotic [3]. Striatal collaterals angiographically seen as "cloudy puff of smoke" which in Japanese language called as Moyamoya Disease [4] (MMD)
Moyamoya in paediatric patients usually have bimodal presentation [5]. Digital subtraction angiography (DSA) presentation correlates with different stages of MMD. Unilateral disease is a rare phenomenon [5].
Contralateral disease develops in up to 40% of patients [6]. Paediatric cerebrovascular disease has a prevalence of approximately 3 cases per 100,000 children [7]. There are twice as many female patients as male patients [8].
The MCA is formation of anastomotic channels within the lateral striate arteries and its sphenoidal segment (M1) & insular segment (M2) have different phylogenetic anatomy. MCA originates as a branch from anterior cerebral artery. M1 segment supplies lenticulostriate & lateral olfactory areas. M2-segment arising from lateral striate artery supplies telencephalon (frontal parietal, occipital lobes), caudate nucleus and anterior limb of the internal-capsule.
M2 segment phylogenetically is seen several years later than the M1 segment. Accessory MCA with an incidence of 0.3% to 4% [9] and supplies basal ganglia. It is primarily a lenticulostriate artery.

Clinical presentation

Adolescent female 11years of age had gradual onset progressive weakness, involving left upper limb (Figure 1). There was no history of headache, vomiting or diminishing of vision, trauma and fever.

Fig 1: Left side hemiparesis. Left hand wrist drop, poor grip (Power-proximally III and–distally grade zero)

Full term normal delivery child received vaccinations as per schedule. Neurologically normal till 4years of her age when she had two generalised seizures with loss of consciousness. Clinical and brain CT examinations showed no abnormality. (Figure 2) Electro-encephalography & routine cerebrospinal fluid studies were normal. Considered epileptic and was kept on oral medication with carbamazepine.

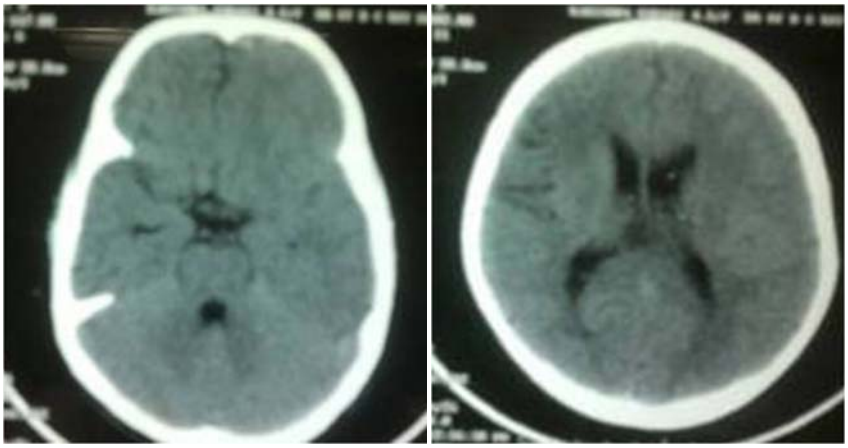
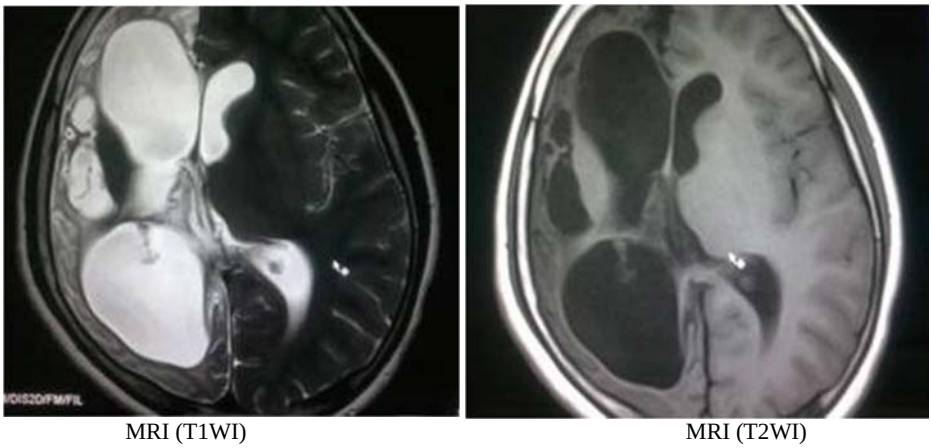


Fig 2: CT Brain (Plain) scan at 4 years of age. Indications: seizures. The CT scan showed no evidence of oedema, trauma or any tumor. No signs of intracranial hemorrhage. Hemispheres and ventricles bilaterally fully developed, no midline shift. Lateral ventricles communicating bilaterally with the third ventricle at foramen monroe. Fourth ventricle normal.

Parents noticed gradual and progressive diminution in her neurocognitive functions, more noticeable in the last 3-4 years. Intelligence, memory and speech were severely affected. MRI brain at 11years of age was performed (Figure 3) and was advised shunt operation



MRI (T1WI) MRI (T2WI)

Fig 3: A) T1 image B) T2-image MRI at 11years of her age showed hydrocephalus-ex vacuo, unilateral-type on the right side. The brain loss confirmed on diffusion weighted MRI-images as due to ischemic atrophy. The fronto-parietal, temporo-occipital, telencephalic affected areas fed by MCA

However upper motor neurone signs prompted us to advice digital subtraction angiography (DSA). The DSA was not accepted by child's' parents and magnetic resonance angiography (MRI) was performed (Figure 4).

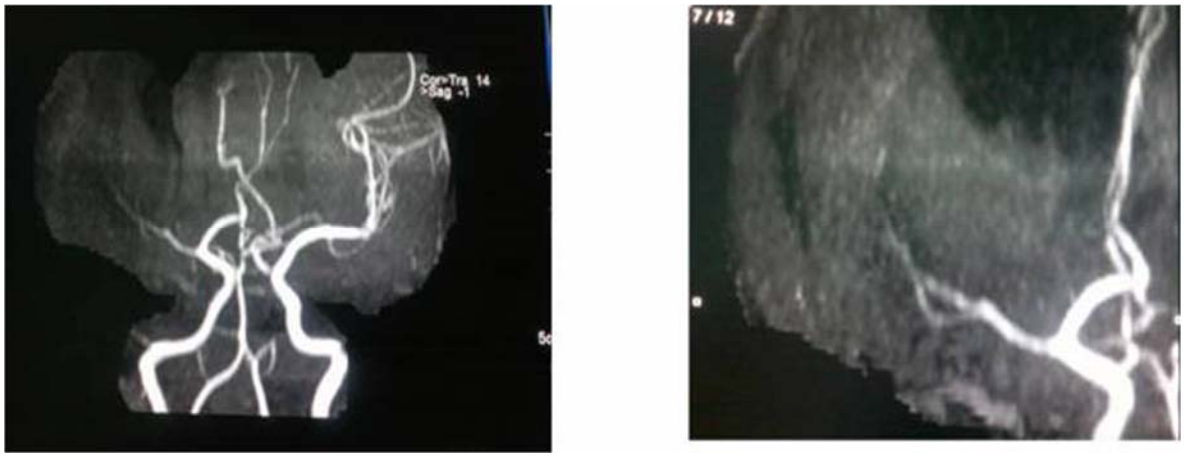


Fig 4: MR-angiography: A &B: Steno-occlusive angiopathy involving the distal (M1) of right MCA only. M2, M3, and M4 all occluded. ICAs, ACA bilaterally and Vertebro-Basilar system normal. Left MCA, M2, M3, M4 were normal.

The neurocognitive functions were deranged. On the right side there were upper motor neurone type of hemiparesis with brisk deep tendon reflexes and up-going plantar response. On the left side hemiparesis was lower motor neurone type (Figure 1**)**.

Discussion

Significant change in radiological features developed within a span of 6 to 7 years. It could be postulated that till 4-years of her age the MCA was well matured and disease-free. Secondly, MCA occlusion was not associated with collaterals in lenticulostriate or with transdural angiogenesis

At 4 years of age well developed normal size cerebral hemispheres and ventricles seen bilaterally. Telencephalon well developed and Foramen Monro well patent.

At 11 years of age hydrocephalus ex-vacuo & cortical hemiatrophy had developed. MR angiography showed underlying atypical unilateral angiopathy of distal M1 segment of MCA. Childhood MMD has peak distribution age at 5-years [10] and 60% of these gradually deteriorate in their cognitive functions [10]. The mortality rate of 4.3% is due to repeated strokes [11]. Only 2.8% Asian children present with the hemorrhagic strokes.[12] Severity of MMD reflects higher grades of occlusion of ICA and disappearance of moyamoya vessels. "Puff of smoke" is the intermediate grade. A few case reports of isolated MCA angiopathy in their initial stages have been reported [13] Encephalomalacia with atrophy could occur with arterial or venous angiopathies.

Venous angiopathy reflects clinically with seizures. The venous back-pressure effects in bleeds and raised intracranial pressure.

Vein of Galen-malformation angiopathy causes atrophy in the occipital and infra-temporal lobes. Theinfratentorial atrophic areas get compensated with CSF cavity formation called as Dandy Walker cyst [14].

Brain atrophies in cerebro-facial metameric syndrome (Sturge-Weber) have clinical manifestation of seizure. DSA shows calcified superficial cortical veins enlarged deep veins, cortical atrophy and angio-genesis [15] Endovascular proliferativeangiopathy occurs during fetal, neonatal, infantile, early childhood or adolescent age groups.

a) Occlusive angiopathy in "PHACE/S" syndrome which include hemangioma, coarctation of aorta, posterior fossa malformation, vascular abnormality in the eye and stroke [16, 17]

b) Proliferative diffuse-angiopathy seen in 20% of vascular diseases in children [18] is telencephalic arteriovenous malformation with diffuse neo-angiogenesis without nidus-formation. Abnormal feeding arteries and draining veins are scattered amongst normal brain parenchyma.

Embryological, phylogenetic (figure5) along with molecular anatomy help understand the disease process.

Phylogenetically MCA a branch from the ACA is recent striato-cortical acquisition. M1 and M2 appear as one continuous artery.M1 segment proceeds by several years before the appearance of M2 segment. MCA does not contribute to form Circle of Willis. It supplies lateral striate (caudate nucleus), anterior limb of internal capsule and cortical territories.11-cortical branches from M4, supply frontal, temporal, parietal & occipital cortical lobes. M1-sphenoidal, M2-insular, M3-opercular and M4-cortical branches are radiological regional descriptive terms (Figure 5).

Accessory MCA (accMCA) is medial striatal artery and can be seen as hypoplastic or dominant type. The type1 - accMCA is more proximal, appears as if arising from the ICA. Type 2 and type 3 accMCA are seen arising from the ACA. The more proximal branch is always cortical branch and the ones which give rise to perforators are the true accMCAs. Type 2 has more striatal and less cortical supply, but arises more proximally than the type 3 accMCA.

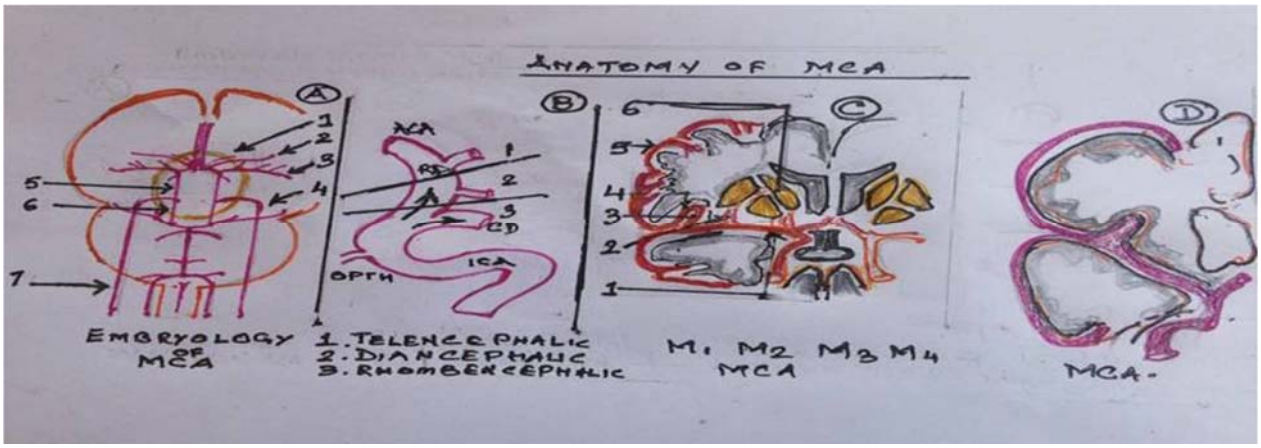


Fig 5: Embryology: MCA: (branch of ACA) A) 1- medial striatal arteries, 2-acc MCA, 3- Cortical branches; 4-Supra-clinoid ICA, 5-rostral division of ICA; 6-caudal division of ICA; 7- ICA B):

Molecular anatomy between arteries & veins and is genetically determined. "Trigger" have qualitative properties on the endothelium and effectively change the arteries or the veins through their molecular actions. This results in increase in the ratio of muscles' cell-mass to their endothelial cells. The molecular level receptors on their endothelial cells viz. ephrin B-2 and ephrin B-4 differentiate the arteries from veins respectively. The reciprocal signalling between these two molecular- receptors initiates the morphogenesis of non-sprouting angiogenesis (angio-ectasia) [19, 20].

Trigger factors in MMD typically affect supraclinoid ICA along with proximal segment of the ACA. It is usually bilateral. "Trigger-factors" have different pathological effects on M1 and M2 segments. In this case spontaneous M1 occlusion, without non- sprouting angiogenesis resulted in complete ischemic atrophy of striato-telencephalic portion.

Conclusion

Only a few case reports of isolated MCA angiopathy in their initial stages have been reported.

Clinically, diminutive- neurocognitive functions of the child at different stages must always be co-related with angiography studies and followed-up at least every two years.

Therapeutic window-period and the time lost, play important role in the overall management and clinical outcome.

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