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Case Series

Ophthalmology Section

# Ocular Features and Visual Outcome in Children with Moyamoya Disease and Moyamoya Syndrome: A Case Series

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## ABSTRACT

Moya Moya Disease (MMD) is characterised by idiopathic vasculopathy affecting the terminal internal carotid arteries resulting in the formation of extensive collaterals at the base of the brain, leptomeninges and parenchymal regions with resultant infarcts and bleeds. Four children presented with clinico-radiological features suggestive of Moyamoya disease/syndrome. This includes global developmental delay, recurrent seizures, transient ischaemic attacks and impaired vision. The first patient had vision of 6/15 in both eyes with bilateral optic disc pallor. Second case also had bilateral optic disc pallor with arteriolar attenuation, but had vision of perception of light only in both eyes. The third child had vision of 6/60 with alternate divergent squint and clinical features suggestive of Neurofibromatosis 1 (NF 1). Fourth patient presented with poor fixation in both eyes with bilateral total cataract. He underwent bilateral cataract surgery with intraocular lens implantation and vision improved to 2/60 with good fixation. We also describe their medical and neurosurgical interventions in this report.

**Keywords:** Developmental cataract, Functional vision, Seizures in children

## CASE SERIES

### Case 1

A 13-year-old male presented with recurrent right focal motor seizures (FMS) and gradual cognitive decline since 10 years of age [Table/Fig-1]. Magnetic Resonance Imaging (MRI) showed bilateral occipital lobe ischemia; Magnetic Resonance Angiography (MRA) confirmed MMD [Table/Fig-2&3a]. Workup for secondary causes was non-contributory. Blood investigations showed haemoglobin (Hb) - 12.7gm/dL, WBC Total 7900 /cumm, APTT 27.9 secs, Fasting blood glucose 97 mg/dL, Sodium (Na) 134 mmol/L, Potassium (K) 3.5mmol/L, ALT 22 U/L, Creatinine 0.63mg/dL, blood borne virus screening - negative. After starting medical management, he underwent staged bilateral encephalo-duro-arteriosynangiosis. Post-surgery he had stabilisation of his deficits with significant reduction in seizure frequency. He had residual deficits of intellectual disability and spasticity in bilateral upper and lower limbs. He presented to the ophthalmology clinic with bilateral decrease in vision. Visual acuity assessment using Cardiff cards was 6/15 in both eyes [Table/Fig-4]. Extraocular movements were complete. Pupils were 3 mm, round and reacting to light; anterior segment examination was normal. Intra Ocular Pressure (IOP) was 12 mmHg in both eyes. Posterior segment showed bilateral optic disc pallor with arteriolar attenuation. There was no oedema or gliosis at the optic disc margin. Cranial nerve examination showed right Upper Motor Neuron (UMN) facial palsy. He had attended school until standard 6, but was now unable to read and write due to cognitive impairment [Table/Fig-5]. After low vision assessment, non-optical devices were advised to encourage reading and writing.

### Case 2

A 14-year-old male presented with recurrent Transient Ischemic Attacks (TIA) followed by stroke [Table/Fig-1] in both anterior and posterior circulation. Imaging was suggestive of MMD involving bilateral anterior and posterior circulation [Table/Fig-2,3b] and secondary work-up was negative. Blood investigations: Hb 11.7 g/dL, Total WBC 8300/ cumm, Platelet count 241000/ cumm, Glucose 2 hours post food 109mg/dL, TSH 2.266uIU/ml, Creatinine 0.45 mg/dL, Calcium (Ca) 9.1 mg/dL, Phosphorus (P) 4.3 mg/dL, ALT 32U/L, AST 32 U/L, Alkaline phosphatise 226U/L.

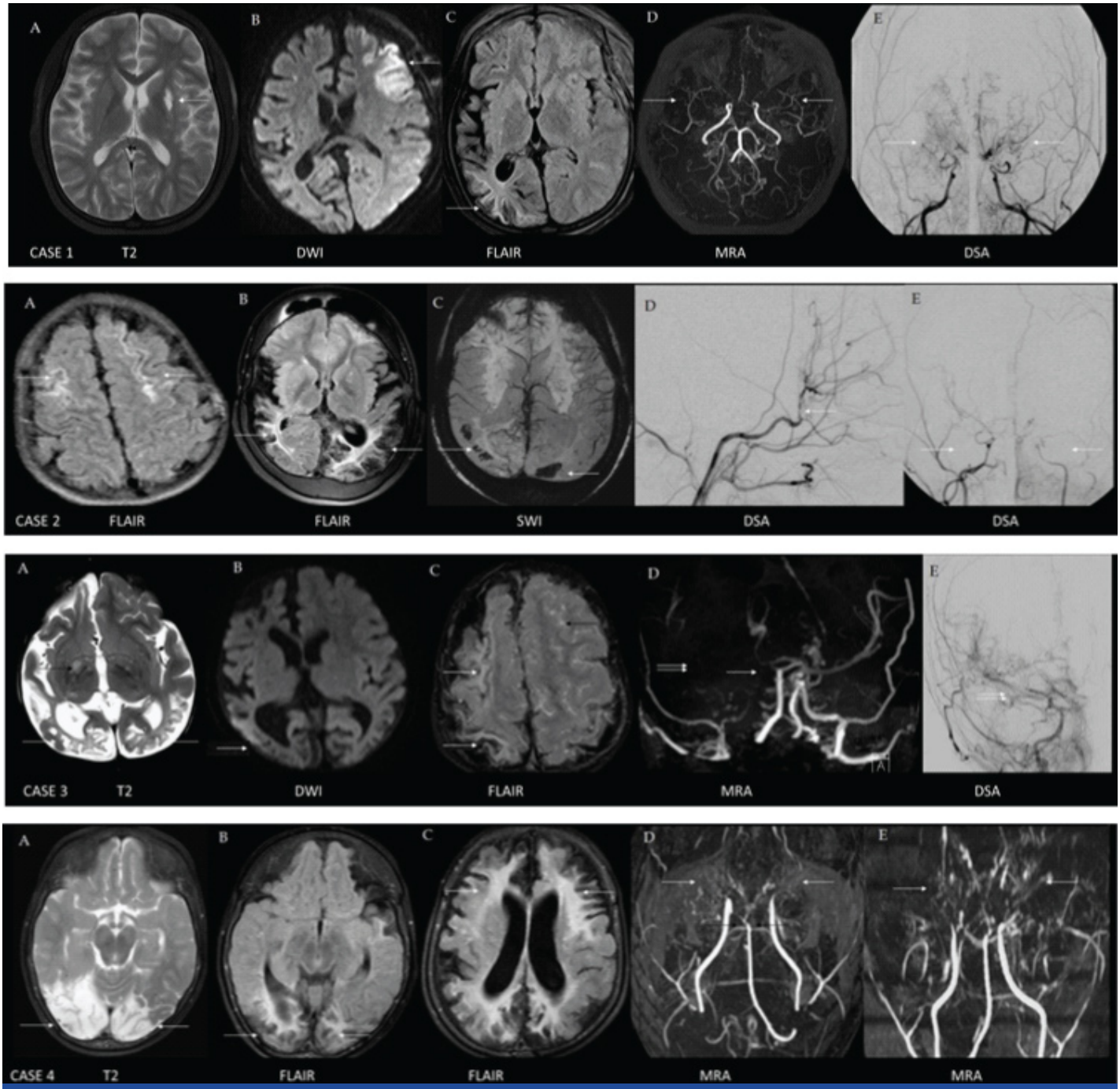
He underwent bilateral encephaloduro-arterio-synangiosis following which there were no new neurological events, but he had sequelae of intellectual disability, low vision and behavioural problems. He also had bilateral Upper Motor Neuron (UMN) facial weakness with spastic dysarthria. He presented to the

| Serial no: | Age at presentation | Sex | Presenting symptom | Systemic association |
|---|---|---|---|---|
| 1 | 13 years | M | Focal motor seizures | Nil |
| 2 | 14 years | M | Transient ischemic attacks | Nil |
| 3 | 3 years | M | Focal motor seizures, hemiparesis | Neurofibromatosis Type 1 |
| 4 | 2 years | M | Focal motor seizures, GDD | Facial dysmorphism, cataract, premature ageing |

**[Table/Fig-1]:** Clinical profile of children with MMD.
GDD – Global developmental delay

| Serial No. | MRI | MRA/DSA | Medical treatment | Surgical management |
|---|---|---|---|---|
| 1 | Acute left frontal infarct. Chronic left basal ganglia and right tempero-parietal and occipital infarct | Bilateral supraclinoid ICA, proximal M1 and A1stenosis, Bilateral PCA involvement on repeat imaging | Antiplatelets, antiepileptics | Bilateral encephalo-duro-arteriosynangiosis |
| 2 | Bilateral anterior watershed infarcts initially, later showing occipital and parieto-temporal infarcts | Pronounced narrowing of bilateral supraclinoid ICA, stenosis of MCA and ACA. Basilar and bilateral PCA involvement | Antiplatelets, antiepileptics | Bilateral encephalo-duro-arterio-synangiosis |
| 3 | Chronic infarcts in bilateral occipito-temporal and parietal lobes, right anterior watershed infarct. Features of NF1 | Near total occlusion of right supraclinoid ICA. Right P1 occlusion. Left P2 stenosis | Antiplatelets, antiepileptics | Bilateral encephalo-duro-arteriosynangiosis |
| 4 | Bilateral chronic occipital, deep and anterior watershed infarcts | Bilateral tight stenosis of supraclinoid ICA Bilateral PCA and terminal basilar occlusion | Antiplatelets, antiepileptics | None |

**[Table/Fig-2]:** Management: Imaging, medical and surgical interventions.
MRI - Magnetic resonance imaging MCA - Middle cerebral artery
MRA - Magnetic resonance angiography M1 - M1 segment of MCA
DSA - Digital subtraction angiography PCA - Posterior cerebral artery
ICA - Internal carotid artery P1 - P1 segment of PCA
ACA - Anterior cerebral artery P2 - P2 segment of PCA
A1 - A1 segment of ACA




**[Table/Fig-3]: (a)** Case 1.T2 axial (A) shows chronic infarct in left basal ganglia (white arrow), DWI image (B) shows hyper intense area in the left frontal lobe suggestive of acute ischemic infarct (white arrows). On FLAIR imaging (C), chronic right temporo parietal and occipital lobe infarct is seen as an area of gyral volume loss and white matter gliosis (white arrows). MRA (D) shows complete non-visualisation of bilateral distal ICA and proximal M1 and A 1 segments (white arrows). DSA (E) images confirm this and shows collaterals giving a "puff of smoke" appearance (white arrows). **(b)** Case 2. FLAIR axial image (A) showing bilateral anterior watershed infarcts (white arrows), FLAIR image at a lower level (B) shows bilateral posterior watershed infarcts (white arrows). SWI (C) images shows bilateral occipital hypo-intense areas suggestive of chronic haemorrhage (white arrows). DSA (D&E) images show bilateral distal ICA and proximal M1 and A1 stenosis (white arrows). **(c)** Case 3. T2 axial (A) images showing bilateral occipito-temporal chronic infarcts with gyral volume loss and white matter gliosis (white arrows). Also note the right basal ganglia hyperintensity (black arrow) suggestive of NF related FASI. DWI (B) axial images show no hyper intensity suggesting chronic nature of infarcts (white arrow). FLAIR axial image (C) shows right anterior watershed infarcts (white arrows) and sulcal hyper intensity ("ivy sign") due to collaterals (black arrow). MRA (D) and DSA (E) images show near total occlusion of right supraclinoid ICA (double arrows) and right P1 occlusion (white arrow). **(d)** Case 4. T2 (A) and FLAIR (B) axial shows bilateral chronic occipital infarcts (white arrows). FLAIR axial at lateral ventricular level (C) also shows additional bilateral anterior watershed infarcts (white arrows). MRA (D) images show bilateral distal ICA and proximal M1 and A1 non-visualisation (white arrows) and bilateral PCA involvement (black arrows). Also note the "puff of smoke" appearance due to collaterals (white arrows in MRA (E).
**Abbreviations:** T2- T2 weighted imaging, DWI- Diffusion weighted imaging, FLAIR - fluid attenuated inversion recovery, MRA- Magnetic resonance angiography, DSA- Digital subtraction angiography, SWI- Susceptibility weighted imaging, ICA- Internal carotid artery, MCA- Middle cerebral artery, PCA- Posterior cerebral artery, M1- M1 segment of middle cerebral artery, A1- A1 segment of anterior cerebral artery, FASI – Foci of abnormal signal intensity.

ophthalmology department with only perception of light in both eyes. On ocular examination, extraocular movements were complete. Pupils were 3 mm, round and reacting to light; the anterior segment was normal. Intraocular Pressure (IOP) was 14 mmHg in both eyes. Posterior segment showed bilateral optic disc pallor with arteriolar attenuation [Table/Fig-4]. Due to severe impairment in vision and cognitive functions, low vision devices could not be prescribed.

## Case 3

A three-year-old boy presented with recurrent alternating focal motor seizures from 4 months of age [Table/Fig-1], followed by recurrent cerebrovascular accidents in both the anterior and posterior circulation from two and a half years of age. In addition to global developmental delay and bilateral spasticity in the limbs, he also had a constellation of clinical features suggestive of Neurofibromatosis 1 (NF1). Cranial nerve examination showed right

| Serial No. | Distant vision right eye | Distant vision left eye | Anterior segment | Posterior segment |
|---|---|---|---|---|
| 1 | 6/15 | 6/15 | Within normal limits | Bilateral optic disc pallor |
| 2 | Perception of light only | Perception of light only | Within normal limits | Bilateral optic disc pallor and arteriolar attenuation |
| 3 | 6/60 | 6/60 | Alternate divergent squint | Bilateral mild temporal pallor of optic disc |
| 4 | Preoperative: Poor fixation Postoperative: 2/60 | Preoperative : Poor fixation Postoperative: 2/60 | Developmental cataract Pseudophakia | No view Bilateral mild pallor of optic disc |

**[Table/Fig-4]:** Vision and ocular features.

| Serial No. | Can walk around | Can recognise faces | Can read | Can write |
|---|---|---|---|---|
| 1 | Able | Able | Unable | Unable |
| 2 | Able | Unable | Unable | Unable |
| 3 | Unable | Unable | Unable | Unable |
| 4 | Unable | Able | Unable | Unable |

**[Table/Fig-5]:** Functional vision in children with MMD.

**[Table/Fig-6]:** Two year old boy with Moyamoya disease and bilateral cataract.

UMN facial palsy. MRI features are described in [Table/Fig-2&3c]. He was diagnosed as Moyamoya syndrome with NF1. Blood investigations: Hb-13.8 g/dL, WBC Total count - 18600/cumm, Platelet count 439000/cumm, erythrocyte sedimentation rate (ESR) at 60'- 5mm, S.Ca 9.7mg/dL, P 4.4 mg/dL, Vitamin D 24.83 ng/ml, AST 22 U/L, ALT 15 U/L, Alkaline phosphatise 268 U/L, Homocysteine 5.87umol/ L, Serum Complement C3 - 87.4 mg/dl, C4-12.2 mg/dl, Anti-thyroglobulin antibodies 10 IU/ml, antinuclear antibody (ANA) - negative, DSDNA 1 IU/ ml, Anticardiolipin 1 u/ ml, CRP <3.45 mg/L, VDRL non-reactive, blood borne virus screen - negative, cytoplasmic and perinuclear anti-neutrophil cytoplasmic antibodies (c ANCA, p ANCA) <2. In view of recurrent TIAs and progressive deficits, he underwent bilateral encephalo-duro-arteriosynangiosis and was kept on a maintenance dose of antiepileptics along with antiplatelet therapy.

When presenting to the ophthalmology clinic at 3 years of age, he had vision of 6/60 with preferential looking method using Cardiff cards. Ocular examination showed alternate divergent squint. Extraocular movements were complete. Pupils were 3mm, round and reacting to light. Anterior segment examination was normal, while posterior segment showed bilateral temporal pallor of the optic disc [Table/Fig-4]. With global developmental delay and poor cognition, he had poor functional vision [Table/Fig-5]; occupational therapy was advised.

### Case 4

A two-year-old boy presented with recurrent right focal motor seizures since 7 months of age with global developmental delay, intellectual disability and spastic quadriparesis. He also had facial dysmorphism, features of premature ageing, bilateral mature cataract and bilateral UMN facial weakness with spastic dysarthria [Table/Fig-1]. Blood investigations: Hb7.7 g/dL, Platelet count 410000/ cumm, S. Na135 mmol/L, K4.7 mmol/L, Bicarbonate 25mmol/L, TSH2.62 uIU/ ml, Creatinine 0.13 mg/dL, Ca 9.8 mg/ dL, P 5.7mg/dL, ALT 99U/L, AST 148U/L, homocysteine 3.93 umol/l, HIV ELISA negative. MRI findings are described in [Table/ Fig-2,3d]. Since his systemic condition had attained a plateau, he was maintained on antiplatelet and antiepileptic therapy.

He presented to the department of ophthalmology at 2 years with bilateral white reflex and poor fixation in both eyes [Table/ Fig-4]. Extraocular movements were complete. Pupils were 3mm, round and reacting to light. Anterior segment showed bilateral total cataract [Table/Fig-6]. IOP was 12 mmHg in the right eye and 14 mmHg in the left eye. He underwent lens matter aspiration, primary posterior capsulotomy and partial anterior vitrectomy with intraocular lens implantation in both eyes. Post-operatively he attained vision of 2/60 with good fixation. Fundus examination showed mild pallor of the optic disc. He was able to recognize family members and is on regular follow up. However due to global developmental delay, he was not ambulant [Table/Fig-5].

## DISCUSSION

Moyamoya disease (MMD) is an idiopathic vasculopathy affecting terminal internal carotid arteries. Moyamoya syndrome is due to recognizable systemic associations or when a specific aetiology is detected. Progressive stenosis of the carotids results in reduced blood flow to the anterior brain resulting in the formation of collaterals at the skull base. Moyamoya in Japanese means a "puff of smoke", the characteristic feature due to abnormally dilated collaterals seen on imaging [1]. MMD is described to have a familial and ethnic predisposition. Familial occurrence is seen in 9-12% of cases [2]. However, in this series a positive family history is not seen. Japan has the highest incidence (0.54) of MMD. It is more in Asia than other parts of the world. Though the female to male ratio is reported as 1.8:1 [3], all patients in this series were males.

The classical presentation in MMD is TIA, ischemic strokes and intracranial haemorrhage [2]. Intracranial haemorrhage is more common in adults. Posterior circulation involvement is considered to be a late manifestation of the disease process. Hence posterior circulation infarct with occipital lobe involvement and resultant visual impairment is rare. All patients in our series had cognitive and visual decline. Moya Moya Syndrome is known to have various associations like Down syndrome, Marfan's syndrome and NF 1 [2]. Case 3 in this series had associated NF1.

Surgical management - Direct, indirect and combined revascularization are the preferred treatments for MMD [2]. Regional blood flow can be achieved by revascularization surgeries, which might reduce re-bleed as compared to conservative management [4]. Early surgical intervention before irreversible haemodynamic changes occur is necessary to attain a good outcome postoperatively.

MMD is the most commonly treated cerebrovascular disease in children [5]. In recent years stroke has been increasingly recognised in children, and diagnosis can be difficult. As MMD can cause severe functional impairment and even death, early diagnosis and prompt management is necessary. Once vascular occlusion has occurred the condition progresses in spite of medical management [6]. Hence surgical intervention aiming at increasing blood flow to the hypoperfused cerebral regions should be attempted at the earliest. MRA is one of the best diagnostic methods for this condition [7]. Various cases of MMD have been reported from India [7-10]. A variety of ocular features and associations have also been described. They include amaurosis fugax [11], morning glory disc anomaly, optic nerve hypoplasia, retinochoroidal coloboma, microphthalmos [12], iris hypoplasia [13], Peter's anomaly [14] and chorio-retinal atrophy [15]. All our

patients had optic disc pallor with arteriolar attenuation without any associated optic disc oedema or gliosis. Visual decline in our case series could be attributed to cortical blindness since all of them had associated occipital lobe ischemia/ infarct on imaging. Alternate divergent squint and bilateral developmental cataract were the other ocular features seen in our case series. Previously there has been a series of patients reported from France with a syndromic association of cataract [16].

## CONCLUSION

Visual problems though rare are not uncommon in Moyamoya disease as reported in this series. Ophthalmic rehabilitation forms an integral part of the holistic management of children with MMD and Moyamoya syndrome. This is also the first report of MMD associated with bilateral cataract in a child from India. MMD is associated with childhood stroke and death. Prompt diagnosis and timely surgical management is essential to reduce systemic morbidity and improve functional outcome.

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