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CASE SERIES

Möbius sequence with varied strabismus presentations in Filipino patients

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ABSTRACT

Objective

To report various presentations of patients diagnosed with Möbius sequence, discuss theoretical basis for the findings, and present treatment options.

Methods

Consecutive cases of patients meeting the minimum criteria of VI and VII cranial-nerve diplegia seen from January 2003 to June 2003 were included in this case series. Their strabis-mus presentations and associated systemic findings were presented. All patients underwent a comprehensive ophthalmologic examination.

Results

Seven patients aged six months to eight years, five males and two females, were identified. Patients were born to mothers 28 to 38 years old with varying parities. First trimester insults in the form of tobacco and alcohol exposure, upper respiratory and varicella infections were seen in three patients. While all patients had bilateral abduction deficit consistent with bilateral VI cranial-nerve palsy, the strabismus deviations varied. Four patients had large-angle esotropia exceeding 40 PD, one of whom had dissociated vertical deviation (DVD), ptosis, and lid fissure narrowing on attempted adduction. The others had 20 PD of exotropia, 10 PD of intermittent esotropia with DVD, and one was orthotropic. Four patients had limb abnormalities, including three with talipes equinovarus or clubfoot and one with absent distal phalanges. Four patients, two of them females, suffered from mental retardation. Two patients had seizure disorder.

Conclusion

Patients with typical Möbius sequence may have varying strabismus presentations despite bilateral VI cranial-nerve involvement. Standard strabismus management principles apply. These patients require a multidisciplinary team for optimal care.

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THE CONSTELLATION of findings often referred to as Möbius (or Moebius) syndrome is more appropriately discussed as Möbius sequence, consistent with a cascade of secondary events after an embryonic insult from hetero-genous causes.[1] There is general agreement that the timing of insult or trigger factors occur during the fourth to sixth weeks of gestation during which time the cranial nerve nuclei undergo the most rapid development.[2] No common cause has been found but a history of benzodiazepine and misoprostol use, bleeding during pregnancy, spontaneous abortion, and chorionic villus sampling in the second month of gestation have been documented.[3,4]

Palsy of the sixth and seventh cranial nerves is the minimum diagnostic criteria for Möbius sequence.[5] Clinically it is characterized by a large-angle esotropia and absence of facial expression (facial lines). Typically, the strabismus deviation is observed during the first six months of life with bilateral limitation in abduction.[6] There may be other associated ocular and orbital findings (Table 1).[7,8]

In many cases, an expanded Möbius sequence is observed with variable cranial-nerve-III to IX involvement.[1] Cases consisting primarily of cranial-nerve involvement are known as Möbius syndrome while those with associated limb abnormalities are known as Hanhart or Poland-Möbius syndrome.[9] Simultaneous disruption of normal blood flow in developing facial arterial networks could account for hypoplasia of the eye, ear, and jaw. Concomitant disruption of the subclavian artery, around the sixth week of embryonic development, could cause the terminal transverse limb defects and Poland syndrome.[10]

Patients with typical Möbius facies with varied strabismus alignment, including large-angle esotropia described above, are presented in this case series. Theoretical basis for the varied presentations and treatment options are discussed.

METHODOLOGY

Consecutive series of patients with typical Möbius facies seen at the pediatric ophthalmology clinic of the University of the Philippines-Philippine General Hospital (UP-PGH) from January 2003 to June 2003 were identified. All Möbius sequence diagnoses were confirmed by pediatric genetics specialists at the University of the Philippines-National Institutes of Health.

All patients underwent a complete ophthalmologic evaluation consisting of gross examination, visual-acuity testing, full cycloplegic refraction, biomicroscopic examination, sensorimotor (strabismus) and amblyopia evaluation, and dilated fundoscopy with both direct and indirect ophthalmoscopes. All refractions were performed following cycloplegia with 0.5 to 1.0% atropine given thrice a day for three days prior to objective refraction. Whenever possible, alternate-prism-cover testing was the preferred method for measuring misalignment with the appropriate correction glasses in place, if necessary. In uncooperative patients, strabismus measurements were estimated by Krimsky/Modified Krimsky method.

Table 1. **Ocular and orbital findings in Möbius syndrome.**[7,8]

- VI cranial-nerve palsy with decreased abduction ability
- Small palpebral fissure
- Epicanthal folds
- Hypertelorism
- Esotropia [E+] [up to 100 prism diopters (PD)]
- Exposure keratitis due to lagophthalmos
- Situs inversus of retinal vessels and tortuous retinal vasculature
- Mild to moderate refractive errors
- Entropion
- Ptosis
- Anomalous head posture
- Head tilt if vertical strabismus is present
- Amblyopia and decreased binocular vision
- III and IV cranial-nerve palsies
- Generally preserved vertical eye movements and convergence
- Normal pupillary function, occasionally poorly reactive and miotic

RESULTS

Seven cases with typical Möbius sequence were included. Their profiles are summarized in Tables 2 and 3.

Case 1

A five-year-old male was born full term via spontaneous vaginal delivery to a 38-year-old multigravid [G6P5 (5-0-0-5)]. There was no identified insult—viral or other illness, teratogenic drug intake, or radiation exposure—during pregnancy. Esotropia, poor suck, and bilateral talipes equinovarus (clubfoot) were noticed at birth. The patient's feet underwent repair at age 4 months. Though developmentally at par with his peers, the patient had persistent esotropia that prompted consultation at our institution.

There was bilateral eccentric fixation with best-corrected vision of 6/9 (20/30) OU and slight right-eye preference. Cycloplegic refraction was +5.50 -1.00 x 90° OD and +6.00 -3.00 x 90° OS. He had prominent epicanthal folds with epiblepharon. The poor orbicularis oculi and oris tone were confirmed. There was lagophthalmos with preservation of upgaze and good Bell's phenomenon. Cranial-nerve-VII palsy was total, but he had intact gross hearing. Gag and corneal reflexes were also intact. His tongue deviated to the right on protrusion. There was 60 PD of esotropia with absence of horizontal gaze (Figure 1). Maximum tolerated plus prescription was given with minimal improvement in ocular alignment. Bilateral transposition surgery with medial rectus weakening was recommended.

Table 2. **Demographic and ocular findings in a series of Möbius sequence patients.**

Features	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
Age(yrs.)/Sex	5/M	1/M	0.5/F	4/M	8/M	6/F	3/M
Maternal Age	38	33	38	28	38	35	27
Pre-/perinatal exposure	No known exposure	8mos: Tobacco, alcohol, UTI[1]	6mos: UTI,[1] 7mos: URTI[2]	6mos: Meclizine HCl	1mo:URTI[2] w/ fever; 3 mos: varicella infection	2mos: URTI[2] w/ fever	No known exposure
Best-corrected visual acuity	OD: 6/9; OS: 6/9	OU: tracts light	OU: inconsistent dazzle (flat VER[3])	OD: 6/9; OS: 6/12	OD: 6/6; OS: 6/6	OU: tracts light; CSM[4]	OU: finger play at 6 meters
Cycloplegic refraction	OD: +5.50 -1.00 x 90° OS: +6.00 -3.00 x90°	OD: +2.75 OS: +2.50	OD: +1.50 OS: +1.25	OD: +2.00 OS: +2.00	OD: +2.00 OS: +2.00	OD: +1.50 -0.50 x180° OS: +1.50	OD: +3.00 OS: +3.00
Prescription glasses	OD: +4.50 -1.00 x90° OS: +4.00 -1.00 x90°	OD: +2.75 OS: +2.50	None given	OD: +2.00 OS: +2.00	OD: +1.00 OS: +1.00	None given	OD: +1.50 OS: +1.50
Strabismus deviation in primary gaze	60 PD[5] ET[6]	45 PD[5] ET[6]	40-60 PD[5] ET[6]	65 PD[5] ET[6] with DVD[7]	20 PD[5] XT[8]	10 PD[5] E(T)[9] with DVD[7]	Orthotropic
Anomalous head position	Right head turn, Right head tilt	None	None	Right head turn, Right head tilt	None	None	Left head tilt
Lateral gaze	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Vertical gaze	Intact	Intact	Intact	Intact	Intact	Intact	Intact
Abduction limitation	OU	OU	OU	OU	OU	OU	OU
Adduction limitation	None	None	None	None	OU	OU partial	OU partial
Eyelids	Epicanthus, Epiblepharon, Lagophthalmos	Epicanthus, Epiblepharon, Lagophthalmos	Epicanthus, Epiblepharon, Lagophthalmos	Epicanthus, Epiblepharon Lagophthalmos, Lid-fissure narrowing on attempted adduction, Right ptosis	Epicanthus, Epiblepharon	Epicanthus, Epiblepharon, Lagophthalmos, Trichiasis	Epicanthus, Epiblepharon, Trichiasis
Fundus Findings	Normal	Normal	Normal	Normal	Normal	Optic-nerve pallor OU	Normal

1. Urinary tract infection; 2. Upper respiratory tract infection; 3. visual-evoked-response; 4. central, steady, maintained; 5. prism diopters; 6. esotropia; 7. dissociated vertical deviation; 8. exotropia 9. intermittent esotropia

Table 3. **Nonophthalmologic findings in Möbius sequence patients.**

Features	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
CN[1] VII palsy	Bilateral & complete	Bilateral & complete	Bilateral & complete	Bilateral; complete left; partial right	Bilateral & complete	Bilateral & complete	Bilateral & complete
CN[1] VIII	Intact gross hearing	Normal BAER[2]	Intact gross hearing	Intact gross hearing	Intact gross hearing	Normal BAER	Intact gross hearing
CN[1] IX-X	Intact gag reflex	Intact gag reflex	Intact gag reflex	Intact gag reflex	Intact gag reflex	Intact gag reflex	Intact gag reflex
CN[1] XII	Tongue deviated to right on protrusion	Not tested; tongue atrophy noted	Not tested	Tongue deviated to right on protrusion	Tongue atrophy	Tongue deviated to right on protrusion	Tongue midline on protrusion
Seizure disorder	None	None	Yes	None	Yes	None	None
Mental retardation	None	Yes	Yes	None	Yes	Yes	None
Chest Findings	Normal	Normal	Normal	Normal	Normal	Normal	Absent left nipple, absent pectoralis muscle
Extremities	Bilateral talipes equinovarus	Normal	Absent/underdeveloped distal phalanges both hands; absent distal phalanx of left big toe; absent toenails of 2nd and 3rd digits of left foot and right big toe.	Bilateral talipes equinovarus	Normal	Normal	Right talipes equinovarus

1. cranial nerve; 2. brainstem-auditory-evoked response

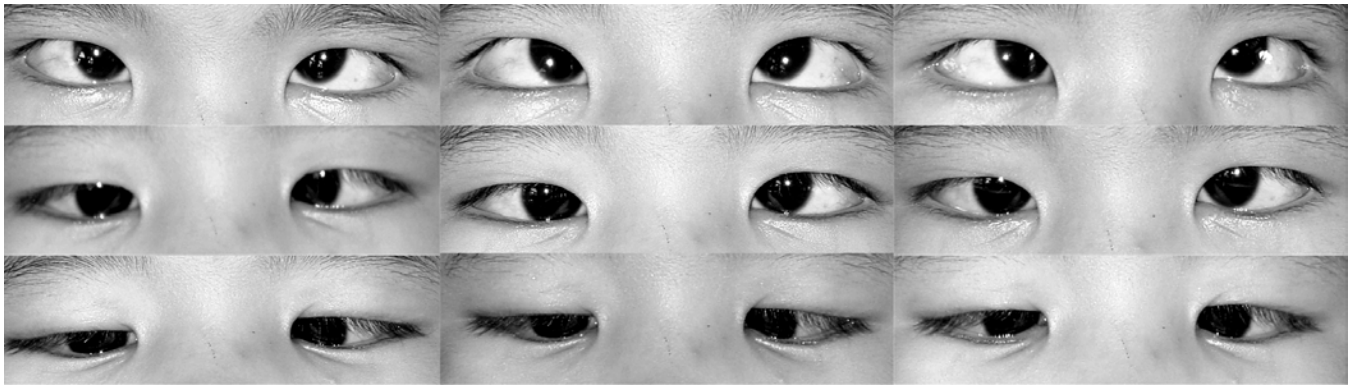

Figure 1. Gaze composite. A 60 PD esotropia with absence of horizontal gaze was evident. Bilateral eccentric fixation and slight right-eye preference were pesent. Esotropia increased on up and down gaze. Vertical eye movements were preserved.

Case 2

A one-year-old male was born full-term to a 33-year-old multigravid [G5P3 (3-0-1-3)] mother assisted by a midwife. The mother smoked one pack of cigarettes a day up to delivery and drank brandy and whisky, about 750 ml per session, twice or thrice weekly up to the third month of gestation. There was maternal urinary-tract infection (UTI)) at 8 months of gestation treated with amoxicillin for a week. Soon after giving birth, the mother noted the baby had poor suck and spilled milk when fed. Dropper feeding was required to sustain nutrition. At one month, expressionless facies, esotropia, and monotone voice on crying were noted. The baby had no lateral gaze. Eyelashes were misdirected toward the cornea with bilateral epiblepharon of the medial third of eyelids and epicanthal folds.

The mother first brought the child for consultation at five months of age. Expressionless facies was observed. He was able to fixate at objects, but tracking of movements was difficult to assess because of bilateral abduction deficits. A 45 PD of esotropia was documented with slight right-eye preference. Corneal and gag reflexes appeared intact. Tongue atrophy was noted but tongue deviation on protrusion was not elicited. There was good gross sound lateralization confirmed by a normal brainstem-auditory-evoked response (BAER). Refraction was +2.75D OD and +2.50D OS. Patient was given full cycloplegic refraction and started on patching therapy for amblyopia. Transposition surgery was suggested.

Case 3

A six-month-old female was born post term via spontaneous vaginal delivery after induction of labor to a 38-year-old [G3P2 (3-0-0-2)] mother at a tertiary-care facility. Pregnancy was confounded by UTI at six months of gestation, treated by a full course of amoxicillin, and upper-respiratory-tract infection (URTI) at seven months treated with paracetamol intake. No first-trimester insult was identified.

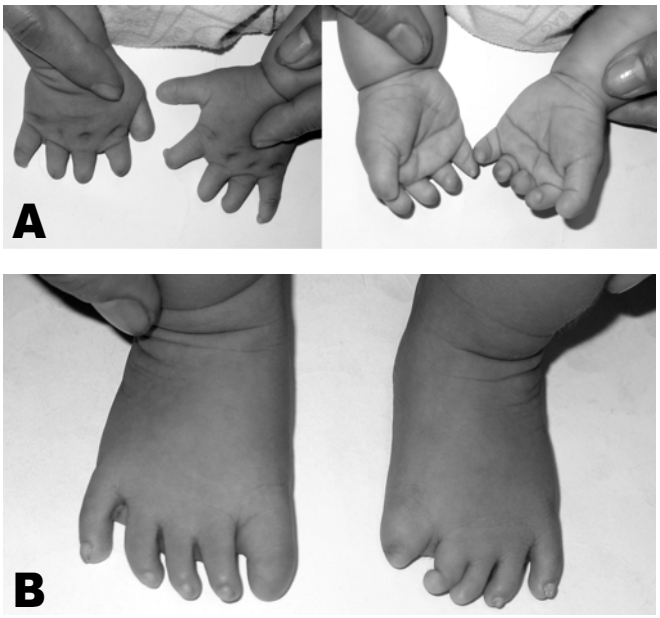

Figure 2. A: Both hands have absent or underdeveloped distal phalanges. Bilateral simian crease was also noted. B: The distal phalanx of the left big toe is absent. Also missing are the toenails of the second and third digits of the left foot and the right big toe. Rocker bottom feet were also noted.

At birth, the patient had poor cry and poor suck, with subsequent development of seizures described as generalized tonic-clonic associated with upward rolling of eyeballs necessitating prolonged hospital confinement. All upper extremities had absent or underdeveloped distal phalanges (Figure 2A). The distal phalanx of the left big toe was absent as well as the toenails of the second and third digits of left foot and the right big toe (Figure 2B). Simian crease, high arched palate, and rocker bottom feet were also identified.

Visual-acuity assessment showed inconsistent dazzle reflex to bright halogen test light. A visual-evoked-response recording revealed no evidence of conduction along the visual pathway. There was bilateral epiblepharon and epicanthus managed conservatively with bland ointments. Variable esotropia ranged between 40 to 60 PD by Krimsky

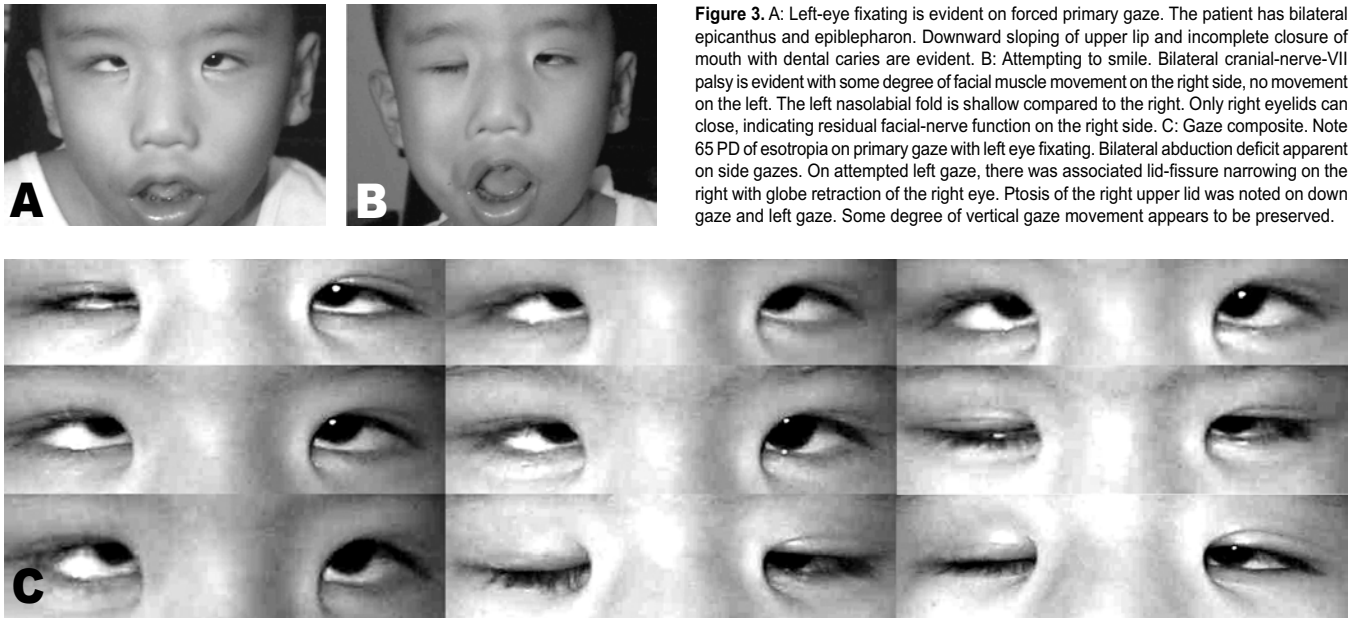

Figure 3. A: Left-eye fixating is evident on forced primary gaze. The patient has bilateral epicanthus and epiblepharon. Downward sloping of upper lip and incomplete closure of mouth with dental caries are evident. B: Attempting to smile. Bilateral cranial-nerve-VII palsy is evident with some degree of facial muscle movement on the right side, no movement on the left. The left nasolabial fold is shallow compared to the right. Only right eyelids can close, indicating residual facial-nerve function on the right side. C: Gaze composite. Note 65 PD of esotropia on primary gaze with left eye fixating. Bilateral abduction deficit apparent on side gazes. On attempted left gaze, there was associated lid-fissure narrowing on the right with globe retraction of the right eye. Ptosis of the right upper lid was noted on down gaze and left gaze. Some degree of vertical gaze movement appears to be preserved.

method. No abduction was elicited. Latest refraction at 7 months old was +1.50D OD and +1.25D OS. Because of poor vision OU, no further treatment except vision stimulation exercises was recommended.

Case 4

A four-year-old male was born full term via spontaneous vaginal delivery to a 28-year-old primigravid assisted by a physician at a local hospital. The mother took meclizine HCl (Bonamine, Pfizer, New York, NY, USA) at 6 months of gestation, but no insult during the first trimester was identified. Bilateral abduction deficit with large-angle esotropia was apparent at birth. Some degree of facial muscle movement was noted on the right side, no movement on the left (Figure 3A-B). Beginning at age 4 months, patient consulted repeatedly for esotropia, facial asymmetry, and frequent drooling.

At last evaluation at age 4, best-corrected visual acuity was 6/9 (20/30) OD, 6/12 (20/40) OS with refraction of +2.00D OU. He had spontaneous alternating fixation with slightly better vision OD. He preferred the right-head turn to assume left gaze, maximizing the use of his right eye. However, because of the right-sided congenital blepharoptosis on forced primary gaze, left-eye fixation was preferred in this position. He also had epicanthus, epiblepharon, and a 65 PD of esotropia with dissociated vertical deviation. Tongue deviates to the right on protrusion (Figure 3B). On attempted left gaze, there was associated lid-fissure narrowing on the right with globe retraction of the right eye. Ptosis of the right upper lid was noted on down gaze (Figure 3C). He was started on full hyperopic prescription and patching of the right eye to treat the amblyopia in the left eye. Bilateral transposition surgery with medial rectus weakening may be required.

Case 5

An eight-year-old male was born full term via spontaneous vaginal delivery to a 38-year-old [G4P3 (3-0-0-3)] at home assisted by a midwife. At around 3 months of gestation, the mother developed systemic varicella infection (chicken pox). There was no known exposure to radiation; mother denied intake of potential teratogens or other drugs.

Patient had episodes of seizure starting on the third day after birth, recurring monthly and associated with fever, upper-respiratory-tract infection as well as aspiration from frequent regurgitation, poor suck, and inadequate swallowing reflexes.

The patient came for an eye examination at 8 years old. At this time, the visual acuity was 6/6 (20/20) OU without correction. Cycloplegic refraction was +2.00D OU. There was 20PD of exotropia on primary gaze with some degree of limited lateral versions (Figure 4). Patient had bilateral partial abduction deficit and bilateral complete cranial-nerve-VII palsy. Atrophy of the tongue was noted. There was bilateral epicanthus that needed no intervention. A trial of +1.00D OU was given to evaluate effect of correction of small hyperopia on his alignment. Patient had not followed up since then.

Case 6

A six-year-old female was born full term and thickly meconium-stained to a 35-year-old multigravid [G5P4 (4-0-0-4)] via spontaneous vaginal delivery. At 2 months of gestation, the mother experienced a 38-40°C fever asso-

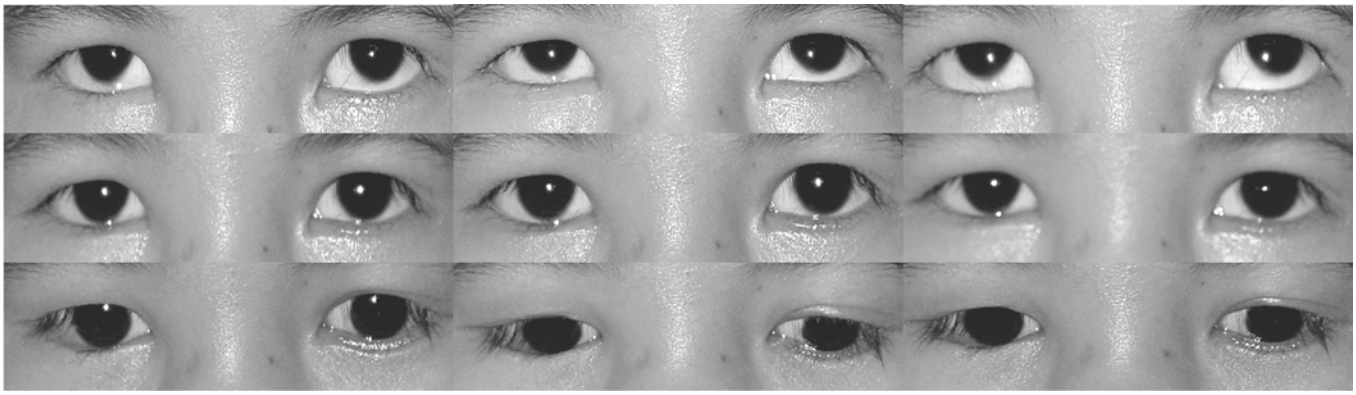

Figure 4. Gaze Composite. A small angle of 20PD of exotropia on primary gaze with some degree of limited lateral versions was evident. There is mild "X" pattern with increase in angle of exotropia on straight up and down gaze. Patient had bilateral partial abduction deficit.

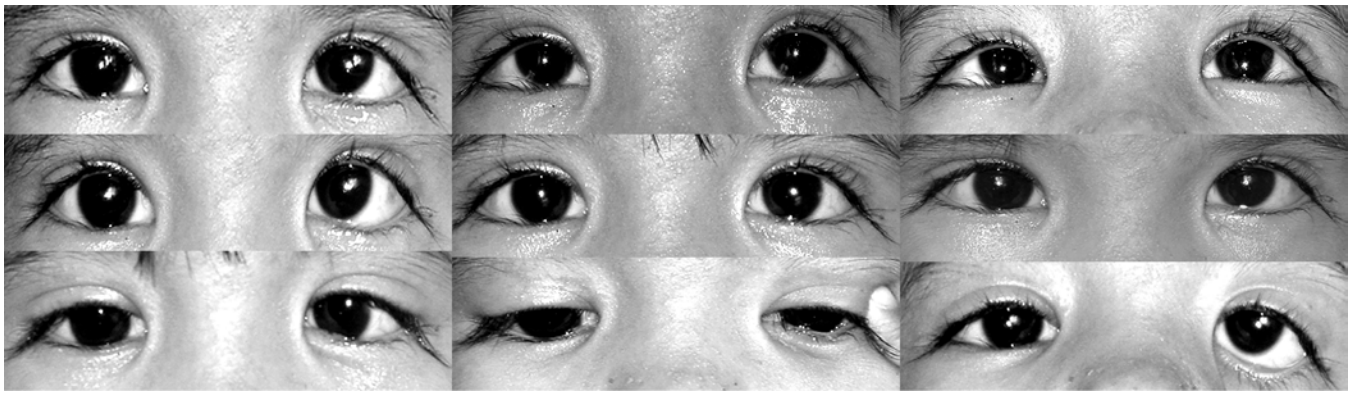

Figure 5. Gaze Composite. A 10 PD of intermittent esotropia was documented on alternate prism cover test. The esodeviation increases on attempted lateral gaze. Small lateral excursion on straight upgaze noted, with a small binocular field of vision apparent on primary and slight upgaze. Vertical up and down gaze somewhat preserved, with a tendency for spontaneous upward deviation suggestive of dissociated vertical deviation. Left eye moves up on attempted right gaze. Either upshoot or dissociated vertical deviation was considered.

ciated with cough and colds. She self-medicated with amoxicillin, paracetamol, and dextromethorphan-paracetamol-phenylpropanolamine HCl (Tuseran Forte) combination. Fever allegedly lasted for 15 days without medical supervision. No other first-trimester insults could be elicited.

At birth, facial asymmetry was noted. No consultations were made until age one year. Throughout her first few years, the patient had feeding difficulties implicating cranial-nerve-IX-X involvement, contributing to her malnutrition.

Patient had profound mental retardation with lack of verbal response. Best qualitative visual-acuity test showed both eyes can maintain central and steady fixation, but with a right-eye preference. There was no associated nystagmus. Mask-like facies with bilateral trichiasis, epicanthus, and epiblepharon was apparent on gross examination. BAER was normal. Gag reflex was intact. Tongue deviated to the right on protrusion with tongue atrophy on the left side. Cycloplegic refraction was +1.50 -0.50 x 180° OD and +1.50D OS. Ten PD of intermittent esotropia was documented on alternate prism cover test. Vertical up-and-down gaze was intact, with a tendency for spontaneous upward deviation suggestive of dissociated vertical deviation. The esodeviation increased on attempted lateral gaze. Fundus evaluation showed minimal pallor of the optic-nerve head with a small cup, but otherwise within normal limits.

Patient had associated severe global developmental delay so that delayed visual maturation was also considered. With intermittent esodeviation in the monofixation range and fairly good motor fusion in primary gaze (Figure 5), no intervention was recommended at this time. The patient remains under the care of a multidisciplinary team.

Case 7

A three-year-old male was born full term to a 27-year-old primigravid via Caesarian section secondary to cephalopelvic disproportion. There was no maternal illness or exposure to teratogens or radiation.

At birth, patient had good cry, movement, and color. There was note of syndactyly of the left hand from second to fifth digits and right talipes equinovarus. The left nipple and pectoralis muscle were absent. Clubfoot was operated on prior to consultation at our institution.

Evaluation done at 3 years of age revealed finger play

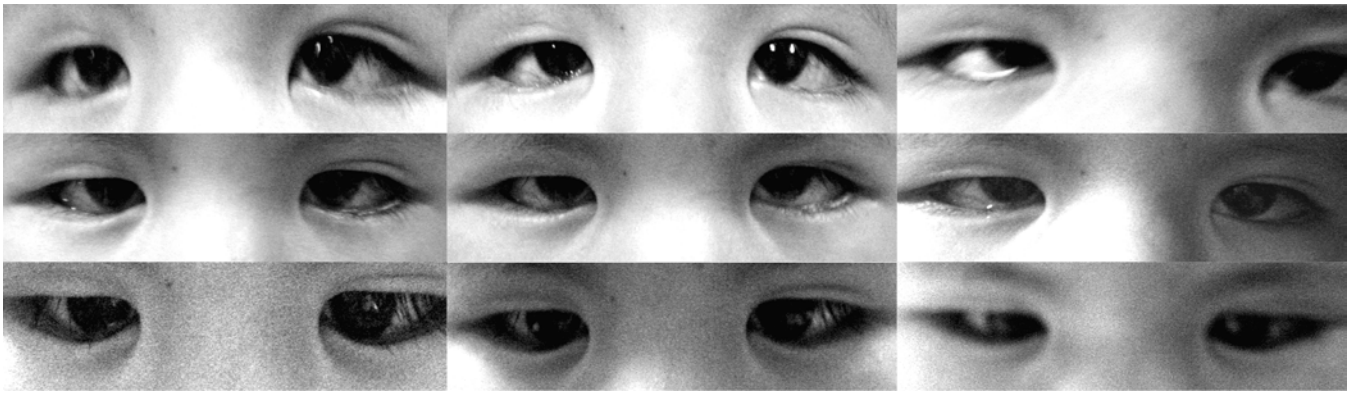

Figure 6. Gaze composite. Patient is orthotropic on primary gaze without refixation movement on alternate prism cover test. Note slight increased esotropia on up and down gaze that may be due to target convergence and preservation of accommodation. There is absence of abduction. Some vertical movements noted.

at 6 meters OU, with bilateral epiblepharon, trichiasis, and epicanthus. There was intact gross hearing. Tongue was midline on protrusion with intact gag reflex. Pupillary and fundus evaluation were normal. In primary gaze, patient was orthotropic without refixation movement on alternate prism cover test. Esotropia was noted only on up-and-down gaze but represented target convergence (Figure 6). Abduction was absent. Cycloplegic refraction was +3.00D OU. Reduced hyperopic prescription of +1.50D OU was given, with plans of bilateral blepharoplasty for trichiasis.

DISCUSSION

Aplasia or hypoplasia of the cranial nerves is believed to result from an ischemic event during the first trimester of pregnancy, usually at about the fourth to the sixth week of gestation. Interruption of the blood supply from compression of fetal vessels near developing cranial-nerve nuclei VI and VII leads to a vascular insufficiency, hence a clinical picture with VI-VII cranial-nerve diplegia.[11] This presents as typical mask-like facies known as Möbius sequence. Multiple causes of blood-flow interruption include trauma, placental abruption,[2] maternal illness, and drug ingestions such as benzodiazepines,[13] thalidomide,[7] and misoprostol.[4] Anomalous development of cerebral circulation has also been implicated.[12] The subclavian-artery-supply-disruption-sequence theory (SASDS) alludes to an interruption of embryonic blood supply during the sixth week of gestation. This theory is supported by the histologic documentation of symmetric calcification (in a vascular distribution) of the dorsal tectum at the midbrain-pons junction, presumably causing hypoxia and ischemia of the affected neural tissues.[2,14]

In this series, first-trimester insults were identified only in three patients (42.9%), with Case 2 exposed to tobacco and alcohol throughout gestation. The two other cases only had a vague history of maternal URTI, although one had confirmed varicella infection. The older maternal age at the time of delivery (mean of 33.9 years) may be indicative of a relative vascular insufficiency and may be contributory.

Most cases appear sporadic but there have been reports exhibiting autosomal-dominant, autosomal-recessive, and X-linked inheritance transmissions.[15] Familial transmission has been reported in 26 patients.[16] A gene was localized in chromosome 3q by linkage analysis in one family with autosomal-dominant Möbius sequence.[17] Deletion in the long arm of chromosome 13 has also been described.[18] Whether these are inherited defects or the result of a trigger event has not yet been clarified.

Recurrence rate in siblings of about 2% in typical isolated cases has been reported.[19] If associated with skeletal defects, the recurrence rate is very low.[7] The syndrome affects both sexes equally.[17] In this series, male patients outnumbered female patients 5 to 2 (2.5:1). Typical bilateral VI cranial-nerve involvement consistently gives a large-angle deviation exceeding 40 PD,[6] and may even reach up to 100 PD,[7,8] especially if associated with secondary changes on the medial rectus muscles. In this series, however, this typical presentation of a large-angle deviation was seen only in Cases 1 to 4.

That other mechanisms may be responsible is suggested by Case 4. Associated lid-fissure narrowing on attempted adduction was present, prompting the patient to prefer his left eye, despite loss of 1 line of Snellen acuity. These findings allude to the presence of cocontraction as that occurring in Duane syndrome.[3,11,14] Cocontraction may explain why Case 5 presented as an exotropia (despite bilateral abduction deficit), intermittent esotropia, and orthotropia. The possibility of an aberrant nerve regeneration occurring in some cranial-nerve palsies cannot be excluded.[20] In fact, in a 1999 series, orthotropia in primary gaze was reported in 10 out of 25 cases, exotropia in 2, and esotropia in only 7.[5]

Bilateral facial-nerve involvement was seen in all patients except Case 4, which had complete left facial-

nerve palsy but partial paresis only on the right. This can be observed as facial asymmetry or mask-like facies, downward sloping of upper lip, incomplete closure of mouth, and lagophthalmos. The involvement of bilateral VII cranial nerve, together with bilateral VI cranial nerve, is necessary before a diagnosis of Möbius sequence can be made. Involvement of the IX-X cranial nerves was gleaned from feeding difficulties, recurrent regurgitation, and aspiration, often complicated with malnutrition as well. In 4 patients, the involvement of the XII cranial nerve was evident with tongue atrophy or deviation.

Limb anomalies consistent with Hanhart (Poland-Möbius) syndrome were seen in four (57%) patients. Findings such as syndactyly, talipes equinovarus, absence of unilateral nipple, breast, and pectoralis muscles, as well as absence or underdevelopment of distal phalanges of hands and absence of toenails were seen. This compares well with the 43% reported by Croenemberger in his series.[19] There are experts, however, who recognize these abnormalities of extremities and trunk as essential feature of Möbius sequence.[21,22] Nonetheless, there was no correlation between limb abnormalities and extent of cranial-nerve involvement.[23]

Mental retardation in this series was seen in 57% of patients (4/7) compared with 75% in a much larger series of 16 patients.[19] Notably, seizure disorder was seen in 2 patients and poor control may have also contributed to poor cortical and visual function.

The typical VI cranial-nerve palsies in Möbius sequence give a large-angle deviation that exceeds 40 PD. Invariably, the medial rectus muscle develops a contracture (Cases 1 to 4). In patients with partial VI nerve function, a recession of the medial rectus combined with a resection of the lateral rectus may suffice.[6,8] Bimedial rectus recession in itself, however, is usually inadequate.[6] In patients with total abduction deficit, especially with preservation of vertical gaze, the superior rectus muscle and the inferior rectus muscle may be transposed beside the lateral rectus muscle. Our preferred procedure is lateral augmentation. This procedure, however, may result in overcorrections.[8,24,25] We reserve medial rectus weakening as a second procedure, and prefer chemodenervation of the contracted medial rectus muscle. A partial transposition with lateral augmentation to decrease the strength of the procedure, as well as preserve a second ciliary blood supply per vertical rectus muscle, has been described.[26] This procedure may prove useful for these patients.

Management of refractive errors, amblyopia, and strabismus follows existing guidelines in treatment.

Many patients with Möbius sequence have multiple problems aside from age deviation, eating and communication difficulties resulting from facial palsy, cleft palate, and tongue anomalies. Cranial-nerve-IX-XII involvement, for example, leads to feeding and speech problems, as well as malnutrition. Developmental delay, seizure disorder, and dental caries all require specialists' care. The recognition and reinforcement of strengths and resiliencies such as family support, faith, sense of self, special skills, determination, and networking help maximize their personal and professional success as adults.

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