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Case Report

A congenital cranial dysinnervation disorder: Möbius' syndrome

Hatice Mutlu Albayrak[1], Nuriye Tarakçı[2], Hüseyin Altunhan[2], Rahmi Örs[2], Hüseyin Çaksen[3]

[1]Department of Pediatrics, Division of Pediatric Genetic Diseases, Necmettin Erbakan University Meram Medical Faculty, Konya, Turkey
[2]Department of Pediatrics, Neonatal Intensive Care Unit, Necmettin Erbakan University Meram Medical Faculty, Konya, Turkey
[3]Department of Pediatrics, Division of Pediatric Neurology, Necmettin Erbakan University Meram Medical Faculty, Konya, Turkey

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Abstract

Möbius' syndrome, also known as Möbius' sequence, is a nonprogressive cranial dysinnervation disorder characterized by congenital facial and abducens nerve paralysis. Here, we report a 5-day-old girl who was conceived after in vitro fertilization with poor suck and facial paralysis. She had bilaterally ptosis and lateral gaze limitation, left-sided deviation of the tongue, dysmorphic face, hypoplastic fingers and finger nails on the left hand, and was diagnosed as having Möbius' syndrome. Involvement of other cranial nerves such as three, four, five, nine, 9 and 12, and limb malformations may accompany this syndrome. However, several factors have been proposed for the etiology, some rare cases have also been reported with artificial reproductive technologies. Feeding difficulties and aspiration are the main problems encountered in infancy. The other cranial nerves should be examined further in newborns who present with congenital facial palsy, and other cranial dysinnervation disorders should be considered in the differential diagnosis.

Keywords: Artificial reproductive technologies, congenital facial paralysis, Möbius' syndrome

Introduction

Moebius syndrome (MS; %157900), also known as Moebius sequence, is a nonprogressive disease characterized by congenital facial and abducens nerve paralysis and is included in the group of congenital cranial dysinnervation disorders (CCDD). Congenital cranial dysinnervation disorders are primary or secondary muscle dysinnervation disorders arising from congenital developmental anomalies or complete absence of one or multiple cranial nerves. They are nonprogressive and may be sporadic or familial. Duane retraction anomaly, congenital fibrosis of extraocular muscles, horizontal gaze palsy, congenital ptosis, and congenital facial palsy are the other disorders included in CCDD.

The seventh and sixth nerves are the most commonly affected cranial nerves in MS, and involvement of the 3rd, 4th, 5th, 9th, 10th, and 12th cranial nerves may also be observed in association in some patients. Dysphagia, cranial dysmorphism, extremity anomalies, hypoplasia of the pectoralis minor muscle (Poland anomaly) and mental deficiency may also be observed in association (1). In these patients, feeding difficulty and aspiration problems are the main problems encountered in infancy. With advancing age, inexpressive face and speech disorder develop, leading to difficulty in social adaptation.

Although the majority of the cases are sporadic, cases showing autosomal dominant, recessive and X-linked recessive inheritance have also been reported. Cytogenetic anomalies in chromosome 1 and 13 have been demonstrated (2). A specific gene region belonging to this syndrome has not been identified up to this time. However, a mutation in the KIF21A gene, which was

Address for Correspondence: Hatice Mutlu Albayrak E-mail: haticemutlu@gmail.com
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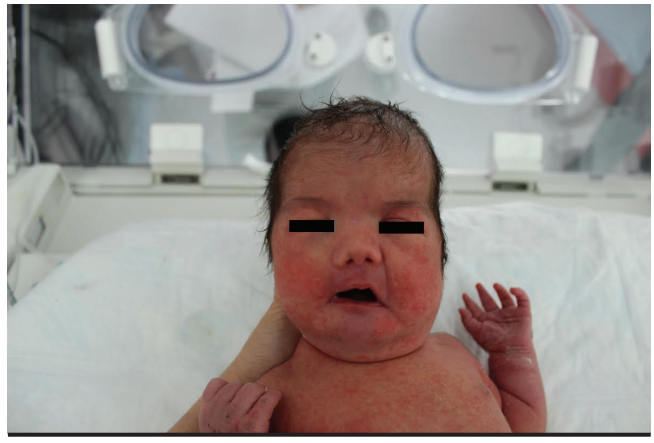
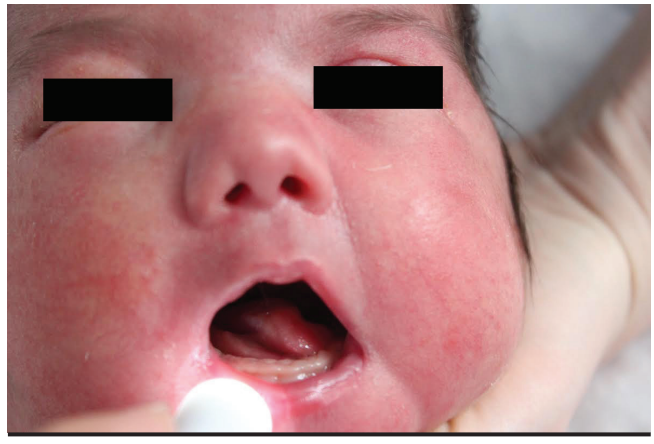
identified in congenital fibrosis of extraocular muscles type 1, has been reported in cases of MS accompanied by additional eye movement disorder (3). In the medical literature, a case of MS and a patient with Hanhart syndrome involving Moebius sequence in relation with intracytoplasmic sperm injection (ICSI), which is one of the assisted reproductive techniques, have been reported (4, 5). Our patient was born by way of in vitro fertilization and we could no other case reports in relation with in vitro fertilization in the medical literature. We presented this patient who was born as a result of pregnancy constituted by in vitro fertilization to draw attention to the potential etiological relationship between MS and in vitro fertilization.

Case

A five-day-old female baby was referred to the Pediatric Genetics Outpatient Clinic because of facial palsy and hypotonicity. The patient was born from the first pregnancy of a 30-year-old mother as the first living child at the 38th gestational week by cesarean section. There was no consanguinity between the mother and the father. It was learned that the mother became pregnant by way of in vitro fertilization. The patient was internalized in the Neonatal Intensive Care Unit because of poor feeding, hypotonicity, and facial palsy. Her body weight was 3100 g (P50), her height was 49 cm (P50), and her head circumference was 36 cm (P50). On physical examination, bilateral ptosis, epicanthus, bilateral limited outward gaze, depressed nasal bridge, anteverted nostrils, thin upper lip, downturned mouth corners, and micrognathia were observed, the labial sulcus was obscure on the right side and the mouth corner was sliding to the left while crying (Picture 1). Her tongue was sliding to the left side and twisting (Picture 2). Pinpoint appearance was present in the 2nd, 3rd, and 4th fingers of the left hand, and the nails were hypoplasic (Picture 3). The patient was hypotonic, she had lively deep tendon reflexes. The Moro reflex was positive. Her grasp reflex was present in all four extremities and her sucking reflex was weak. She was being fed with the help of a feeding tube because the patient had dysphagia and difficulty in sucking due to tongue palsy. Considering all the findings, the patient was diagnosed as having MS. The patient's hearing test was found to be normal. Cranial magnetic resonance imaging (MRI) and contrast-enhanced MRI of the temporal bone revealed no pathologic finding in the brain parenchyma and cranial nerves. Chromosomal analysis revealed 46, XX karyotype. On the follow-up, dysphagia continued in the third month and the family reported that she was drooling from her mouth. Written informed consent was obtained from the family to share the patient's data in a scientific setting.



Picture 1. Convergent strabismus and right facial palsy, dysmorphic facial appearance

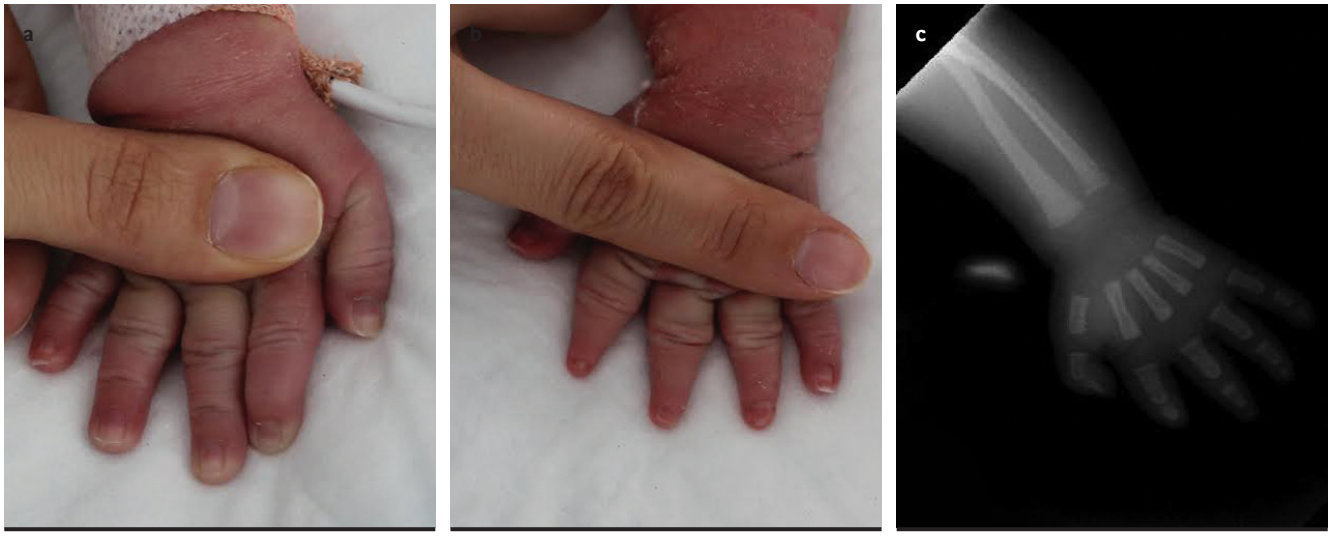


Picture 2. Unilateral tongue paralysis

Discussion

Moebius syndrome is defined as a congenital, non-progressive syndrome presenting with typical association of facial and abducens nerve palsy. The seventh and sixth cranial nerves are the most commonly affected cranial nerves. However, oropharyngeal involvement (secondary glossopharyngeal and hypoglossal nerve palsy) mostly accompanies MS, though it is sometimes overlooked (6). Here, we reported a case of MS with unilateral facial palsy and bilateral abducens nerve palsy. We think that involvement of the 9th, 10th, and 12th nerves accompanied because our patient had tongue palsy and dysphagia in addition to 7th and 6th cranial nerve palsy,.

The clinical findings of patients with Moebius syndrome show variability. Orofacial dysmorphism, cognitive retardation, extremity defects, Klippel-Feil anomaly, Poland syndrome, and epilepsy may also be



Picture 3. a-c. Right hand with normal appearance (a), Pen-point appearance of the fingers in the right hand (b), left hand antero-posterior graphy revealing hypoplasia in the distal phalanges (c)

observed in Moebius syndrome (7). Our patient had facial malformations (depressed nasal bridge, anteverted nostrils, thin upper lip, downturned mouth corners, bilateral epicanthus, and micrognathia), and hypoplasic distal phalanxes and nails in the left hand as additional anomalies.

Although the etiology has not been elucidated fully, some hypotheses thought to be involved in the pathogenesis of MS have been proposed. These include; 1) Absence or hypoplasia (the most common type) of the central brain nuclei, 2) Destructive degeneration of the central brain nuclei, 3) Peripheral nerve involvement and myopathy. In some studies, it was shown that hypoxic/ischemic injury of the brain stem in the first trimester and rombencephalic developmental disorders secondary to fetal vascular failure or exposure to teratogen (misoprostol) might lead to this syndrome (8). However, Jacob et al. (9) found no MRI anomalies in two cases of unilateral MS. In our patients, MRI revealed no brainstem developmental disorders, structural brain anomalies or venous anomalies.

There are two main techniques used for fertilization in IVF treatment including in vitro fertilization, which is the classic tube baby and ICSI. Studies have shown that some major and/or minor anomalies occur more commonly in babies of mothers who became pregnant by way of assisted reproductive techniques compared with groups that were pregnant through intercourse (2). A case of MS and a case of Hanhart syndrome (MS-associated syndrome) in relation with the intracytoplasmic sperm injection method have been reported previously (4, 5). Although studies conducted in recent years have reported that there was no increase in the general risk of congenital anomaly in relation with in vitro fertilization, an increased risk has been reported in under certain conditions (10). We could no case reports of MS related with in vitro fertilization in the medical literature. It seems to be insufficient to talk about a relationship between in vitro fertilization pregnancy and Moebius syndrome with only one case, studies with large series are needed.

In a study involving follow-up and treatment of patients with Moebius syndrome, it was observed that facial palsy had little effect on sucking function and tongue movements were more important in terms of early sucking pattern. Thus, sucking and swallowing disorders are present in cases accompanied by tongue paralysis in this syndrome. In patients who have facial palsy and tongue paralysis in association, speech disorder is also an important problem. Sensory-motor stimuli are applied in order to strengthen facial and tongue muscles, certain swallowing and speech therapies are given, facial exercises are recommended, and some assistive compensation mechanisms are taught. The symptoms tend to decrease with advancing age.

In conclusion, MS is basically a CCDD, though it may show clinical variability according to the etiopathogenesis and has a wide clinical variation. Although the expected finding is congenital 6th and 7th nerve palsy, paralysis of the other cranial nerves may also accompany. The life standards of patients can be increased with precautions and therapies directed to complications by early diagnosis of the syndrome and additional findings. History of birth by assistive reproductive techniques should be carefully interrogated in the etiology.

Informed Consent: Written informed consent was obtained from patients' parents who participated in this case.

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