Moebius syndrome: A review of literature
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Abstract
Moebius syndrome is a congenital neurological disorder, which frequently shows facial diplegia with bilateral lateral rectus palsy, but there are variations. The definition and diagnostic criteria for Moebius syndrome vary among authors, it is defined as congenital facial weakness with abnormal ocular abduction. Deformities such as muscular dystrophies and mental retardation have also been associated with this syndrome. The list of signs and symptoms mentioned in various sources for Moebius syndrome includes more than 20 peculiar features. This review of literature includes classification and grading system of Moebius syndrome, their features, etiology, and management.

Keywords:
Cranial nerves, facial palsy, Moebius syndrome, oral health

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Introduction
Moebius syndrome is a neurological disease, non-progressive congenitally occurs unilaterally or bilaterally weakness or palsy of more than 2 cranial nerves, mostly the abducens and facial nerves. The third and twelfth cranial nerves are also frequently involved. This type of syndrome was reported by Von Graefe in 1880 and Moebius in 1888. Prevalence is approximately 1/200,000 in live birth populations and equally distributed in male and female.

An International Group of Experts in 2007 prepared a criterion about how to diagnose Moebius syndrome. They are as follows: First, congenital facial paralysis affecting of both sides or complete paralysis of one limb, they affect lower efferent neuron of the peripheral nervous system, and second, unable to move lateral movements of the eyeball and abnormal alignment of the eyes because of abducens nerve paralysis.

The syndrome may also include cranial nerves such as III, V, VIII, XI, and XII with other abnormalities such as tongue fasciculations, cleft palate, and mandibular hypoplasia; skeletal abnormalities such as fusion of one or more digits, shortening of fingers and toes, abnormal curve of spine, curving of joints, absence of pectoral muscles, delayed puberty, impaired sense of smell, lack of production of certain hormones, and Carey–Fineman–Ziter syndrome which is combined with Moebius syndrome and Pierre Robin syndrome, and skin abnormalities such as macules and axillary web syndrome. Some patients reported autism and poor connection with society around 30–40% according to Ana et al. due to loss of facial expression. Figures of Moebius syndrome of a girl is given from Figure 1-3.

Classification and Grading System
The first district, “C” as cranial nerve, is divided into three groups based on severity of paralysis:

Group A: Bilateral complete paralysis of abducens and facial nerves (Moebius syndrome).
Group B: Paralysis of abducens and facial nerves with residual function of some nerve muscle units of the face unilaterally (incomplete Moebius syndrome).
Group C: Unilateral facial paralysis (Moebius-like syndrome).

Towfighi et al. classified Moebius syndrome into four categories according to alterations in their pathology

Category A includes underdevelopment of cranial nerve nuclei and presumably as.
Category B includes the main lesions of the surrounding cranial nerves. Category C comprises focal necrosis in brainstem nuclei indicating fetal infection and blood loss and shock due to less oxygen supply of the mother during gestation period. Category D includes no lesions in the CNS or having disease of the muscle.

Some pathogenesis are investigated, and suggestive causative factors are intrauterine vascular, toxic, genetic, and infections. The etiopathogenesis of Moebius syndrome remain unknown and still discuss, if it is caused genetically. The suggested etiological factors include lack of motor nuclei of the VI and VII cranial nerves, loss of function, and organs such as hypoxic–ischemic encephalopathy, brain injury (caused by

**Table 1: Of Moebius syndrome: Authors' findings and management**

<table>
<thead>
<tr>
<th>Authors</th>
<th>Findings</th>
<th>Management</th>
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<tr>
<td>Nagaraj et al. in 2016</td>
<td>Magnetic resonance imaging of a 2-year-old girl showed the following findings:</td>
<td>Since the disease is congenital and non-progressive, no definitive and established treatment has been described</td>
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<td>• Absent of cisternal and canalicular segments of left facial nerve</td>
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<td>• Flattened floor of fourth ventricle with absence of bilateral facial colliculi</td>
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<td>The magnetic resonance imaging of a 15-month-old male child brain showed complete agensis of the corpus callosum with superior vermian hypoplasia with prominent fourth ventricle which is consistent with the Dandy-Walker variant (includes vermian hypoplasia and cystic dilation of the 4th ventricle without enlargement of the posterior fossa)</td>
<td>Since the disease is congenital and non-progressive, no definitive and established treatment has been described</td>
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<td>A case of 18-year-old male showed the theory of nuclear hypoplasia that appears to hold good for III, VI, and VII nerve involvement and the gaze palsy, but the associated features like maldevelopment of foot and palm with webbing of fingers showed that the diverse manifestations of Moebius sequence are due to some noxious agents acting on the embryo at the time of development</td>
<td>Since the disease is congenital and non-progressive, definitive and established treatment has been described</td>
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<td>A case of a 2½-year-old female showed classical features of Moebius syndrome in association with a deletion of chromosome 13 (46, XX, del (13) (q12.2))</td>
<td>Since the disease is congenital and non-progressive, no definitive and established treatment has been described</td>
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<td>A case of male infant which is associated with unilateral cerebellar hypoplasia is unusual but consistent with a vascular disruption occurring in the basilar artery early in its development</td>
<td>Since the disease is congenital and non-progressive, no definitive and established treatment has been described</td>
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<td>A case of a 32-year-old male showed loss of function of the abductors of the eye and paresis of the muscles of the lower portion of the face and the tongue. The underdeveloped mandible could possibly have resulted from that paresis. Except for slight arthritic changes in both legs, other anomalies of the extremities or trunk were not present (Henderson, 1939)</td>
<td>Surgical treatment such as Obwegeser sagittal osteotomy of maniple and chin reposition and rhinoplasty was done</td>
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<td>A case of a 6-year-old boy evaluated for congenital strabismus. This review showed that the use of thalidomide in early pregnancy associated with non-progressive facial, extraocular, lingual, and pectoral muscle agenesis, together with the skeletal deformity of symbrachydactyly represents the result of an intrauterine mesodermal defect impairing the development of these structures</td>
<td>Since the disease is congenital and non-progressive, definitive and established treatment has been described</td>
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<td>In the Moebius patients, the constant limitation of temporomandibular joint movement during growth seems to lead to the permanent limitation in the articular movement range. It is well known that the Moebius syndrome affects mimic muscles activity when muscles related to mandibular opening, protrusive and lateral movements are not directly damaged</td>
<td>These observations suggest the importance of an adequate functional rehabilitation program, starting from an early age, to improve temporomandibular joint movements</td>
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<td>A case of newly born boy to a 17-year-old woman showed that brainstem calcification on computed tomography confined to the abducens nuclei was strongly suggestive of Group III Moebius syndrome</td>
<td>Since the disease is congenital and non-progressive, no definitive and established treatment has been described</td>
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Authors                                                                                                               Findings                                                                                                          Management                                                                                                     
10. Ha and Messiah in 2003[21]                                         A case of an 18-year-old Hispanic male reported with a chief complaint of teeth hurt                              Surgical correction of facial paresis was done. Surgical treatment for the relief of bilateral facial paralysis has been attempted using the temporalis muscle for transplantation or using platysma muscle. Bilateral transfer of the anterior third of the masseter muscles to the corners of the mouth also has been attempted

11. Elsahy in 1973[22]                                                 Due to taking of thalidomide during miscarriages and throughout the last pregnancy, a 1-year-old girl showed mask-like facies, more apparent during crying. All facial movements were absent, unable to close eyelids completely, no conjugate movements of the eyes to either side could be detected; however, vertical elevation and depression were infrequently noted. The mouth was always open and the corners drooped, shrunken tongue, unable to protrude beyond her teeth, atrophic papillae. Right hand smaller than the left, syndactyly

12. Budic et al. in 2016[23]                                           A case of a 10-year-old girl with Moebius syndrome was scheduled for multiple tooth extraction surgery. Characteristic clinical expressions such as mask-like facies, strabismus, severe hypotonia, microglossia, micrognathia, high palate, limited mouth opening, inadequate coughing and swallowing reflexes, and respiratory problems due to frequent aspirations, nasal ulceration, crescent-shaped ulceration at the right corner of the mouth, trophic changes of the skin bilaterally along the third division of the trigeminal cranial nerve, hypoplastic corpus callosum, ventriculomegaly, developmental delay, limb anomalies (clubfoot), and hypoplastic right pectoral muscle

13. Krajcirik et al. in 1985[24]                                        A case of a 13-year-old girl with Moebius syndrome and recurrent pulmonary aspiration was scheduled for diagnostic fiber-optic bronchoscopy because of persistent left lower lobe pneumonia. Previous examination revealed expressionless facies, marked bilateral facial paralysis, and dysarthria, could not gaze fully to right or left, gag reflex was present, but poor elevation of uvula, bilaterally impaired corneal reflex

14. Mussi et al. in 2016[25]                                           The study included 30 subjects, MS group (n=15) and the healthy control group (CG, n=15). The salivary flow rate was measured from unstimulated and stimulated whole saliva and bilateral PS by calculating milliliters of saliva per minute. The right and left paraffin stimulation was evaluated separately

Moebius syndrome and repeated episodes of aspiration and pulmonary complications tolerated well nitrous oxide-fentanyl anesthesia with a d-tubocurarine-pancuronium mixture, during fiber-optic bronchoscopy. However, after the bronchoscopy, the patient developed acute respiratory failure due to excessive secretions in the airway and required tracheal intubation and respiratory support for 48 h. We recommend that these patients be medicated preoperatively with an antialalgogue and receive intensive respiratory support postoperatively, preferably with the tracheal tube in place, to facilitate bronchial toilet

The salivary changes found in MS subjects, as the reduced salivary flow, increased amylase activity and a lower buffering capacity, may be related to higher incipient carious lesions in MS group. These results provide novel information regarding the dental caries increased risk on individual with MS
oxygen deprivation to the brain, which occurs in between 5 and 6 weeks of gestation period), diseases of the blood vessels, gastrointestinal tract infections, exposure to drugs (thalidomide or misoprostol), alcohol, cocaine, and a genetic component such as remodeling of PLXND1 and REV3L genes. It is already reputed that a major problem show an occurrence of damage of brainstem in one or more particular areas where the phase of embryogenesis occurs. Oral manifestation includes thin or small upper lip, congenital or acquired reduction in the size of the oral aperture, hanging corner of the mouth, micrognathia, high arch palate, weakness of tongue, grooves in tongue, loss of tongue papilla, and inability to close mouth.

Magda et al. in 1999 found a 14-month-old baby boy diagnosed as Moebius syndrome due to misoprostol taken in the 8th week of intrauterine life which includes disorder manifesting as sleep-associated alveolar hypoventilation, which mostly seen

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**Table 1: (Continued)**

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<td>15. Julia <em>et al.</em> in 2010⁶</td>
<td>A data collection was performed by retrospective review on six patients with Moebius syndrome who underwent direct tongue neurotization. Each patient was videotaped for 30 min preoperatively and postoperatively according to a standardized protocol</td>
<td>Result showed considerable improvement in speech intelligibility and articulation. Higher improvement was noted in patients with partial bilateral hypoglossal involvement than in patients with complete unilateral involvement of the hypoglossal nerve, as well as in younger patients. Tongue neurotization has therefore an important role in restoring the ability of these patients to communicate and obtain the potential to develop normal social skills</td>
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<td>16. Fernandes <em>et al.</em> in 2013⁷</td>
<td>A case of a 7-month-old boy, first twin, weighing 6.5 kg presented with Moebius syndrome was admitted for clubfoot repair. The patient had malignant hyperthermia after exposure to sevoflurane and succinylcholine, which was readily reversed with dantrolene maintained for 24 h. Ten hours after dantrolene discontinuation, there was recrudescence of malignant hyperthermia that did not respond satisfactorily to treatment, and the patient died</td>
<td>Musculoskeletal disorders in children are associated with increased risk of developing malignant hyperthermia, although Moebius syndrome has not yet been reported. Dantrolene is the drug of choice for treating this syndrome; prophylaxis is indicated during the first 24–48 h of the episode onset. The main risk factors for recurrence are muscular type, long latency after anesthetic exposure, and increased temperature. The child had only one risk factor. This case leads us to reflect on how we must be attentive to children with musculoskeletal disease and maintain treatment for 48 h</td>
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**Figure 1:** Facial profile

**Figure 2:** Unable to close eyelids (lagophthalmos)
in the early stage after birth. Symptoms may include bluish discoloration of the skin due to inadequate oxygen supply of the blood, cessation of breathing, respiratory arrest, and congenital central hypoventilation syndrome. Many authors had given findings and management of Moebius syndrome in Table 1.

Conclusion

It is important to diagnosis and rehabilitate to get proper information. It is also necessary to counsel both the child and parent about this syndrome. For management, this type of patient needs multidisciplinary approach which involves qualified trainers to perform different types of therapies. And at last, we should analyze large number of populations and need more investigation to find out the etiology and complications of this type of syndrome.

References
