

# Marden-Walker syndrome

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## Abstract

*Marden and Walker described in 1966 a female infant with blepharophimosis, joint contractures, arachnodactyly and growth and developmental delay, who died of pneumonia at 3 months. Since 1966, about 30 cases of Marden-Walker syndrome (MWS) have been reported. MWS signs are mostly present in the neonatal period and the most frequent manifestations include multiple congenital joint contractures, dysmorphic features with a mask-like face, blepharophimosis, ptosis, micrognathia, cleft or high-arched palate, low-set ears, arachnodactyly, decreased muscular mass. Disease course is always characterized by failure to thrive and psychomotor retardation. Initially described as a syndrome, this condition is more likely to be the phenotypic expression of various heterogeneous diseases and belongs to group II in the classification of arthrogyrosis. The underlying pathological mechanism has not been clearly established. The diagnosis is only based on clinical criteria. The treatment is only symptomatic, with multidisciplinary management (kinesitherapy, psychomotricity, orthophony).*

## Key-words

Marden-Walker syndrome, dysmorphism, arthrogyrosis, psychomotor retardation

## Definition / diagnostic criteria

Marden-Walker syndrome (MWS) is a rare congenital connective tissue disorder (1). Over 75% of children with MWS have blepharophimosis, small mouth, micrognathia, kyphosis/scoliosis, radioulnar synostose and multiple contractures (2). Minimal diagnosis criteria have been defined by Williams (3): severe developmental delay, congenital joint contractures and blepharophimosis should be present in every patient, while 2 out of the 3 following signs should be manifested: post natal growth retardation, mask-like facies, decreased muscular mass. Shrandner (4) defined criteria

which require additional signs: micrognathia, high arched or cleft palate, low set ears, kyphoscoliose. On the basis of these criteria (3,4), it is almost impossible to establish the diagnosis of MWS with certainty in the newborn period.

## Differential diagnosis

The differential diagnosis is relatively limited (3), encompassing 2 other syndromes: Freeman-Sheldon syndrome and Schwartz Jampel syndrome (5), which share some features with MWS, although they are usually both associated with normal mental development. Moreover, Freeman-Sheldon

syndrome is characterized by the absence of joint contractures, which are progressive and not present at birth in Schwartz Jampel syndrome. Many children of the series described with the diagnosis of Pseudo-trisomy 18 match diagnostic criteria suggested by Williams et al. (3) and are probably MWS. Presence of some symptoms, such as myotony should rule out MWS.

### **Etiology**

Etiology of MWS is probably heterogeneous. Initially described as a syndrome, this condition is more likely to be the phenotypic expression of various heterogeneous diseases and belongs to the group II in the classification of arthrogryposis (6,7). The report of two affected sibs, with a female presenting a typical Marden-Walker syndrome and a normocephalic male fetus with severe distal arthrogryposis without facial dysmorphism (6), suggest that Marden-Walker syndrome and isolated distal arthrogryposis may be variable manifestations of the same entity. Unknown congenital myopathy has been suspected to underlie MWS (8) due to muscular involvement, but extensive evaluation of the neuromuscular system (EMG, muscle biopsy and CPK data) failed to identify a primary myopathy in patients with MWS. Secondary muscle involvement from a CNS lesion may occur, as suggested by prenatal central nervous system dysfunction (mainly of the cerebellum and brainstem which may play a significant role in the pathogenesis of the MWS). This could produce a picture of congenital weakness with hypotonia, reduced muscle mass and hypoactive deep tendon reflex .

### **Clinical description**

Most MWS signs are present in the neonatal period (9). The most frequent signs include multiple congenital joint contractures, dysmorphic features with a mask-like face, blepharophimosis, ptosis, micrognathia, cleft or high-arched palate, low-set ears, arachnodactyly, decreased muscular mass. Camptodactyly, chest deformation as pectus (excavatus or carinatus), kyphoscoliosis and absent deep tendon reflexes are frequent. Minor malformations have also been described and consist of renal anomalies (10) (renal microcysts and cystic dysplasia, unilateral kidney hypoplasia, unilateral mild hydronephrosis), cardiovascular abnormalities (dextrocardia, abnormal connexion between inferior and superior

vena cava, multiple ventricular septal defects), hypospadias, omphalomesenteric duct, hypertrophic pyloric stenosis (11), duodenal bands, hypoplastic right lower lobe of the lung, displacement of the larynx to the right and vertebral abnormalities. Cerebral malformations, such as hydrocephalus, hypoplastic corpus callosum, cerebellar vermis hypoplasia, enlarged cisterna magna may be associated with microcephaly (9,12).

### **Natural history**

Disease course is always characterized by failure to thrive and psychomotor retardation. Mental retardation remains severe, whereas contractures are not progressive and decrease with advancing age and physiotherapy. Nevertheless, the natural history of MWS is not well-known: many patients died in infancy and clinical follow-up has only been reported in few surviving adult patients. Moreover, diagnosis may be more difficult to establish in adult patients (13): blepharophimosis, contractures, growth retardation, and developmental delay persist, whereas minor face anomalies are less noticeable as the patient grows older. Behaviour changes from kindness in childhood to restlessness, hyperactivity and aggressiveness in adolescence.

### **Diagnostic methods**

The diagnosis is based on clinical criteria (see **Definition/diagnostic criteria**).

### **Frequency**

Since 1966, about 30 cases of Marden-Walker syndrome (MWS) have been reported (4,8,10,11,13,14,15,16,17,18,19,20,21,22,23,24,25,26,27,28,29,30,31).

### **Genetic counseling**

Genetic counseling remains unclear, but the possibility of autosomal recessive inheritance (2,25) should be considered since cases of affected sibs and parental consanguinity have been reported. Frequent spontaneous abortions have been described.

Intrauterine growth retardation, renal cystic disease, decreased fetal movements, polyhydramnios, talipes equinovarus and arthrogryposis should be considered as non specific antenatal presentation: Marden-Walker syndrome must be suspected as one of the possible pathologies in children presenting with heterogeneous fetal a(hypo)kinesia deformation sequence.

## Management

The treatment is only symptomatic, with multidisciplinary management (kinesitherapy, psychomotricity, orthophony).

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