

## P-09

### MX-LINKED CENTRONUCLEAR MYOPATHY: FROM CLINICAL DIAGNOSIS TO GENETIC COUNSELING

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**Background:** X-Linked Centronuclear Myopathy is a rare congenital myopathy characterized by hypotonia, muscle weakness and respiratory distress at birth, although the presentation may be delayed. It is the most severe and the most common of the three inheritance forms, which also include the autosomal dominant and the autosomal recessive centronuclear myopathies. While muscle biopsy is crucial to differentiate centronuclear myopathies from other congenital myopathies and muscular dystrophies, genetic testing is essential to establish a definitive diagnosis and to perform a precise genetic counseling.

**Clinical report:** We report a proband, first son of healthy non-consanguineous parents, who presented with severe congenital hypotonia, global muscle weakness and bilateral hand contractures. He was born prematurely, shortly after polyhydramnios diagnosis, at 30 gestational weeks. Ventilatory support was required since his birth. At examination, dolichocephaly was evident and he had ptosis and ophthalmoparesis, facial diparesia, as well as a weak cry. Muscle biopsy revealed fibers with variable diameter, including round atrophic fibers, with centrally located nuclei, as well as central areas of increased oxidative activity surrounded by a bright halo, which was compatible with a centronuclear myopathy. The previously reported pathogenic missense variant c.566A>G (p.Asn189Ser) was detected in the *MTM1* gene, in hemizygosity in the proband and heterozygosity in the mother, confirming the diagnosis of X-Linked Centronuclear Myopathy.

**Discussion:** The genetic testing of the X-linked form is warranted as a first-tier investigation in male infants with a severe phenotype and a characteristic muscle biopsy, since the autosomal forms of centronuclear myopathies present with a relatively mild phenotype in both males and females. The identification of a pathogenic *MTM1* mutation will enable preimplantation genetic diagnosis or prenatal diagnosis, as additional reproductive options for this couple.

## P-10

### PRENATAL DIAGNOSIS: A CASE OF PARTIAL TRISOMY 6Q

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Partial distal trisomy 6q is a rare event and is characterized by a distinct phenotype which includes microcephaly, acrocephaly, joint contractures and profound psychomotor retardation. The authors present a case of a 30-year-old pregnant woman referred to prenatal diagnosis due to ultrasound anomalies. It was the first pregnancy of a non-consanguineous couple with no familial or personal story of anomalies. Parents karyotype was performed. Cytogenetic analysis revealed a chromosome 15 with an increase p arm similar to a variation in length of heterochromatic stalks on the short arm. Both parents presented a chromosome 15 with satellites but different from the one detected at the amniocytes. Subtelomeric FISH analysis revealed a trisomy of 6q27-qter present at p arm of chromosome 15 - it was a *de novo* rearrangement. The parents decided to terminate the pregnancy and foetal autopsy was required. Several polymorphic variants were described in human chromosome 15 including increased amounts of short arm heterochromatin (ph+), interpreted as a normal polymorphism. In the majority of cases partial trisomy 6q results from a balanced chromosomal rearrangement in one of the parents, usually of maternal origin. There have also been rare cases in which partial trisomy 6q has appeared from spontaneous (*de novo*) errors very early in embryonic development. The authors compared the cytogenetic and the foetal autopsy findings with those described in the literature. Every new case of a rare chromosomal alteration should be reported in order to establish a genotype/ phenotype correlation, improving risk evaluation and genetic counseling.