Charcot-Marie-Tooth Disease, So Which Type?

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Introduction

- Charcot-Marie-Tooth disease (CMT) is an inherited motor and sensory neuropathy of the peripheral nervous system characterized by progressive loss of muscle tissue and tactile sensation in various parts of the body
- This disease is the most common inherited neurological disorder, affecting about 1 in 2500 people
- Charcot-Marie-Tooth disease is a phenotypic and genetically heterogeneous disease. There are more than 70 types described in the literature
- Genetic mutations that cause defects in neuronal proteins lead to disease. Although these mutations are predominantly inherited in an autosomal dominant manner, they can be inherited either autosomal recessively or X-linked. Although most mutations in CMT affect the myelin sheath, there are also mutations that affect the axon
- CMT is divided into several types and subtypes. CMT is most commonly seen (60-70% of cases) due to duplication of a large region containing the PMP22 gene on the short arm of chromosome 17
- A case of type 4C which is less common, and autosomal recessive inherited gene mutation of CMT is reported

Case

- A ten-year-old male patient
- **Complaint:** Inability to walk and food deformity
- **History:** While he had no known disease before, scoliosis was noticed at the age of 5 and later on, gait disturbance and foot deformity developed
- **Physical and neurological examination:** The patient, who had kyphoscoliosis, had facial and neck muscle weakness, tongue atrophy, bilateral pectoral and thenar-hypothenar atrophy, decreased bilateral lower extremity muscle strength (4/5) and bilateral pes cavus in his neurological examination. Bilateral lower extremities deep tendon reflexes were absent
- **Electromyography:** Severe sensorimotor demyelinating neuropathy
- **Echocardiography:** Normal
- **Cranial magnetic resonance imaging:** Normal
- **Genetic tests:** The patient's PMP22 gene analysis was normal. In the whole exome sequence analysis of the patient, c.3328_3329insGCTTCTGTTCCTAGG homozygous pathogenic mutation was detected in the SH3TC2 gene. This variant has not been reported before, but evaluations in databases show the variant as likely pathogenic. It was confirmed by Sanger sequence analysis, and it was seen that both parents were heterozygous carriers for this mutation. The patient was diagnosed with Charcot-Marie-Tooth disease type 4C
- **CMT Type 4C:**
  - Charcot-Marie-Tooth Type4C disease is seen due to the mutation of the SH3TC2 (SH3 domain and tetratricopeptide repeats 2) gene located on chromosome 5q32
  - It is a demyelinating neuropathy characterized by severe spinal deformities (scoliosis or kyphoscoliosis) and foot deformities (pes cavus, pes planus, or pes valgus) typically occurring in the first decade of life
  - Treatment is symptomatic and multidisciplinary

Conclusion

- PMP22 gene mutation is the most common genetic cause of Charcot-Marie-Tooth disease
- A single-gene analysis regarding PMP22 deletion or duplication should be performed in all patients
- Whole exome or whole genome sequence analysis should be performed in patients with normal single gene analysis
- Genetic counseling should be given to families

References

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