

Steroid-Responsive Benign Hereditary Chorea: A Case of Unexpected Therapeutic Benefit

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Background: *NKX2-1*-related disorders range from benign hereditary chorea (BHC) to choreoathetosis, congenital hypothyroidism, and neonatal respiratory distress syndrome (also known as brain-lung-thyroid syndrome). Childhood-onset chorea, the hallmark feature of *NKX2-1*-related disorders, may or may not be associated with pulmonary disease or congenital hypothyroidism. Current treatment options are symptomatic and frequently unsatisfactory. We report the case of a patient with a genetically confirmed *NKX2-1* mutation who manifested sustained clinical improvement after steroid therapy—an unexpected result for a non-inflammatory genetic disease.

Case Report: we presented a case of generalized chorea in a 43-year-old man. The patient reports difficulty in acquiring motor milestones, with gait instability, and the presence of generalized choreo-athetotic movements. Brain MRI revealed bilateral, non-specific gliotic changes localized to the corona radiata. Genetic testing for Huntington's disease was negative. The patient was unsuccessfully treated with tetrabenazine. At the age of 32, he underwent orthopedic surgery on his right hip, which was followed by treatment with corticosteroids. A few hours after corticosteroid treatment, a clear improvement in choreoathetosis was reported. From that moment, the patient takes chronic therapy with prednisone 12.5 mg/day. The patient was referred to our attention for a second evaluation. Neurological examination revealed mild choreoathetotic movements involving all four limbs and the head. Extrinsic ocular movements were preserved. No bradykinesia was observed. All distractibility tests -such as cognitive tasks and motor-dual-tasking, failed to modulate the involuntary movements. After excluding several secondary causes of chorea, we performed an extended genetic panel, that showed a heterozygous c.429G>A (p.Arg143Gln) mutation in *NKX2-1*. A diagnosis of benign hereditary chorea (BHC) was made. During a screen for thyroid and/or pulmonary diseases, given their common association with BHC, the patient was diagnosed with nodular thyroid disease and is currently being monitored.

Discussion and Conclusion: this is the first case of steroid-responsive benign hereditary chorea reported in the literature. Potential mechanisms could involve unknown inflammatory pathways, epigenetic influences, or steroid off-target effects.[1][2]

[1] E. Falkenstein e M. Wehling, «Nongenomically initiated steroid actions», *Eur. J. Clin. Invest.*, vol. 30, fasc. s3, pp. 51–54, dic. 2000, doi: 10.1046/j.1365-2362.2000.0300s3051.x.

[2] M. Wehling, «SPECIFIC, NONGENOMIC ACTIONS OF STEROID HORMONES», *Annu. Rev. Physiol.*, vol. 59, fasc. 1, pp. 365–393, ott. 1997, doi: 10.1146/annurev.physiol.59.1.365.