

Congress Abstract

An Atypical *WNK1*-Associated Disorder with Severe Familial Hypertension and Sensory-Autonomic Neuropathy: A Case Report

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ABSTRACT

Background: *WNK1* encodes a serine/threonine kinase involved in renal electrolyte transport, blood-pressure regulation, and peripheral nervous system function. Pathogenic variants are associated with pseudohypoaldosteronism type II (PHAII; Gordon syndrome) and hereditary sensory and autonomic neuropathy type IIA. We report an unusual phenotype involving severe familial hypertension, mild autonomic manifestations, and recurrent seizure-like episodes.

Case presentation: A 39-year-old man presented with severe arterial hypertension and seizure-like episodes occurring daily, sometimes twice per day. Episodes began with hand tremor, progressing to generalized muscle rigidity, transient loss of consciousness, and facial and hand swelling. Observed sustained rigidity predominantly affected the upper body and thighs, with relative sparing of the gastrocnemius muscles. Psychological stress and blood-pressure elevations were common triggers. Blood pressure was 160/100 mmHg approximately five minutes before one attack; symptoms were less pronounced at systolic pressures of 130–140 mmHg. His mother and maternal grandfather had severe hypertension, whereas siblings were unaffected.

Brain 3-T MRI showed no explanatory structural abnormalities. Twenty-four-hour video-EEG monitoring demonstrated no convincing epileptiform activity, prompting consideration of a non-epileptic mechanism. Whole-genome sequencing identified a heterozygous *WNK1* frameshift variant, NM_018979.4.1748dup (p.Gln584AlafsTer27), classified as pathogenic by AIRS and Franklin, with sequencing evidence supported by manual IGV review.

Biochemical findings were atypical for classical PHAII. Potassium (4.0 mmol/L), sodium (143 mmol/L), magnesium (0.78 mmol/L), total calcium (2.16 mmol/L), phosphate (0.89 mmol/L), and creatinine (70.25 μ mol/L) were within reference intervals. Venous pH (7.39) and bicarbonate (23.7 mmol/L) were normal. Mild hyperchloremia (109 mmol/L), decreased ionized calcium (1.05 mmol/L), and vitamin D deficiency (12.11 ng/mL) were present, with normal PTH (28.07 pg/mL) and aldosterone (131.06 pg/mL). Twenty-four-hour urinary sodium excretion was elevated (232 mmol/day). Treatment comprised hydrochlorothiazide 12.5 mg once daily, calcium citrate 1,000 mg, and magnesium citrate 400 mg. At the two-month follow-up, the patient reported only one stress-triggered episode during the preceding month, compared with daily episodes before treatment.

Conclusion: This presentation raises the possibility of an atypical *WNK1*-associated phenotype, although the variant's contribution requires further clarification. The absence of hyperkalemia and metabolic acidosis differs from classical Gordon

syndrome, while ionized hypocalcemia may contribute to neuromuscular hyperexcitability. The reported reduction in episode frequency suggests clinical improvement following treatment. Long-term follow-up, including blood-pressure and electrolyte monitoring and further characterization of paroxysmal events, is required to evaluate sustained response and clarify the underlying mechanism.

Keywords: WNK1 Mutation; Familial Hypertension; Whole Genome Sequencing; Gordon Syndrome