Adrenomyeloneuropathy (AMN) manifesting in a genetically confirmed female carrier with a pathogenic heterozygous mutation in the X-linked ABCD1 gene.

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Background

AMN is an X-linked recessive disorder affecting the nervous system white matter and adrenal cortex. Males manifest in their twenties to middle age with symptoms of progressive leg stiffness and weakness, bowel/bladder dysfunction and adrenal cortex dysfunction. The majority of female carriers do not show symptoms but a minority can present with spastic paraparesis usually in middle age. The diagnosis of AMN is established with elevations in very long chain fatty acids (VLCFAs) and a heterozygous pathogenic mutation in the ABCD1 gene.

Design and Methods

Case report of a patient seen at the University of California, Irvine Neuromuscular clinic.

Examination

We report a 46-year-old woman with 6 years of progressive gait difficulty, bowel/bladder dysfunction, and history of infertility. Examination was significant for marked leg spasticity and symmetric proximal and distal bilateral leg weakness of MRC grade 4-4+/5 with hyperreflexia limited to the lower extremities. Vibration and proprioception loss was demonstrated in the legs only. She had a spastic gait with obvious leg scissoring.

A

Figures A:
Marked adduction of thighs during stride.
Figure B:
Normal posture when standing.

B

Results

Workup was unrevealing for: B12, copper, HIV, HTLV1-2, RPR, brain MRI, and EMG/NCS. Spinal MRI demonstrated atrophy of posterior cord. VLCFAs were elevated. Previous adrenal testing by an endocrinologist was unrevealing. Genetic testing revealed a pathogenic heterozygous mutation c.1415_1416delAG (p.Q472R) in the ABCD1 gene.

Conclusion

While typically a male disease (given the X-linked recessive inheritance), we present a case of adrenomyleoneuropathy in a female manifesting carrier with a heterozygous mutation in the ABCD1 gene. Although often asymptomatic, female carriers of heterozygous mutations can manifest symptoms of AMN and should be considered in cases of myeloneuropathy.

References

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