The Endocrine-Genetics Clinic

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Introduction:

The field of Endocrinology has witnessed a rapid expansion in the taxonomy of monogenic disorders, which can be detected by genetic tests. The Endocrine-Genetics Clinic was established in September 2020. Since then, ~240 patients have been evaluated for diverse clinical diagnoses, including: endocrine tumor syndromes, metabolic disorders, bone metabolism and hormonal dysfunction. The following presentation of an ultra-rare diagnosis illustrates the complexity of the Endocrine-Genetics field.

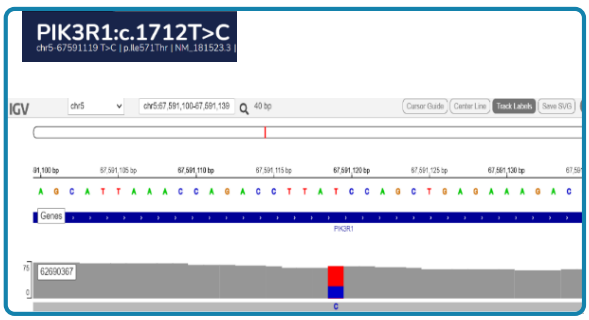
Case report:

A 37-year-old patient with *papillary thyroid carcinoma. F*ollowing total thyroidectomy and radioiodine treatment complained of constant debilitating severe myalgia, necessitating chronic opioid treatment. Extensive evaluation, including muscle MRI and biopsy, nerve conduction studies, EMG, and medical treatment reevaluation were all negative.

- Past medical history: thyroiditis, dyslipidemia, speech delay, delayed dentition, myopia, diabetes-adult onset, hypogonadism, hearing impairment.
- Family History: Unremarkable. No known consanguinity.
- Physical exam: height 153 cm, weight 85 kg, BMI=35.
- Central obesity with sparing of the extremities, ocular depression, temporal wasting, gynecomastia.

Molecular analysis:

- NGS-based gene panel for muscular disorders – Negative.
- Whole Exome Sequencing (WES) trio analysis during his daughter's pregnancy performed (Centogene) due to IUGR and shortening of long bones - Negative.
- Revision of WES raw data: The patient and his daughter carry a heterozygous *PIK3R1* c.1712T>C, p.Ile571Thr likely pathogenic variant.



Discussion:

Pathogenic variants in the gene *PIK3R1* are associated with SHORT syndrome. This rare syndrome (~50 cases published to date) manifests as IUGR, short stature, partial lipodystrophy, insulin resistance, hearing loss and dental abnormalities. Herein we present a familial case of a proband and his daughter, with a phenotype consistent with SHORT syndrome. Though myalgia is reported as a rare chronic complication of radioiodine treatment, it may also be triggered by predisposing lipodystrophy. We suggest that the confirmed molecular diagnosis of SHORT syndrome provides an etiological explanation for this enigmatic manifestation of myalgia.

Conclusion:

This case illustrates the value of an Endocrine-Genetics Clinic, which combines the expertise of these two disciplines and provides personalized medicine for such complex cases.