Thoughts on The Results of Genetic Map of a Family

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Background:

Neuroendocrine tumors associated with MEN1-4 genetic syndrome are more and more recognized. The evolving understanding of genotype-phenotypic relationships and disease progression is changing the way we manage affected patients.

Methods:

The blood samples of the patient's mother, the mother's brother and sister and their next generation, the patient and her brother and their next generation were collected and tested.

Demonstration:

The patient, a 47-year-old female, underwent left parathyroidectomy for parathyroid tumor and elevated PTH in 2013. Pancreatic tumor resection was performed in 2021, confirmed pancreatic neuroendocrine tumor. no germline mutant gene was found at that time. Fatigue began to appear in 2022, PTH 235.54pg/mL, Ca 2.83mmol/L, and bilateral parathyroidectomy was performed again. In terms of family history, her brother was diagnosed with Adult Still Syndrome in 2007 and lung metastasis of renal clear cell carcinoma in 2021; her mother was considered with lung cancer at the age of 40; and the niece was diagnosed with pituitary adenoma at the age of 16.

Conclusions/Main Findings: In the case of typical clinical features and clear family history, if the results of the first gene test are negative, further expanded gene testing can be expanded. Further provide genetic counseling for patients, and conduct corresponding clinical and genetic screening of patients' first-degree relatives according to the actual clinical situation.

Keywords: family, germline mutant, MEN1

No confficts of interest.

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Results/Data:

Blood samples were collected and germline testing was carried out in 2023, and 6 out of 11 people detected MEN1 mutation (c.35C>T) and interpreted it as likely-pathogenic. Particularly, the patient has a pair of 18-year-old twin sons, one of whom has the pathogenic mutation and the other is negative. The sequence change replaces proline with leucine at codon 12 of MEN1 protein (p.Pro12Leu). Proline residues are highly conserved, while there are moderate physical and chemical differences between proline and leucine, which may affect the function of MEN1.

Number	MEN1 Mutation	Interpretation
1*	c.35C>T	likely_pathogenic
2	c.35C>T	likely_pathogenic
3	None	None
4	c.35C>T	likely_pathogenic
5	None	None
6	None	None
7	None	None
8	c.35C>T	likely_pathogenic
9	c.35C>T	likely_pathogenic
10	None	None
11	c.35C>T	likely_pathogenic