INTRODUCTION

- Multiple endocrine neoplasia type 4 (MEN4) syndrome is an autosomal dominant disorder caused by a germline mutation in the CDKN1B gene.
- CDKN1B codes p27, a tumor suppressor protein involved in cell cycle.
- MEN4 is characterized by occurrence of hyperparathyroidism (HPT), pituitary adenomas (PA), and neuroendocrine tumors (NET), similar to MEN1 syndrome.
- Possible genotype-phenotype correlation in MEN4 have not been thoroughly assessed.

OBJECTIVES

- Review the literature on MEN4 clinical course.
- Assess for possible genotype-phenotype association in MEN4.
- Describe new Israeli cases harboring a pathogenic variant in CDKN1B.

METHODS

A literature review on published and unpublished data from previously reported MEN4/CDKN1B cases (Figure 1).

Data gathered: clinical presentation, age of diagnosis and characteristics of each tumor, family history, CDKN1B variants reported.

Additional three families with CDKN1B pathogenic variant described.

Univariate analysis analysed time-dependent risks for developing PHPT, PitAd, or NET by variant type and position along the gene.

RESULTS

A total of 74 cases of MEN4 were identified and analyzed

Three unrelated Ashkenazi Jewish families described, with identical CDKN1B mutation p.Q107fs in seven carriers

Family 1 (Figure 2), comprised one carrier with HPT, and one untested deceased family member with NET, family 2 had a patient with acromegaly and HPT, family 3 had no clinical symptoms

CONCLUSIONS

MEN4 is a rare syndrome, with 74 cases (including the presented case reports) described thus far

MEN4 is clinically distinct from MEN1, with lower risk and older age for HPT diagnosis and a relatively early presentation of PitA

We report possible genotype-phenotype correlations

REFERENCES

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Halperin et al, Endo Relat Cancer, in press

ACKNOWLEDGMENT

We thank Dr. Frederiksen and Dr. Nielsen for providing additional information on the cohort published on Frederiksen et al (JCEM, 2019)