INTRODUCTION

The autosomal dominant Multiple Endocrine Neoplasia Type 1 (MEN1), characterized by parathyroid hyperplasia (PH), neuroendocrine digestive tumours (NET) and pituitary adenomas (PA), is due to mutations in the tumor suppressor gene MEN1 (11q13.1) encoding a 610-amino acid protein, menin. Guidelines recommend MEN1 mutational analysis in index cases with two or more MEN1-associated tumors, in 1st degree relatives of mutation carriers and if clinical data suggest MEN1.

AIM

To compare our results in MEN1 genetic analysis from patients referred by Spanish endocrinologists and geneticists from 1997 to 2013 with the inclusion criteria from MEN1 guidelines in order to improve our insight on mutations and phenotype spectrum.

PATIENTS AND METHODS

164 index-cases, 117 females and 47 males from 13 hospitals in Spain (decision to study was taken by referring centers).

Coding regions and intron-exon boundaries of the MEN1 gene were analyzed. When no mutation was thus found, MLPA was performed.

RESULTS

164 index-cases: 117 female and 47 male (R:2.4)

No MEN1 mutations

108

106: no findings

1 CaSR and 1 AP2S1 (familiar PH)

56

MEN1 mutations

35/115 (30%)

21/47 (44%)

(cases are better selected in males than in females)

RELATIONSHIP OF N° OF MEN1-RELATED TUMORS AND FAMILY HISTORY (FH) WITH PRESENCE OF MEN1 MUTATIONS

INDEX CASES WITH 3 MEN1-RELATED TUMORS

INDEX CASES WITH 2 MEN1-RELATED TUMORS

INDEX CASES WITH 1 MEN1-RELATED TUMOR

PH + NET + PA (N=38)

PH + NET (N=27)

NET + PA (N=2)

MEN1 MISSENSE MUTATIONS IN FAMILIAL PH AND RELATED WITH NUMBER OF MEN1 TUMORS: no association was observed (p value=0.72)

CONCLUSIONS

Our data support clinical current referral criteria for MEN1 molecular genetic testing.

The probability of finding a MEN1 mutation in a patient is positively correlated with the presence of family history and the number of MEN1-related tumors (NET).

Cases that present only one tumor + family history, or even one tumor if this is a NET, should be analysed.

According to our results missense mutations are not associated with familial hyperparathyroidism or milder phenotype.

REFERENCES: