INTRODUCTION

Pituitary adenomas (PA) in pediatric and young patients comprise a rare pathology of unknown prevalence. The majority are sporadic, but 5% occur in a familial setting, either as isolated (FIPA) or as part of a syndrome (1,2). Somatic changes in GNAS and USP1 have been identified in an important percentage of sporadic somatotropinomas and adrenocorticotrophic tumours (3). However, only 10-12% of young patients with sporadic PA carry germline mutations in AIP or MEN1 (4). Other genes such as CDKN1B, PRKAR1A, SDHD, and DICER1 predispose to PAu (5).

AIM

We describe the clinical characteristics of patients with sporadic pituitary adenomas arising before the age 35 years and perform a thorough genetic screening for germline variants in probands and relatives.

RESULTS

Clinical characteristics

Among the total cohort, mean age was 19.5 years and 64.1% were females. Local mass effect symptoms were present in 22.4% and prolactinomas were the most frequent type of tumour (46.3%). Genetically positive patients were younger and had larger tumor size at diagnosis (Table 1).

Genetic findings

We identified disease-causing germline variants in 20 patients (Table 2). Healthy family carriers were also identified.

PATIENTS & METHODS

Patients

Clinical characteristics were collected from 276 patients (<35 years at disease onset) with apparently sporadic PA. Genetic screening

Genomic DNA from peripheral blood leukocytes was tested using a targeted gene panel (Thermo Fisher Scientific) including MEN1, AIP, PRKAR1A, CDKN1B, GNAS, DICER1, SDHD, SDHC, and SDHD genes. After bioinformatic analysis and in silico studies, we classified genetic changes according to recommendations (6). Patients’ relatives were tested by PCR and Sanger sequencing. We performed a comparative genomic hybridization array (aCGH) and GPR101 gene amplification on patients with gigantism/acromegaly. In cases with a constitutively active gene was amplified by PCR and sequenced.

CONCLUSIONS

Variants in genes associated with syndromic forms of pituitary adenomas were detected in a large cohort of apparently sporadic pituitary tumours. Longer follow-up of these positive patients and their relatives is essential to accentuate this statement.

We have identified novel variants in well-known genes, such as CDKN1B, and set the possibility of incomplete disease penetrance in carriers of MEN1 alterations or a limited clinical expression of the syndrome.

Despite the low penetration observed, genetic screening of AIP and MEN1 in young patients and relatives is of clinical value.

CONTACT INFORMATION

Icíar Castaño de las Almeidas
idiaz.martinezdelasalvacion@canarias.usalud.es

REFERENCES


ACKNOWLEDGEMENTS