Tyrotroph adenoma

Thyrotropin-secreting pituitary neuroendocrine tumors (TSHomas) represent a rare subtype of pituitary tumors.

They are a rare cause of hyperthyroidism, and the genetic aberrations responsible remain unknown.

Whole-Exome Sequencing Study

A single-nucleotide polymorphism (SNP) array analysis was performed on 8 TSHomas. Four tumors with no allelic losses or limited loss-of-heterozygosity were selected and whole-exome sequencing was performed including their corresponding blood samples. Somatic variants were confirmed by Sanger sequencing. A set of 8 tumors was also assessed to validate candidate genes. PATIENTS: Twelve patients with sporadic TSHomas were examined. INTERVENTION: No intervention was performed. RESULTS: The overall performance of whole-exome sequencing was good, with an average coverage of each base in the targeted region of 97.6%. Six novel DNA variants were confirmed as candidate driver mutations, with an average of 1.5 somatic mutations per tumor. No mutations were recurrent. Two of these mutations were found in genes with an established role in malignant tumorigenesis (SMOX and SYTL3) and four with unknown roles (ZSCAN23, ASTN2, R3HDM2, and CWH43). Similarly, a SNP array analysis revealed frequent chromosomal regions of copy number gains, including recurrent gains at loci harboring 4 of these 6 genes.

We identified several candidate somatic mutations and changes in copy numbers for TSHomas. Our results showed no recurrence of mutations in the tumors studied, but a low number of mutations, thereby highlighting their benign nature. Further studies on a larger cohort of TSHomas, along with the use of epigenetic and transcriptomic approaches may reveal the underlying genetic lesions [1].

Treatment

Surgery is still considered the first-line therapy.

Reviews

Fujio S, Yoshimoto K. [TSH-Secreting pituitary neuroendocrine tumor]. No Shinkei Geka. 2018 Dec;46(12):1053-1063. doi: 10.11477/mf.1436203868. Japanese. PubMed PMID: 30572302 [2].

Case series

2014

A retrospectively evaluation of thirteen patients diagnosed for TSHomas (9 M; age range 27-61). Ten patients had a magnetic resonance evidence of macroadenoma, three with slight visual field defect. In the majority of patients, thyroid ultrasonography showed the presence of goiter and/or increased

gland vascularization. Median TSH value at diagnosis was 3.29 mU/L (normal ranges 0.2-4.2 mIU/L), with median fT4 2.52 ng/dL (0.9-1.7 ng/dL).

Three patients (two microadenoma) were primarily treated with NCH and achieved disease remission, whereas ten patients (nine macroadenomas) were initially treated with somatostatin analogs (SSA). Despite the optimal biochemical response observed during medical treatment in most patients (mean TSH decrease -72 %), only two stayed on medical therapy alone, achieving stable biochemical control at the end of the follow-up. The remaining patients (n = 7) underwent NCH later on during their clinical history, followed by radiotherapy or adjuvant SSA treatment in two cases. Noteworthy, five of them developed hypopituitarism. All patients reached a biochemical control, after a multimodal therapeutic approach.

Neurosurgery ultimately led to complete disease remission or to biochemical control in majority of patients, whereas resulting in a considerable percentage of post-operative complications (mainly hypopituitarism, 50 %). In the light of the optimal results unanimously reported for medical treatment with SSA, this experience suggests that a careful evaluation of risk/benefit ratio should be taken into consideration when directing the treatment approach in patients with TSHoma [3].

1)
Sapkota S, Horiguchi K, Tosaka M, Yamada S, Yamada M. Whole-Exome Sequencing Study of Thyrotropin-Secreting pituitary neuroendocrine tumors. J Clin Endocrinol Metab. 2016 Nov 17:jc20162261. [Epub ahead of print] PubMed PMID: 27854551.
2)
Fujio S, Yoshimoto K. [TSH-Secreting pituitary neuroendocrine tumor]. No Shinkei Geka. 2018 Dec;46(12):1053-1063. doi: 10.11477/mf.1436203868. Japanese. PubMed PMID: 30572302.
3)
Gatto F, Grasso LF, Nazzari E, Cuny T, Anania P, Di Somma C, Colao A, Zona G, Weryha G, Pivonello R, Ferone D. Clinical outcome and evidence of high rate post-surgical anterior hypopituitarism in a cohort of TSH-secreting adenoma patients: Might somatostatin analogs have a role as first-line therapy? Pituitary. 2014 Oct 19. [Epub ahead of print] PubMed PMID: 25326851.