Gonadotroph adenoma

pituitary neuroendocrine tumors with FSH- or LH-positive immunohistochemistry.

Pathogenesis

Long non-coding RNAs (lncRNAs) have received increased research interest owing to their participation via distinct mechanisms in the biological processes of clinically nonfunctioning pituitary neuroendocrine tumors. However, changes in the expression of lncRNAs in gonadotropin secreting pituitary neuroendocrine tumor, which is the most common nonfunctional pituitary neuroendocrine tumors, have not yet been reported.

Li et al., performed a genome-wide analysis of lncRNAs and mRNAs obtained from gonadotrophin adenoma patients' samples and normal pituitary tissues using RNA-seq. The differentially expressed lncRNAs and mRNAs were identified using fold-change filtering.

They identified 839 lncRNAs and 1015 mRNAs as differentially expressed. Gene Ontology analysis indicated that the biological functions of differentially expressed mRNAs were related to transcription regulator activity and basic metabolic processes. Ingenuity Pathway Analysis was performed to identify 64 canonical pathways that were significantly enriched in the tumor samples. Furthermore, to investigate the potential regulatory roles of the differentially expressed lncRNAs on the mRNAs, they constructed general co-expression networks for 100 coding and 577 non-coding genes that showed significantly correlated expression patterns in tumor cohort. In particular, they built a special sub-network of co-expression involving 186 lncRNAs interacting with 15 key coding genes of the mTOR pathway, which might promote the pathogenesis of gonadotrophin tumor. This is the first study to explore the patterns of genome-wide lncRNAs expression and co-expression with mRNAs, which might contribute to the molecular pathogenesis of gonadotrophin adenoma [1)].

Diagnosis

Gonadotroph adenomas are difficult to diagnose because they are usually non-secreting, or they secrete biologically inactive peptides with no clinical effects, and they classically grow silently until neurological symptoms develop.

Clinical signs or symptoms of gonadotropin hypersecretion are very rarely reported, involving a few premenopausal women with ovarian hyperstimulation syndrome and men with macro- orchids.

A large proportion of the adult patients undergoing surgery for clinically nonfunctioning pituitary neuroendocrine tumor had a silent gonadotroph adenoma: the definitive diagnosis can only be established from a positive FSH/LH immunoreactivity.

Most are endocrinologically silent, and neurological symptoms due to their large volume are the first clinical signs; they are rarely reported to be secreting gonadotropins, this usually occurring in cases with clinical endocrine findings.

Among gonadotropinomas, female gender (77%), macroadenoma (84%), young age at diagnosis (28

± 12 years), delay from first symptoms to diagnosis (up to 15 years), and ovarian cysts/menstrual disorders in females or macro-orchidism in males were the foremost clinical and neuroimaging features.

Male gonadotropin-secreting pituitary neuroendocrine tumors may have a variable clinical expression secondary to testosterone excess. Somatostatin analogs, dopamine agonists or temozolomide may have a role that needs to be assessed case by case.

Treatment

Gonadotrophinomas are often treated surgically because they are unresponsive to conventional medical therapies. Temozolomide was recently recommended for non-responder aggressive pituitary neuroendocrine tumor management [2].

1)
Li J, Li C, Wang J, Song G, Zhao Z, Wang H, Wang W, Li H, Li Z, Miao Y, Li G, Zhang Y. Genome-wide analysis of differentially expressed lncRNAs and mRNAs in primary gonadotrophin adenomas by RNA-seq. Oncotarget. 2016 Dec 15. doi: 10.18632/oncotarget.13948. [Epub ahead of print] PubMed PMID: 27992366.
2)
Ceccato F, Occhi G, Regazzo D, Randi ML, Cecchin D, Gardiman MP, Manara R, Lombardi G, Denaro L, Mantero F, Scaroni C. Gonadotropin secreting pituitary adenoma associated with erythrocytosis: case report and literature review. Hormones (Athens). 2014 Jan-Mar;13(1):131-9. PubMed PMID: 24722134.