Familial isolated pituitary neuroendocrine tumor

Most familial pituitary neuroendocrine tumors occur in the setting of multiple endocrine neoplasia-type 1 (MEN-1), Carney complex (CNC) or isolated familial somatotropinomas (IFS) [1)]

Familial isolated pituitary neuroendocrine tumor (FIPA) is an autosomal dominant disease, characterized by low penetrance, early-onset disease, more invasive tumor growth, as well as somatotroph and lactotroph adenomas in most cases.

Only 20 to 30 percent of individuals with an AIP gene mutation develop a pituitary neuroendocrine tumor.

Less common tumor types in FIPA include somatolactotropinomas, nonfunctioning pituitary neuroendocrine tumors, adrenocorticotropic hormone-secreting tumors (which cause a condition known as Cushing disease), thyrotropinomas, and gonadotropinomas. In a family with the condition, affected members can develop the same type of tumor (homogenous FIPA) or different types (heterogenous FIPA).

In FIPA, pituitary tumors usually occur at a younger age than sporadic pituitary neuroendocrine tumors, which are not inherited. In general, FIPA tumors are also larger than sporadic pituitary tumors. Often, people with FIPA have macroadenomas.

Familial pituitary neuroendocrine tumors can occur as one of many features in other inherited conditions such as multiple endocrine neoplasia type 1 and Carney complex; however, in FIPA, the pituitary neuroendocrine tumors are described as isolated because only the pituitary gland is affected.

It has been indicated that the aryl hydrocarbon receptor interacting protein (AIP) gene is a tumor suppressor gene. Many heterozygous mutations have been discovered in AIP in about 20% of FIPA families. However, the exact molecular mechanism by which its disfunction promotes tumorigenesis of pituitary is unclear [2)].

Reviews

A review of Beckers et al. assesses the current clinical and therapeutic characteristics of more than 200 FIPA families and addresses research findings among AIP mutation-bearing patients in different populations with pituitary neuroendocrine tumors [3)].

Case reports

Marques et al. report a five-generation kindred with two brothers with pituitary gigantism due to AIP mutation-positive GH-secreting pituitary neuroendocrine tumors and their first-cousin coincidently also having gigantism due to Marfan syndrome [4].

1)
Asa SL, Ezzat S. Genetics and proteomics of pituitary tumors. Endocrine. 2005 Oct;28(1):43-7. Review. PubMed PMID: 16311409.
2)
Cai F, Zhang YD, Dai CX, Liu XH, Yang YK, Yao Y, Wang RZ. [Aryl hydrocarbon receptor interacting protein gene and familial isolated pituitary neuroendocrine tumors]. Zhongguo Yi Xue Ke Xue Yuan Xue Bao. 2012 Dec;34(6):640-4. doi: 10.3881/j.issn.1000-503X.2012.06.021. Review. Chinese. PubMed PMID: 23286415.
3)
Beckers A, Aaltonen LA, Daly AF, Karhu A. Familial isolated pituitary neuroendocrine tumors (FIPA) and the pituitary neuroendocrine tumor predisposition due to mutations in the aryl hydrocarbon receptor interacting protein (AIP) gene. Endocr Rev. 2013 Apr;34(2):239-77. doi: 10.1210/er.2012-1013. Epub 2013 Jan 31. Review. PubMed PMID: 23371967; PubMed Central PMCID: PMC3610678.
4)
Marques P, Collier D, Barkan A, Korbonits M. Coexisting pituitary and non-pituitary gigantism in the same family. Clin Endocrinol (Oxf). 2018 Sep 17. doi: 10.1111/cen.13852. [Epub ahead of print] PubMed PMID: 30223298.