Lactotroph pituitary neuroendocrine tumor

- Estimating diagnostic delay in patients with pituitary adenomas in Sweden: a cross-sectional study
- Baseline testosterone levels as a predictor of hypogonadism resolution in male patients with isolated hyperprolactinemia
- Hyperprolactinemia caused by extra-pituitary prolactin secretion: a systematic review
- Cabergoline counteracts adipose and skeletal muscle lipid accumulation: A novel therapeutic approach to obesity?
- Whole genome sequencing and single-cell transcriptomics identify KMT2D inactivation as a potential new driver for pituitary tumors: a case report
- Subtle cognitive impairments and psychological complaints in patients with prolactinoma despite biochemical control
- Advances in drug treatments for male patients with prolactinomas
- Lights or shadows, a promising future for positron emission tomography in pituitary tumors: a systematic review

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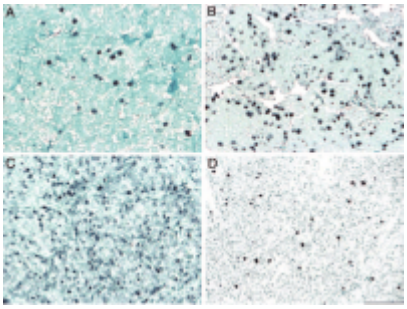

New term for prolactinoma.

It is a hormonally active pituitary tumor.The most common secretory adenoma. Arise from neoplastic transformation of anterior pituitary lactotrophs.

Epidemiology

Over 95 % of prolactinomas are microadenomas (< 10 mm diameter).

Prolactinomas are the most common type of hormone-secreting pituitary tumors and they represent 40% of all pituitary tumors [1)].

Classification

Current classification systems rely on phenotypic elements and have few molecular markers for complementary classification.

Giant prolactinoma

Macroprolactinoma

Microprolactinoma (At the time of diagnosis , 90 % of prolactinomas in women are microadenomas, vs. 60 % for males probably due to gender specific differences in symptoms resulting in earlier presentation in females).

Cystic prolactinoma

Etiology

Neoplastic transformation of lactotrophs.

Genetics

Somatic GNAS and USP8 mutations have been implicated in sporadic somatotrophinomas and corticotrophinomas, respectively. However, no genes are known to be recurrently mutated in sporadic prolactinomas. The prevalence of copy number variants (CNV), which is emerging as a mechanism of tumorigenesis in sporadic pituitary neuroendocrine tumors in general, is also unclear in prolactinomas. To characterize the genetic events underpinning sporadic prolactinomas, we performed whole exome sequencing of paired tumor and germline DNA from 12 prolactinoma patients. We observed recurrent large-scale CNV, most commonly in the form of copy number gains. We also identified sequence variants of interest in 15 genes. This included the DRD2, PRL, TMEM67, and MLH3 genes with plausible links to prolactinoma formation. Of the 15 genes of interest, CNV was seen at the gene locus in the corresponding tumor in 10 cases, and pituitary expression of eight genes was in the top 10% of tissues. However, none of our shortlisted somatic variants appeared to be classical driver mutations as no variant was found in more than one tumor. Future directions of research include mechanistic studies to investigate how CNV may contribute to prolactinoma formation, larger studies of relevant prolactinoma subsets according to clinical characteristics, and additional genetic investigations for aberrations not captured by whole exome sequencing [2)].

Seltzer et al. aimed to summarize prior research exploring gene and protein expression in prolactinomas in order to highlight molecular variations associated with tumor development, growth, and prolactin secretion. A PubMed search of select MeSH terms was performed to identify all studies reporting gene and protein expression findings in prolactinomas from 1990 to 2014.

1392 abstracts were screened and 51 manuscripts were included in the analysis, yielding 54 upregulated and 95 downregulated genes measured by various direct and indirect analytical methods. Of the many genes identified, three upregulated (HMGA2, HST, SNAP25), and three downregulated (UGT2B7, Let7, miR-493) genes were selected for further analysis based on our subjective identification of strong potential targets.

Many significant genes have been identified and validated in prolactinomas and most have not been

fully analyzed for therapeutic and diagnostic potential. These genes could become candidate molecular targets for biomarker development and precision drug targeting as well as catalyze deeper research efforts utilizing next generation profiling/sequencing techniques, particularly genome scale expression and epigenomic analyses [3)].

A total of 52 genes were identified as being significantly different between prolactinomas and normal samples which were classified into 29 COG functional categories. Three TFs, ZIC3 (Zic family member 3), NGFIC (nerve growth factor-induced protein C) and SP1 (Specificity Protein 1) were screened out, which can regulate part of DEGs. Two down-regulated genes, FSHB (follicle stimulating hormone β subunit) and LHB (luteinizing hormone β subunit) were involved in GnRH (gonadotropin-releasing hormone) signaling pathway [4)].

Clinical features

Some tumors secrete both PRL and GH.

see Lactotroph adenoma Clinical Features

Diagnosis

Blood tests can show if too much prolactin is being made. They can also show whether levels of other hormones controlled by the pituitary gland are within the standard range. A pregnancy test is typically recommended for females of childbearing age.

Differential diagnosis

hyperprolactinemia

Treatment

see Lactotroph pituitary neuroendocrine tumor treatment.

Books

MRI of the Pituitary Gland By Jean-François Bonneville, Fabrice Bonneville, Françoise Cattin, Sonia Nagi

This clinically oriented book will familiarize the reader with all aspects of the diagnosis of tumors and other disorders of the pituitary gland by means of magnetic resonance imaging (MRI). The coverage includes acromegaly, Cushing’s disease, Rathke cleft cysts, prolactinomas, incidentalomas, Clinically Non-Functioning Pituitary Neuroendocrine Tumors, other lesions of the sellar region, hypophysitis, and central diabetes insipidus. Normal radiologic anatomy and the numerous normal variants are

described, and guidance is also provided on difficulties, artifacts, and other pitfalls. The book combines concise text and high-quality images with a question and answer format geared toward the needs of the practitioner. MRI is today considered the cornerstone in the diagnosis of diseases of the hypophyseal-hypothalamic region but the relatively small size of the pituitary gland, its deep location, the many normal anatomic variants, and the often tiny size of lesions can hinder precise evaluation of the anatomic structures and particularly the pituitary gland itself. Radiologists and endocrinologists will find MRI of the Pituitary Gland to be full of helpful information on this essential examination, and the book will also be of interest to internists and neurosurgeons.

Literature review

A systematic literature review was performed utilizing the PRISMA guidelines. Seltzer et al. aimed to summarize prior research exploring gene and protein expression in prolactinomas in order to highlight molecular variations associated with tumor development, growth, and prolactin secretion. A PubMed search of select MeSH terms was performed to identify all studies reporting gene and protein expression findings in prolactinomas from 1990 to 2014.

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Case series

Lactotroph adenoma case series.

Case reports

2016

Two cases of well-controlled prolactinoma on dopamine agonists with the development of acromegaly 10-20 years after the initial diagnoses. In both patients, a mixed PRL/GH-cosecreting adenoma was confirmed on the pathology examination after transsphenoidal surgery (TSS). Therefore, periodic routine measurements of IGF-1 should be considered regardless of the duration and biochemical control of prolactinoma.

Acromegaly can develop in patients with well-controlled prolactinoma on dopamine agonists.The

interval between prolactinoma and acromegaly diagnoses can be several decades.Periodic screening of patients with prolactinoma for growth hormone excess should be considered and can lead to an early diagnosis of acromegaly before the development of complications [6].

2014

A case of sarcomatous transformation of a prolactin (PRL)-producing pituitary neuroendocrine tumor in a 27-year-old man, originally presented with bitemporal visual disturbance, headache, and hyperprolactinemia 8 years earlier. Tumor shrinkage was confirmed by magnetic resonance imaging (MRI) during treatment with dopamine-receptor agonist. However, 3 years later transsphenoidal surgery had to be performed because of tumor re-growth. Histopathological examination revealed a PRL-producing adenoma with fibrotic changes. One year later, he presented with right-sided visual disturbance, and tumor re-growth was confirmed using MRI. He underwent transcranial surgery, followed by radiation therapy (50 Gy in 25 fractions). The histological and immunostaining features were similar in both specimens obtained from the two operations. Four years later, he presented with left-sided visual disturbance, and tumor re-growth was confirmed using MRI. The mass lesion dramatically increased in size within 2 months, and partial removal of the tumor by craniotomy was performed. The specimen was histologically diagnosed as malignant fibrous histiocytoma (MFH). Regardless of aggressive chemotherapy, his clinical symptoms and imaging findings worsened rapidly. He died 7 months after the diagnosis of MFH. Because patients with pituitary tumor undergoing radiotherapy face the possibility of developing such neoplasm, long-term follow-up is required [7].

1)
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7)
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