PRIMEVIEW

CRANIOPHARYNGIOMA

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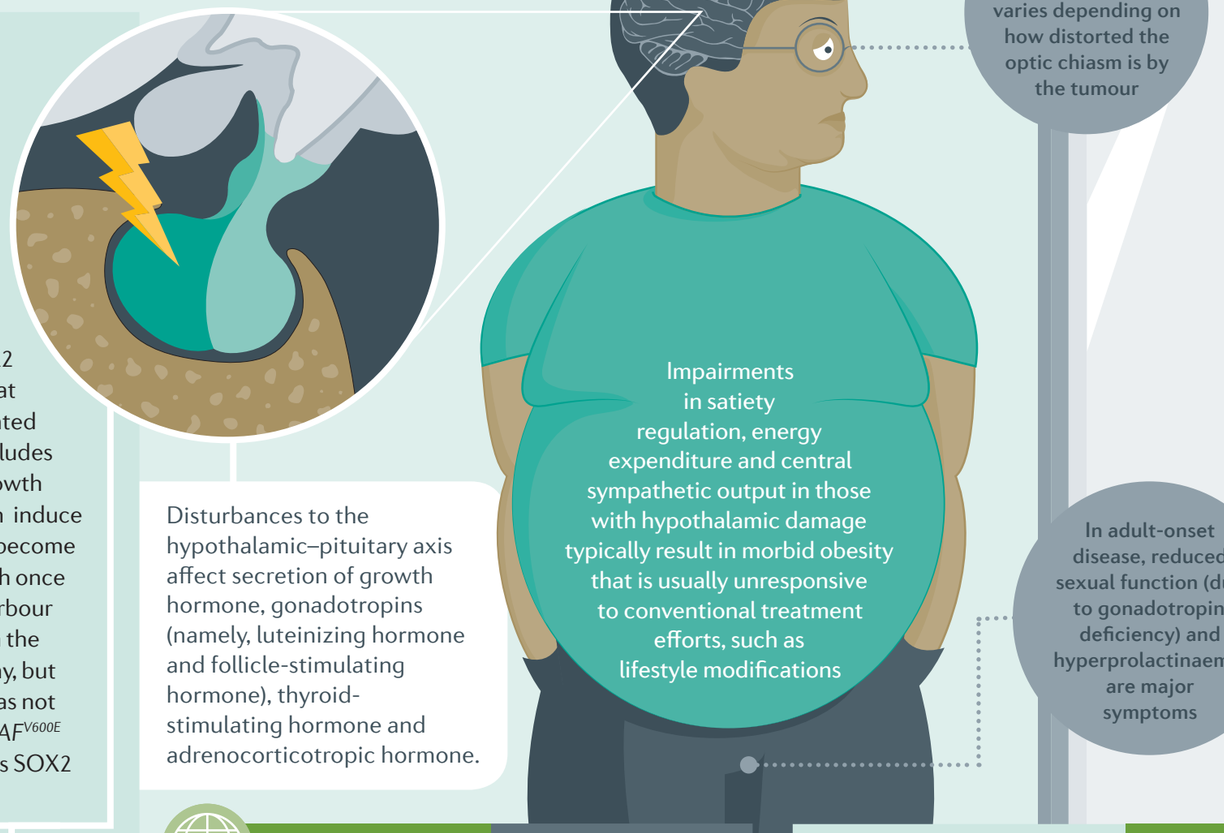
Craniopharyngiomas (CPs) are rare embryonic tumours that arise along the craniopharyngeal duct in the skull. Although survival is high, the close anatomical proximity of CPs to the optic chiasm, hypothalamus and pituitary gland can impair quality of life.

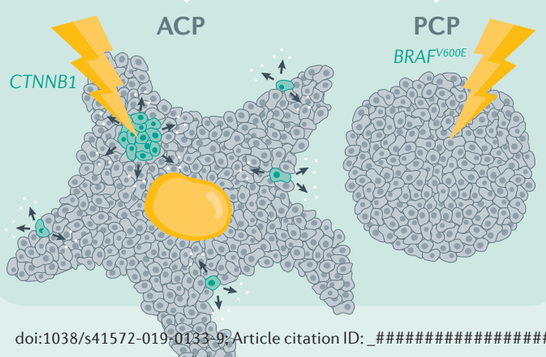
QUALITY OF LIFE

Hypothalamic damage is a major consequence of CPs, either preoperatively (owing to adhesion of the tumour to the hypothalamus), or postoperatively (as a result of surgical and/or radio-oncological treatment).



MECHANISMS

There are two histological subtypes of CP, namely adamantinomatous craniopharyngioma (ACP) and papillary craniopharyngioma (PCP). ACPs are driven by somatic mutations in *CTNNB1* (encoding β-catenin). Mouse models suggest that expression of oncogenic β-catenin in precursor cells that express the transcription factor SOX2 results in the formation of cell clusters that exhibit a pro-tumour senescence-associated secretory phenotype. This phenotype includes secretion of various factors, including growth factors, cytokines and chemokines, which induce transformation of a neighbouring cell to become tumour-initiating, and fuel tumour growth once initiated. By contrast, PCPs frequently harbour somatic $BRAF^{V600E}$ mutations that result in the activation of the MAPK signalling pathway, but the causative effect of these mutations has not yet been demonstrated. However, the $BRAF^{V600E}$ mutation may transform cells that express SOX2 to initiate tumour development.



Disturbances to the hypothalamic–pituitary axis affect secretion of growth hormone, gonadotropins (namely, luteinizing hormone and follicle-stimulating hormone), thyroid-stimulating hormone and adrenocorticotropic hormone.

EPIDEMIOLOGY

CPs constitute 1.2–4.6% of all intracranial tumours globally. ACPs affect all age groups (but have a bimodal peak incidence in children aged 5–15 years and adults aged 45–60 years) and are the more common subtype. PCPs are mostly restricted to adults (mean age at diagnosis of 40–55 years).

OUTLOOK

Alongside infrastructural improvements to ensure diagnostic and therapeutic quality globally, efforts are underway to develop better treatments for CP. For example, targeted therapies in PCPs habouring $BRAF^{V600E}$ mutations are being tested and cytokine inhibition is being considered in ACP.

DIAGNOSIS

Patients with CP typically present with features of increased intracranial pressure (for example, headache), visual impairment and endocrine abnormalities (for example, diabetes insipidus). Typically, patient history, biochemical assessment and detailed neuroimaging can confirm a diagnosis. On imaging, ACPs can be described using the '90% rule' — in which ~90% of tumours are predominantly cystic, ~90% show prominent calcifications and ~90% take up contrast media in the cyst walls. PCPs are more frequently uncalcified, 'solid' and usually lack cysts. The major differential diagnoses for CPs include low-grade gliomas and germ cell tumours.

Hypothalamic dysfunction is also a risk factor for impairments in body image, social functioning and physical ability; long-term neurocognitive complications problems affecting attention and executive function.

MANAGEMENT

Treatment options include surgery or radiotherapy or, more commonly, a combination of the two. However, surgery as a sole treatment is only appropriate for tumours that can be completely resected without neurovascular injury or visual impairment. In children in particular, such an approach must be carefully planned. For CPs that have invaded the hypothalamus, partial resection and radiotherapy may be the best option for treatment.

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