Chapter

Craniopharyngioma

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Abstract

Craniopharyngioma (CP) is a rare, benign, slow-growing, but clinically aggressive tumor located mainly in the sellar and suprasellar regions. While it occurs equally in children and adults, there are two peaks in the age distribution: first in 5–14 years of age and second in 45–74 years of age. The clinical presentation varies according to the age of patients, while the predominant symptoms are visual disturbances, headache, and endocrine dysfunctions. CPs are topographically classified in several subgroups based on the relationship of the tumor to the sella, diaphragma sellae, optic chiasm, stalk, and third ventricle; whereas the pathological classification includes two types: adamantinomatous (aCP) and papillary (pCP). Distinctive features of aCP are cysts with content of "motor-oil" fluid, calcification, wet keratin, peripheral palisading of basal cells, stellate reticulum, and mutations in CTNNB1/β-catenin gene; and those of Pcp are regular stratified squamous epithelium, devoid of cilia, papillary projections, no calcification, rare cyst with a clear fluid, and mutations in BRAF V600E. The surgical approaches include transcranial (subfrontal, pterional, transcallosal, and transcortical-transventricular) and transsfenoidal approaches, having different selection criteria, advantages, and disadvantages. Despite complete resection and radiotherapy, CPs are inclined to recur causing high morbidity and mortality.

Keywords: adamantinomatous, craniopharyngioma, papillary, sellar tumor, suprasellar tumor, surgery

1. Introduction

New information about tumor types and subtypes based on molecular studies were introduced first by 2016 update, and then lately by 2021 update of the World Health Organisation (WHO) Classification of Tumors of the Central Nervous System (CNS) [1]. One of the updated tumors is Craniopharyngoma (CP), particularly in the aspects of molecular pathology. We aim to review CPs with the new updates by 2016 and 2021 WHO classification systems highlighting important implications for clinical practice including diagnosis and management. We also intend to include a brief consideration of epidemiology and demographics, clinical manifestations, morphologic and molecular features, behavior, and prognosis of craniopharyngioma along with the current treatment modalities – surgery, radiosurgery, radiation therapy – with a thorough review of the literature.

2. Terminology and staging

Craniopharyngioma (CP) is a benign primary brain tumor originating from epithelial remnants of craniopharyngeal duct (Rathke's pouch, a diverticulum arising from the embryonic buccal cavity and rising to form the anterior pituitary gland) [2].

CP is a WHO grade I neoplasm often with a low proliferation index (MIB-1 < 10%) [1]. Although it is classified as a benign tumor, it has a tendency to recur due to its invasive nature, and inability to complete excision, particularly when MIB-1 is higher than 7% [3].

Despite its current WHO grade I classification with no malignant subtype, more and more case reports of a malignant form of CP occurring de novo or transforming from a benign variant have been published in recent years [4–10]. The exact pathogenesis and biological behavior of malignant change in CP are not yet clear; however, some reports have suggested that radiation may be a contributing factor to carcinogenesis [4, 6, 7, 9] though such a link has not been proven yet by any studies with high level of evidence [8, 11, 12]. Although malignant CP is still a rare clinical entity with less than 40 reported cases in the current literature, it may induce a new update in the WHO classification system in the future.

3. Epidemiology

CP is overall rare accounting for 1.2–4.6% of all brain tumors; [2, 13] yet, its incidence is higher in children, accounting for 5–13% of all pediatric brain tumors [14–16]. The overall incidence of CP was reported as 0.13 per 100,000 person-years in the USA with no difference between genders or races [17]. CPs occur almost equally in children and adults, and there is a bimodal age distribution with the first peak in children at the age of 5–14 years, and the second peak in older adults aged 45–74 years [14, 17, 18]. Between two types of CPs (adamantinomatous and papillary), the adamantinomatous CP (aCP) occurs predominantly in children, while papillary (pCP) is seen almost exclusively in adults [19, 20]. About 90% of CPs are aCP, and 10% are pCPs [14, 19].

4. Anatomy

4.1 Location

CPs may originate from anywhere along the pituitary stalk, extending from the tuber cinereum to the pituitary gland, where the remnants of an incompletely involuted hypophyseal-pharyngeal duct may locate [21, 22]. Most frequently, CPs originate in the suprasellar location; while some cases can be exclusively intrasellar or extend in any direction to encompass crucial structures, such as pituitary stalk, optic chiasm, optic tracts, third ventricle, hypothalamus, and thalamus [14, 15].

4.2 Topographical classification

CP has been anatomically classified based on the relationship of the tumor to the sella, diaphragma sellae, optic chiasm, stalk (infundibulum), and third ventricle

mainly to assist in planning optimal surgical approach [21, 23]. The first classification was introduced by Gazi Yaşargil based on his microsurgical experience with CPs [23]. According to his scheme, type A is confined within the sella (intrasellar infra diaphragmatic); type B is both intra- and suprasellar, infra- and supradiaphragmatic; type C is supradiaphragmatic, parachiasmatic, and extraventricular; type D is intra- and extraventricular; type E is paraventricular with respect to the third ventricle; type F is purely intraventricular [24].

Upon the development of endoscope and advances in transsphenoidal endoscopic surgeries, Kassam et al [25] have suggested a different classification system based on the relationship of the lesion to the infundibulum, which is the key anatomical consideration determining the amount of additional exposure needed in expanded endonasal approach (EEA). Accordingly, type I is preinfundibular, type II is transinfundibular, type III is post- or retroinfundibular, and type IV is isolated third ventricular. However, CPs are rarely restricted to only one location but spread widely engulfing the entire suprasellar and prepontine cisterns. In the latter case, the authors of this classification suggest surgeons consider the predominant site in which the greater part of the solid component is located to be the primary target when determining the specific EEA module [25]. Later, Jamshidi et al. [26] added an additional subtype to this scale, called type 0, which describes fully subdiaphragmatic tumors located within the sella.

Recently, Fan et al [27] also suggest a new classification system, called QST, based on tumor origin. They classified CPs into three types as follows: infrasellar/subdiaphragmatic CPs (Q-CPs), subarachnoidal CPs (S-CPs), and pars tuberalis CPs (T-CPs). Q-CPs arise from the subdiaphragmatic infrasellar space with an enlarged pituitary fossa, and the gland is scarcely recognizable; S-CPs arise from the middle or inferior segment of the stalk and tend to extend among cisterns, and the entire stalk can be recognized on MRI; and T-CPs arise in the top of the pars tuberalis, mainly extend upward, and occupy the space of the third ventricle [27]. This new scheme has been proposed to guide the surgeons in choosing the best surgical approach between endoscopic endonasal and transcranial surgery and to predict the outcomes.

Despite the several topographical classifications of CPs, there has not been a consensus on a standard reference classification system [28].

5. Diagnosis

5.1 Clinical presentation

The origin and size of CPs and the patient's age significantly affect the symptoms and signs. Clinical presentations are generally related to the mass effect, high intracranial pressure, and hypothalamic and endocrinologic dysfunctions. Overall, the most frequent symptoms are headache and visual problems due to pressurized optic structures and obstructive hydrocephalus. Patients with CP frequently exhibit the manifestations of hypothalamic-pituitary axis dysfunction, including growth hormone deficiency, adrenocortical insufficiency, central hypothyroidism, hypogonadism, precocious puberty, hyperprolactinemia, central diabetes insipidus, and hypothalamic obesity [14, 19, 20, 29, 30]. Fatigue, nausea/vomiting, somnolence, and memory impairment are the other signs of the clinical presentation related to CPs [2].

5.2 Microscopic histopathology

CP is known to be arising from rest of pharyngeal epithelium remaining from embryogenesis. Histopathologically, two types of CPs are recognized: adamantinomatous and papillary. The distinction between the two types is made by the encapsulating epithelial lining [15].

Adamantinomatous CP (aCP) has internal layers of stratified squamous epithelium anastomosing with the basal layer of columnar cells and forming stellate reticulum. The surface of aCP is usually irregular and infiltrative, with long epithelial extensions penetrating the adjacent neuroglial tissue. Dysmorphic calcification, lamellar keratin formation ("wet keratin"), and fibrosis can be often noted [14, 15, 31]. It generally has multi-cysts with contents of cholesterol crystals giving the fluid a dark, "motor-oil" appearance [19].

Papillary CP (pCP) has a more regularly stratified mature squamous epithelium, with papillary projections of epithelial cords into the surrounding tissues, but without significant infiltration [15, 31]. They are more commonly solid, with rare cyst formation and no calcification, and if cystic, the contents are clear without significant cholesterol crystals [19, 20].

5.3 Molecular pathology

Owing to advances in technology, the genetic mutations of CPs have been identified. Wnt/β-catenin signaling pathway in particular is important in the development of pituitary [32]. aCP and pCP also differ genetically, as BRAF V600E mutations are detected in pCP and CTNNB1 mutations in aCP [1, 2, 19, 33–35]. CTNNB1 gene encodes β-catenin, mutations of which have been found in 70–90% of aCPs and seem to play important role in the tumorigenesis of aCP [34, 36, 37]. BRAF V600E is reported to be the most common mutation in pCPs (65–100%) [34, 35]. These findings have important implications for the diagnosis and treatment of these neoplasms.

5.4 Macroscopic features

The typical macroscopic appearance of aCP is a small solid portion and large single or multiple cysts containing dark, viscous, "motor-oil" colored fluid rich in cholesterol crystals. aCP has calcification and irregular surfaces adhered to the surrounding normal structures [14]. On the other hand, pCP is usually solid, has a smooth surface and a cauliflower-like appearance, is rarely cystic, and if so filled with clear fluid [14].

5.5 Imaging features

Radiological appearances of aCPs and pCPs also differ due to their distinct histopathological features. aCPs present with 90% calcifications, 90% enhancement, and 90% cysts containing cholesterol-rich fluid; whereas, pCPs appear mostly solid, rarely cystic, with more homogeneous enhancement and without calcifications [2, 13, 38].

5.5.1 Computed tomography (CT)

A large conglomerate suprasellar mass with an area of calcification is a common computed tomography (CT) finding in CPs [13]. CT is superior to magnetic

resonance imaging (MRI) in detecting the presence of calcification, and therefore, seems more specific in establishing the diagnosis of CP (**Figure 1**) [39]. It may present as a suprasellar ring lesion with a peripheral rim of increased enhancement after contrast administration. CPs are generally mixed solid and cystic tumors, the former having well defined hyperdense appearance, while the latter presenting an area of low density on CT [13]. The sella turcica is usually intact or only minimally enlarged, suprasellar cistern is distorted, and hydrocephalus is common [13].

5.5.2 Magnetic resonance imaging (MRI)

MRI is the preferred method in the evaluation of tumor extent and recurrence. MRI is valuable in preoperative and radiation therapy planning due to its multiplanar capabilities [39]. Signal intensity on MRI varies with cyst contents [14]. CPs mostly demonstrate high signal intensity on both T2- and T1-weighted images (**Figures 2** and **3**) [38, 39]. High intensity on T1-weighted images corresponded to high cholesterol content or presence of methemoglobin in cystic lesions. Tumors lacking significant cholesterol or blood show moderate intensity (hypo- or iso intensity) on T1-weighted images [39]. While the CP cysts are variably hyperintense on FLAIR scan, the solid portion of the lesion does not suppress (**Figure 2**) [14]. CPs generally appear as mixed solid and cystic, lobulated lesions extending superiorly with the third ventricle compression, and reticular enhancement of the solid portion (**Figures 2** and **3**) [40].

5.6 Differential diagnosis

Most common lesions involving intrasellar and suprasellar regions include pituitary adenoma, CP, and Rathke cleft cyst. Pituitary adenoma has often a snowman shape, solid characteristics with less cystic changes, and more homogenous contrast enhancement; while CPs frequently present with superiorly lobulated shape, cystic changes, calcification, and heterogeneity of enhancement with enhancing solid

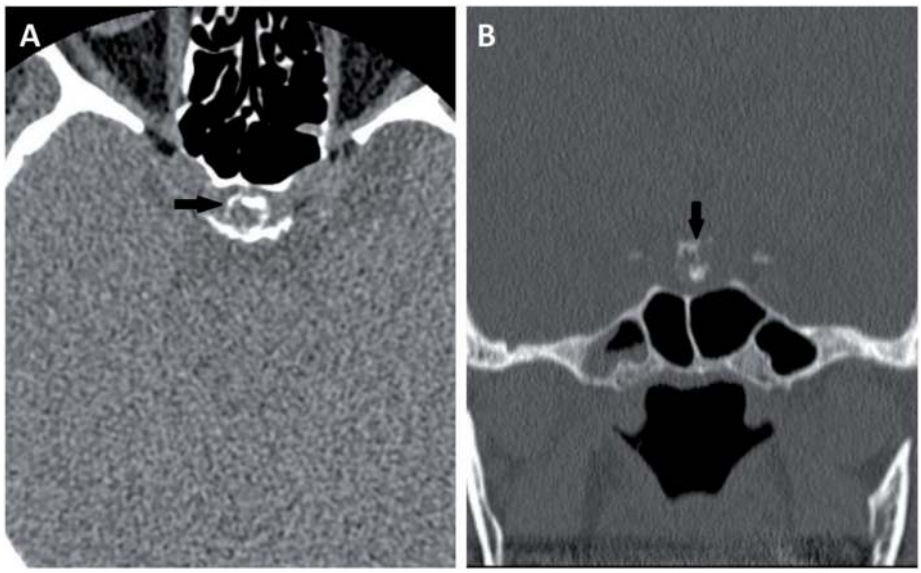

Figure 1.
Axial (A) and coronal (B) non-enhanced CT shows suprasellar dispersed calcifications (black arrow) in a patient with adamantinomatous craniopharyngioma.

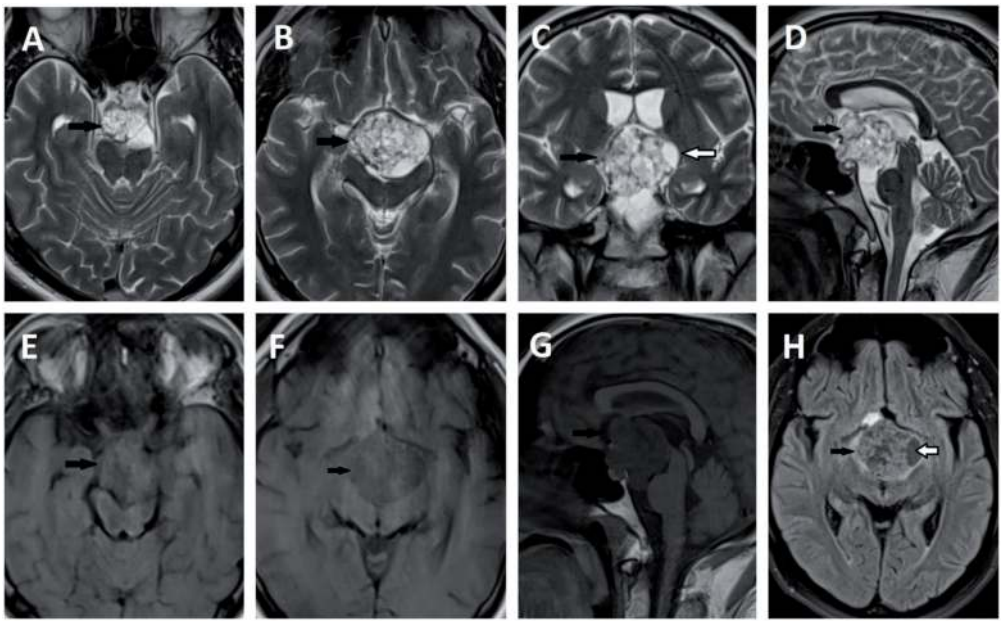

Figure 2.
The MRI of a 33-year-old man shows a lobulated sellar and suprasellar mass that is hyperintense on axial (A, B), coronal (C) and sagittal (D) T2-weighted scans; and nearly isotense or slightly hyperintense on axial (E, F) and sagittal (G) T1-weighted, and FLAIR scans (black arrow) with some small cystic areas (white arrow), radiologically suggesting craniopharyngioma.

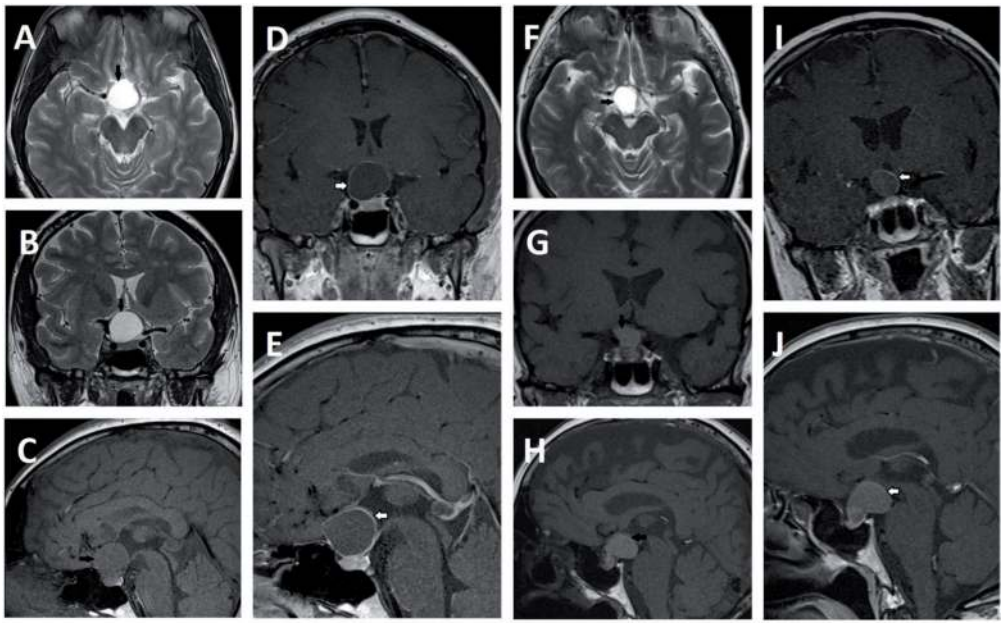

Figure 3.
The sellar and suprallar masses appear hyperintense on axial (A, F) and coronal (B) T2-weighted images; isointense and slightly hiperintense on sagittal (C, H) and coronal (G) T1-weighted images (black arrow). Coronal (D, I) and sagittal (E, J) contrast enhanced T1-weightes scans show thin rim enhancement around the mass with a small tumor nodule at the base of the mass (white arrow).

portion and unenhanced areas on contrast-enhanced T1WI [38, 40]. On the other hand, Rathke cleft cysts are in ovoid shape, with cystic lesions with no or thin cyst wall enhancement without calcification [14, 40].

6. Management

Because of the high variability in the manifestations of CPs, the management strategy should be tailored to the patient. The important parameters for treatment planning are the volumes of the solid and cystic parts of the tumor, its proximity and adhesion to the hypothalamus and optical structures, and the neurological and endocrinological state of the patient [41]. Moreover, the management of CP should be carried out by multidisciplinary teams including neurosurgeons, endocrinologists, ophthalmologists, and oncologists.

6.1 Observation alone

Although the mere observation of the tumor without treatment is currently not recommended, it gives the opportunity to observe natural course of the disease. Nevertheless, the natural growth of the CP seems unpredictable. In the literature, there have been a few case reports of CPs presented with long-term survival (up to 60 years), in spite of receiving no treatment and having some degree of morbidity [42, 43]. In these cases, tumors were mostly calcified, had low proliferative activity, and with partly cessation growth.

6.2 Surgical treatment

Microsurgical resection should be preferred when the solid part of the tumor is large and if the resection is feasible with a low risk of morbidity and mortality. The position of optic chiasm in relation to the sella is an important criterion for the selection of an approach. The chiasm may be above the tuberculum (prefixed), above the diaphragm or the middle of the sellae (normal), or above the dorsum sellae (postfixed) [44].

Postoperative care is vital in CP management. Endocrine dysfunctions often ensue from the surgery. Therefore, following the removal of a CP, patients must be carefully monitored, including for their urination as total removal of a CP frequently leads to diabetes insipidus. To overcome the risk of hypocortisolism, preoperative doses of dexamethasone should be continued for a period of time and tapered off without causing insufficiency. Thyroid function, sexual function, and growth should be carefully observed, as a replacement therapy may be needed [22].

The ideal surgical approach is still controversial. However, some criteria can guide surgeons to choose the best approach to surgery.

6.2.1 Transcranial Approaches

6.2.1.1 Subfrontal approach

CPs that are considered prechiasmatic can be more easily resected via subfrontal approach. A right-sided unilateral frontal craniotomy usually suffices and a unilateral approach along the falx provides approximately equal visualization of both sides of the optic chiasm [45]. Osmotic diuretics and lumbar drainage of cerebrospinal fluid can be used to minimize the retraction of the frontal lobe. If there is a need for approaching the tumor through lamina terminalis behind the optic chiasm, the necessity of removing a small strip of the undersurface of the frontal lobe from the frontal pole to the chiasm along the falx might arise, which is the main limitation

of subfrontal approach [45]. Moreover, inevitable dissection of the olfactory nerves brings about the risk of olfaction impairment [46].

6.2.1.2 Pterional approach

The pterional approach has been traditionally used most frequently because it allows early identification of the stalk, anterior circulation, and protection of the chiasm while giving access to virtually all parts of even very large tumors [24, 46]. The exposure through pterional craniotomy can be widened by adding the resection of the orbital rim and zygoma, which gives access to the skull base and minimize brain retraction [46]. Dissection can be performed through several corridors in the parachiasmal spaces: prechiasmatic, opticocarotid (between carotid artery and optic nerve), and carotidotentorial triangles (superior to the carotid artery bifurcation) or through the opening of the lamina terminalis [24, 46]. The main limitation of the pterional approach is the tumor extending into the upper part of the third ventricle and retrosellar region [46]. When tumors extend superiorly in the third ventricle, the pterional approach can be combined with the transcallosal approach because the pure pterional approach may be insufficient for proper dissection of the superior and posterior portions of the tumor within the third ventricle [23, 24]. CPs are usually subarachnoid tumors; therefore, they may be easily dissected from the surrounding structures covered with their own arachnoid layers. Nevertheless, great care should be paid to differentiating the tumor from hypothalamus and pituitary stalk. To avoid dreadful hypothalamic and infundibular injuries, tumor removal should be done stepwise, starting with the most easily accessible tumor portions, through internal decompression and dissection of the capsular-arachnoid plane [24, 46].

6.2.1.3 Transcallosal approach

Transcallosal approach is used for tumors primarily involving the third ventricle. Following a unilateral paramedian frontal craniotomy, the brain is retracted away from the falx and the corpus callosum will be exposed. A small callosal incision is made and intraventricular parts of the tumor can be removed through foramen of Monro [24]. With the pure transcallosal approach, optic chiasm and pituitary stalk cannot be identified early, and the anterosuperior portions of the tumor under chiasm and lamina terminalis may not be visible, in case of which a combined pterional-transcallosal approach is recommended [24, 46].

6.2.1.4 Transcortical-transventricular approach

Transcortical-transventricular approach via a frontal craniotomy was first introduced by Busch in 1944 mainly for tumors of the third ventricle [47]. It was used for CPs with giant cysts extended to the dorsal surface of the frontal lobe; nevertheless, it is unfavorable for the risk of producing porencephalic cyst or postoperative epilepsy [24].

6.2.2 Transsphenoidal Approach

If predominant portion of the tumor is intrasellar, the approach should be transsphenoidal (TS). TS approaches were traditionally reserved only for intrasellar

infradiaphragmatic tumors; [24] yet, with technological developments, new transsphenoidal approaches, such as expanded endonasal approach (EEA), the exclusive or additional use of the endoscope, have been introduced also for the resection of suprasellar craniopharyngiomas [25, 48]. Nevertheless, TS approach can be combined with the pterional approach in cases of CPs with supradiaphragmatic extensions to achieve a total resection (**Figure 4**). [24]. Reconstruction of the sellar floor is one of the most crucial steps of TS as it was associated with a high incidence of cerebrospinal fluid (CSF) leak [49]. To prevent this complication, autologous grafts, such as fascia, muscle, or adipose tissue can be fixed with fibrin glue and patched to the base of the sella. On the other hand, shorter hospital stays, and a higher rate of preservation of pituitary function are its main advantages [50, 51].

6.2.2.1 Expanded endonasal approach (EEA)

Exposure of suprasellar tumor components is improved with the development of EEA [46]. Currently, EEA is considered the first-line therapy when the distance between the optic chiasm and the surface of the pituitary gland is large, the lateral extension does not go beyond the internal carotid artery, and there is no extension beyond the posterior clinoid process; whereas, poorly developed sphenoid sinus, the pituitary stalk traveling anterior to the tumor, and CPs predominantly in the third ventricle are limitations of EEA [48].

In EEA, the bone of the sellar floor, tuberculum sellae, and planum sphenoidale are removed; while the optic canals mark the lateral limits, and the posterior ethmoidal arteries mark the anterior limit of the bony resection. The medial opticocarotid recess is a very important landmark marking the medial aspect of carotid and

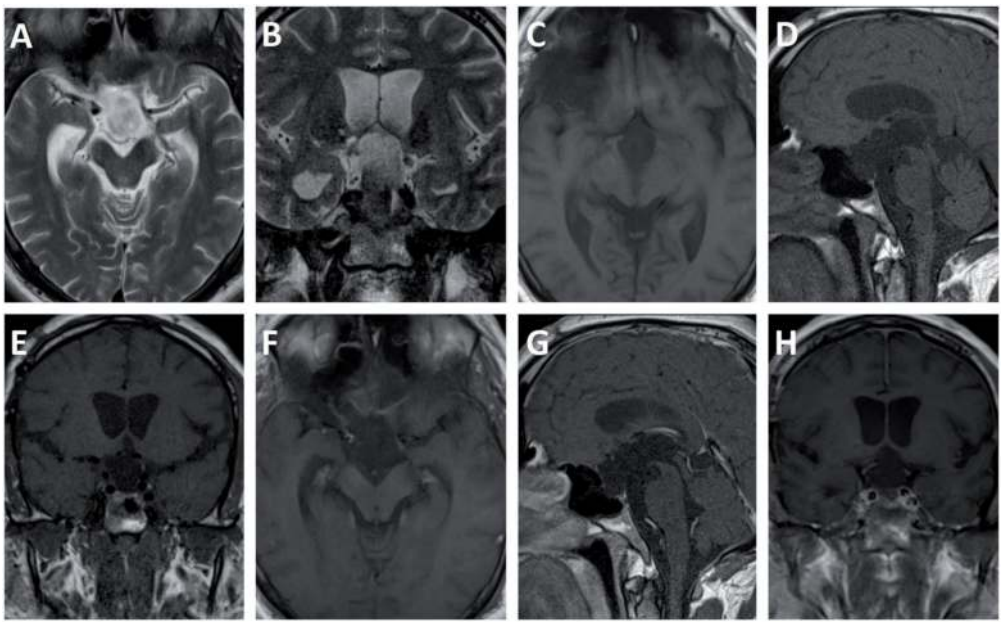

Figure 4.
*The postoperative MRI of the patient on the **Figure 2** following the surgery by combined transsphenoidal and pterional approach reveals total resection without residue or recurrence after 5 years. Papillary craniopharyngioma was diagnosed at histopathology. (A) axial T2-, (B) coronal T2-, (C) axial T1-, (D) sagittal T1-, (E) coronal T1, (F) axial contrast enhanced T1-, (G) sagittal contrast enhanced T1-, (H) coronal contrast enhanced T1-weighted images.*

optic canals [52]. In CPs confined to the sella, removal of the anterior sella wall only would suffice, while preinfundibular tumors require larger bone resection over tuberculum sella and planum sphenoidale, rather than the anterior sellar wall. Whereas, in transinfundibular CPs, additional bone removal from the anterior sella; and in retroinfundibular CPs, extensive bone removal from the sellar floor, posterior clinoid processes, and dorsum sella may be needed [52].

6.3 Radiation therapy

Due to the proximity and adhesiveness of CP to critical structures, including the optic chiasm, pituitary stalk, and hypothalamus, a complete removal is not always feasible, which increases the risk of recurrence. Postoperative radiation therapy (RT) is beneficial in patients with subtotal resection and recurrence, increasing the 10-year progression-free survival rates from 30 to 50% (of incomplete excision alone) to 75–90% (of incomplete excision followed by conventional RT) [20, 53]. Moreover, the tumor control rates were reported over 90% with newer higher precision techniques such as fractionated stereotactic conformal radiotherapy [53–56]. Radiation-related toxicities include impairment of endocrinological functions and vision, necrosis, radiation-induced tumors, and cognitive decline.

6.3.1 Conventional radiation therapy

The standard conventional radiotherapy technique is fractionated 3-dimensional (3D) conformal external beam radiotherapy (3DCRT) using computerized 3D treatment planning coupled with imaging for conforming to the shape of the tumor and delivering photons through a linear accelerator under precise immobilisation [53]. A more complex computerized treatment planning, called intensity-modulated radiotherapy (IMRT), using the modulation of the intensity of radiation can be preferred for more individualized beam shaping, particularly for the avoidance of some critical normal structures [53].

6.3.2 Stereotactic radiosurgery

Stereotactic radiosurgery (SRS) is an efficient option of radiotherapy for recurrent CPs following the surgical removal, ensuring tumor shrinkage and clinical improvement, without significant complications [57, 58]. Radiation can be delivered using gamma rays from multiple cobalt sources arranged in a hemisphere focused through a static collimator system onto the tumor (defined as Gamma Knife Radiosurgery) [53]. In this treatment modality, the use of a fixed frame entails completing the treatment in one day with a single fraction. Hypofractionated SRS may be useful for protecting the visual nerve and neuroendocrine function [58].

6.3.3 Fractionated stereotactic radiotherapy

Fractionated stereotactic conformal radiotherapy was developed to provide more localized irradiation administered in fractions over weeks with a steeper dose gradient between the tumor and surrounding normal structures compared to conventional radiotherapy [54]. This method has been found as effective and safe adjuvant therapy in the treatment of cystic CPs [55, 56].

6.3.4 Intracavitary irradiation

Stereotactic intracavitary brachytherapy with injection of colloidal phosphorus-32 (P-32) is a minimally invasive treatment modality for patients with cystic CP, resulting in improvement of symptoms and cyst regression [59, 60]. Some reports suggested that stereotactic intracavitary irradiation should be considered as the initial surgery for cystic CPs since it seems a safe and effective treatment [59, 60].

6.4 Chemotherapy

Chemotherapy is an option of adjuvant therapy in cases of multiple recurrences of CP despite surgical and radiotherapeutic treatments. Systemic chemotherapy includes vincristine, procarbazine, cisplatin, etoposide, anthracyclines (Adriamycin/doxorubicin), and nitrourea-derivates (BCNU, CCNU/lomustine) can be administered at six weeks intervals and found to be effective in preventing recurrence [61–63].

In cases of subtotal resection, injection of some chemotherapeutical agents such as bleomycin, and interferon alpha into the remaining tumor has been also introduced as a postoperative adjuvant therapy [64–68]. The intratumoral chemotherapy was found to reduce the volume of cystic CPs, and was considered a new therapeutic alternative, proposed to be more advantageous than total excision for cystic-type CPs; [64–69] still, it is not without serious risks of side effects due to its probable toxicity on deep brain structures [70].

7. Outcomes and prognosis

CPs may behave aggressively despite their benign histological nature. Tumor recurrence is very common because of their location and tendency to invasion into surrounding structures, such as the hypothalamus, pituitary gland, and optic apparatus, which makes total resection difficult [18]. Even after complete resection and radiotherapy, CPs have a propensity to recur. Most recurrences appear during the first five years following the first surgery, and during the first three years following repeated surgery [29]. Recurrence rates were reported between 5% and 59% in some series [24, 71].

The recurrence rate and outcomes are mainly dependent on the extent of surgical resection. Katz [72] reported the surgical outcomes of a case series of 34 surgically treated for the first time and 24 reoperated patients with CP. In their series, they noted 74% of cure rate without recurrence after radical primary excision and 16% of cure after reoperation. In the follow-up of 31 living patients of this series, the quality of survival was reported as 39% excellent, 29% good, 29% fair, and 3% poor [72]. In another study among patients with limited surgery (biopsy or removal of less than 25% of the tumor) followed by conventional radiotherapy, the outcomes were good in 50%, poor in 43%, and death in 7% [73]. Yaşargil [24] reported 90% complete resection, with 16% mortality and 7% recurrence rates in their case series of 144 CPs, suggesting that primary total removal of CPs yields the best long-term outcome for the patients.

Perioperative mortality rates were reported between 0% and 25% with higher rates in repeated surgeries [24, 29, 72]. Overall, one- and three-year survival rates are 91% and 86%, respectively [18].

Some studies suggested some potential predictor factors for poor prognosis including histopathological subtype of adamantinous pattern, higher proliferative index (MIB-1/Ki67 > 7%), nuclear atypia, hyperchromatic nuclei of basaloid cells, vascular invasion, coagulative necrosis, and p53 expression pattern [3, 71, 74]. Younger age, smaller tumor size, subtotal resection, and radiation therapy were associated with prolonged survival [17, 18].

The quality of life during follow-up after surgery is closely associated with the extent of removal during surgery. Total and near total resections have more risks of complications, such as hypothalamic syndrome (intellectual impairment, increased appetite, and weight gain) and hypopituitarism (hypogonadism, growth hormone deficiency, hypothyroidism, and hypocortisolemia) [51, 75, 76]. Furthermore, the incidence of CSF leak is much higher after EEA, reaching up to 58% [49].

8. Conclusions

CPs are histopathologically benign, but clinically aggressive suprasellar masses arising from Rathke's pouch. Despite its rarity overall, it is the most common non-glial brain tumor in childhood. It may present with visual and endocrine disturbances, growth retardation, secondary sexual dysfunction, weight gain, polyuria, headache, nausea, and vomiting. aCPs are lobulated, calcified, cystic with cholesterol-rich fluid, and infiltrative lesions; while pCPs are mostly solid, without significant infiltration to the surrounding tissue. Although the management of CPs is controversial, the current consensus is that surgical resection is the first-line therapy for primary and recurrent tumors, while radiation therapy and chemotherapy should be considered adjuvant treatments for subtotal or limited resected and recurrent tumors. Based on individual characteristics and selection criteria; pterional, transsfenoidal, transcallosal, or transcortical-transventricular approaches may be preferred for surgery. Radiation therapy includes the options of conventional radiotherapy, stereotactic radiosurgery, or intracavitary irradiation. Finally, if needed, chemotherapy can be administered intravenously or intralesionally. Owing to the advances in diagnostic and treatment modalities, the outcomes and survival rates have increased despite their inclination to recur.

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Conflict of interest

The authors declare no conflict of interest between any person/persons or institution/institutions and the authors in this study. The materials used in the study are extracted from the archives of the authors and have not been published before. The authors declare no conflict of interest for the materials used in the study.

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