Pathological and Topographical Classification of Craniopharyngiomas: A Literature Review

James Lubuulwa1 Ting Lei1

1 Department of Neurosurgery, Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China

Address for correspondence Ting Lei, MD, PhD, Department of Neurosurgery, Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology, Number 1095 Jie Fang Avenue, Wuhan 430030, China (e-mail: tlei@tjh.tjmu.edu.cn).

Abstract

Craniopharyngiomas (CPs) are clinically relevant tumors of the sellar region and are associated with high morbidity and occasional mortality. There are two different subtypes of CPs that differ clinically and pathologically: adamantinomatous CP and papillary CP. The differential diagnosis is still challenging even with developments in preoperative imaging as several tumors of the sellar/parasellar region share a continuum of clinical characteristics and imaging similarities. Several topographical classifications of CPs have been mentioned in literature, but to date, there has not been a consensus on a standard reference classification system and there is need to develop such a model.

Keywords

► craniopharyngioma
► classification
► pathological features
► topography

Introduction

Craniopharyngiomas (CPs) are tumors of the sellar and parasellar region and constitute approximately 3% of all intracranial tumors. They are the most common form of nonneuroepithelial neoplasm in pediatric population.1,2 They originate from epithelial remnants anywhere along the obscured craniopharyngeal duct from Rathke’s cleft to the floor of the third ventricle.3–5 Though classified by World Health Organization as grade 1 tumors,6 there have only been rare reports of malignancy transformation.7–9 CPs can cause significant morbidity due to their intimate involvement and mass effect on surrounding structures. Treatment is mainly through surgical resection. Several surgical approaches have been developed depending on topographical location of the tumor.1,4,10–12 and post neuroendoscopy radiotherapy,13 Gamma Knife surgery,14,15 and occasional use of Ommaya reservoir placement,16,17 proton beam therapy,18,19 and intracavitary β-irradiation20,21 have been reported in literature.

In this parochial literature review, we focus on the pathological classification and topographical location of CPs, highlighting the differences in two CP subtypes, their clinical presentation, imaging characterization, and the salient pathological and topographical location, and, finally, briefly discuss the differential diagnosis of CPs. For more specific clinical and pathological studies on classification of CPs, other published reviews are recommended.22–27

Classification According to Tumor Pathology

There are two different subtypes of CPs that differ clinically and pathologically: adamantinomatous CP (ACP) and papillary CP (PCP). The adamantinomatous variant occurs predominantly in the pediatric population, whereas the papillary variant is seen mostly among adults. The ACPs are much more common than PCP (9:1) and are pathologically distinct.26 ACPs are composed of cystic “motor oil-like” component and solid components and frequently contain calcifications that are readily identifiable on neuroimaging. Histologically, they contain nodules of wet keratin, a palisading basal layer of cells, surrounding gliosis, and profuse Rosenthal fiber formation. In contrast, PCPs are rarely calcified, mostly solid, and better circumscribed, and, if cystic, contents are clear. Müller postulated that PCPs are caused by metaplasia of the adenohypophyseal cells in the pars tuberalis of the adenohypophysis, leading to the formation of squamous cell nests.27 Histologically, they consist of mature squamous epithelium and pseudopapillae with no stellate...
reticulum or ghost cells. Immunohistochemically, a study by Esheba and Hassan demonstrated that cytoplasm/nuclear β-catenin accumulation as an exclusive characteristic hallmark that can used as a reliable marker for distinguishing between ACP and PCP. However, there exist some overlapping features between the two subtypes that led to the hypothesis that CPs fall on a histopathological continuum with other cystic epithelial sellar lesions. Crotty et al found no significant differences between the two CP subtypes with respect to respectability, efficacy if radiation therapy, and overall survival.

The salient features of these tumors are summarized in Tables 1 and 2.

### Classification According to Tumor Topography

Craniopharyngiomas can arise anywhere along the craniopharyngeal canal, although majorities arise in the sella/parasellar region. Because of their benign nature, they grow silently and are usually present clinically when they are already large with extension into the surrounding sellar region, usually adhering and compressing vital neurologic structures within their vicinity, consequently causing neurologic signs and symptoms. The majority of CPs have supra- and suprasellar components, whereas strictly intrasellar CPs are the least common. Furthermore, ectopic and fetal CPs add to the continuum of possible locations of CPs. Several authors have reported primary ectopic CPs in various locations of the cranium: temporal lobe, extracranial infrasellar, cerebellopontine angle, ethmoid sinus, and petroclival. However, there is no consensus for the mechanism for ectopic occurrence. Theories have been described that stipulate contamination with tumor cells along the surgical tract and vertical spread via cerebrospinal fluid, but more important is the embryogenical theory that CPs may arise from any location along the craniopharyngeal duct. Fetal ACPs have been reported in utero by several authors. Kostadinov et al reported an echodense structure at the intracranial midline with an irregular outline measuring 3.1 × 2.69 cm, which displaced the lateral ventricles and choroid plexus detected by prenatal ultrasound and further histology studies of the fetus specimen revealed an ACP. In the same report, they suggested that CP account for approximately 11% of fetal tumors.

Various grading systems have been suggested by several authors to aid in planning of surgical route either from preoperative images of MRI scans or based on intraoperative views of the anatomical structures involved with or surrounding the tumor. Pascual et al reported no significant relation between age and CP topography and noted significant association between topography and occurrence of postoperative hypothalamic damage and a strong relation between CP location, and the type of surgical approach and degree of tumor removal. Several authors have reported cases where a mistaken surgical approach was used due to topographical misdiagnosis of the location of CP despite the use of magnetic resonance (MR) images. It is important to consider each case on an individual basis as the imaging characteristics of each pathology and individual anatomical variation strongly influence whether a lesion is treated via a particular approach. Although there has been no consensus

### Table 1 Comparison of clinical and imaging features of adamantinomatous and papillary craniopharyngiomas

| Feature                        | Adamantinomatous craniopharyngioma | Papillary craniopharyngioma |
|-------------------------------|-----------------------------------|----------------------------|
| Incidence, %                  | 90                                | 10                         |
| Age28                         | Bimodal, peak incidences 1–5 y and 50–60 y | Almost exclusively adult51  |
| Sex2,52                       | No gender preference observed     | No gender preference observed |
| Visual disturbances27         | Frequent                           | Frequent                   |
| Hypothalamic disturbances27    | Possible                           | Frequent                   |
| High ICP symptoms27,39        | Usual                             | Frequent                   |
| Endocrine disturbances28      | Frequent                           | Unusual                    |
| Headache27                    | Frequent                           | Frequent                   |
| Mental disturbances           | Frequent                           | unusual                    |
| Ataxia23                      |                                   |                            |
| Imaging characteristics44     |                                   |                            |
| General imaging features      | Supra- and intrasellar, multilobulated and multicystic mass | Usually suprasellar, mostly solid and spherical mass |
| MRI                           | T1: solid regions are hypo- or isointense, cystic regions are hyperintense Strong heterogeneous enhancement | T1: hypointense; cystic regions, if present, are hypointense Moderate homogenous enhancement |
|                              | Hyperintense on T2                | Hyperintense on T2         |
| CT23                          | Solid regions and cyst wall enhancement Califications visible | Contrast enhancing with no califications |

Abbreviations: CT, computed tomography; ICP, intracranial pressure; MRI, magnetic resonance imaging.
on a single standard classification system, several authors have attempted to topographically grade CPs according to preoperative MR images and/or with intraoperative findings. Table 3 summarizes some of the most notable classification systems from studied literature.

### Differential Diagnosis with Other Tumors of Sellar Region

The differential diagnosis in pathology of sellar masses includes hypothalamic glioma, optic glioma, Langerhans
### Table 3  Summary of topographical classification of craniopharyngiomas from published literature

| Authors                  | Year | Basis of classification                      | Classification system                                                                 |
|--------------------------|------|----------------------------------------------|---------------------------------------------------------------------------------------|
| Yasargil et al<sup>57</sup> | 1990 | Relation with diaphragm                      | Purely intrasellar–infradiaphragmatic  
Intra- and suprasellar, infra- and supradiaphragmatic  
Supradiaphragmatic parachiasmatic, extraventricular  
Intra- and extraventricular  
Paraventricular in respect to the third ventricle  
Purely intraventricular |
| Hoffman<sup>1</sup>       | 1994 | Relation with ventricle                      | Preventricular  
Subventricular  
Retrochiasmatic  
Intraventricular |
| Samii and Tatagiba<sup>58</sup> | 1997 | Tumor extension                              | I: intrasellar or infradiaphragm  
II: occupying the cistern with/without an intra-sellar component  
III: lower half of the third ventricle  
IV: upper half of the third ventricle  
V: reaching the septum pellucidum or lateral ventricles |
| Kassam et al<sup>59</sup> | 2008 | Relation with stalk                          | Preinfundibular  
Transinfundibular  
Retroinfundibular  
Isolated intraventricular |
| Pascual et al<sup>39</sup> | 2004 | Relation with third ventricle                | Suprasellar tumor pushing the intact third ventricle floor upward  
Suprasellar mass breaking through the third ventricle floor and invading the third ventricle cavity  
Intraventricular mass within the third ventricle cavity and floor, the latter being replaced by the tumor  
Intraventricular mass completely located within the third ventricle cavity and with the intact floor lying below its inferior surface |
| Qi et al<sup>60</sup>     | 2011 | Growth pattern of arachnoid envelope around the stalk | Infradiaphragmatic  
Extra-arachnoidal  
Intra-arachnoidal  
Subarachnoidal |
| Fatemi et al<sup>61</sup> | 2009 | Anatomic extension of tumor                  | Retrochiasmal  
Sellar and suprasellar  
Cavernous sinus invasion  
Far lateral extension |
| Jeswani et al<sup>42</sup> | 2016 | Endoscopic view of Infundibular              | Infundibular I  
Infundibular II  
Infundibular III |
| Matsuo et al<sup>62</sup> | 2014 | Anatomic association between CP and sellar diaphragm, hypophyseal stalk, and optic nerve | Relation with diaphragm  
Subdiaphragmatic (complete, incomplete)  
Supradiaphragmatic  
Relation with hypophyseal stalk  
Preinfundibular  
lateroinfundibular  
retoinfundibular  
transinfundibular  
Relation with optic nerve  
Prechiasmatic type  
Retrochiasmatic type  
Other (pure intrasellar)  
Tumor extension  
Third ventricle |
cell histiocytosis, Rathke’s cleft cyst, xanthogranuloma, intracranial germinoma, epidermoid tumor, thrombosis of arachnoid cysts, colloidal cyst of third ventricle, pituitary adenoma, aneurysm, and rare inflammatory variations. Clinically, it is not easy to distinguish because patients with these tumors usually present with nonspecific features such as headache, hypopituitarism, or visual disturbances. On the contrary, Choi et al found that despite the characteristic MR imaging (MRI) findings of the most common sellar region tumors including pituitary adenoma, CPs, and Rathke’s cleft cyst, which are well known and significantly distinct to each tumor, it is still challenging to arrive at a differential diagnosis of these tumors, although their study demonstrated that tumor characteristics and enhancement patterns could be accurately used in the diagnostic flowchart generated to differentiate these three tumors. The introduction of new technologies, such as the recently developed intraoperative high-field MRI with microscope-based neuronavigation and brain perfusion imaging of CPs by transcranial duplex sonography, might lead to a more advanced way of developing a preoperative-intraoperative basis for a standard topographical classification. Immunohistochemically, CP is positive for pancytokeratin but negative for CK28 or CK20, which is exclusively expressed in Rathke’s cyst, yet another marker for differential diagnosis for CP. Additionally, Kim et al recently reported a BRAF V600E mutation as a useful marker in differentiating Rathke’s cleft cyst with squamous metaplasia from PCp. Scaglotti et al demonstrated that ACPs are devoid of terminally differentiated pituitary hormone producing cells, which aid in differential diagnosis from other pituitary or sellar region tumors.

**Conclusion**

The topographical classification of these subtypes is not purely distinct compared with other tumors of the sellar region, and in as much as it aids in the surgical approach, it has not fully been beneficial in the differential diagnosis from other tumors, with histopathological immunostaining remaining the mainstay for confirming a diagnosis of CP. To date, no standardized topographical classification system has been agreed among neuroradiologists and surgeons, and further studies are necessary to design a clinical-based classification system, which could aid in the surgical planning for determining tumor extent for surgery and radiotherapy, as well as posttherapy monitoring.

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**Table 3 (Continued)**

| Authors                          | Year | Basis of classification | Classification system |
|----------------------------------|------|-------------------------|-----------------------|
|                                    |      |                         | Interpeduncular cistern |
|                                    |      |                         | Prepontine cistern     |
|                                    |      |                         | Frontal base           |
|                                    |      |                         | Cavernous sinus        |
|                                    |      |                         | Sphenoid sinus         |
|                                    |      |                         | Sellar type            |
|                                    |      |                         | Presellar type         |
|                                    |      |                         | Concha type            |

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