

Infundibulo-tuberal or not strictly intraventricular craniopharyngioma: evidence for a major topographical category

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Abstract

Purpose This study investigates retrospectively the clinical, neuroradiological, pathological and surgical evidence verifying the infundibulo-tuberal topography for craniopharyngiomas (CPs). Infundibulo-tuberal CPs represent a surgical challenge due to their close anatomical relationships with the hypothalamus. An accurate definition of this topographical category is essential in order to prevent any undue injury to vital diencephalic centres.

Methods A systematic review of all scientific reports involving pathological, neuroradiological or surgical descriptions of either well-described individual cases or large series of CPs published in official journals and text books from 1892 to 2011 was carried out. A total of 1,232 documents providing pathological, surgical and/or neuroradiological evidence for the infundibulo-tuberal or hypothalamic location of CPs were finally analysed in this study.

Findings For a total of 3,571 CPs included in 67 pathological, surgical or neuroradiological series, 1,494 CPs (42%) were classified as infundibulo-tuberal lesions. This topography was proved in the autopsy of 122 non-operated cases. The crucial morphological finding charac-

terizing the tubero-infundibular topography was the replacement of the third ventricle floor by a lesion with a predominant intraventricular growth. This type of CP usually presents a circumferential band of tight adherence to the third ventricle floor remnants, formed by a functionless layer of rective gliosis of a variable thickness. After complete surgical removal of an infundibulo-tuberal CP, a wide defect or breach at the floor of the third ventricle is regularly observed both in the surgical field and on postoperative magnetic resonance imaging studies.

Conclusions Infundibulo-tuberal CPs represent a major topographical category of lesions with a primary subpial development at the floor of the third ventricle. These lesions expand within the hypothalamus itself and subsequently occupy the third ventricle; consequently, they can be classified as not strictly intraventricular CPs. A tight attachment to the hypothalamus and remnants of the third ventricle floor is the pathological landmark of infundibulo-tuberal CPs.

Keywords Craniopharyngioma · Hypothalamus · Infundibulum · Pituitary stalk · Tuber cinereum · Third ventricle

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Introduction

Craniopharyngiomas (CPs) are histologically benign epithelial lesions which may develop at any point along the pituitary-hypothalamus axis, from the sella turcica to the third ventricle [105, 123, 151, 159]. These lesions remain among the most challenging for neurosurgeons due to the everlasting controversy about the most appropriate therapy to be chosen for each patient. A major reason for this controversy is the high variability regarding the age at

onset, topographical relationships, size and consistency, degree of adherence and biological behaviour of these lesions. CPs involving the third ventricle include the lesions that present the utmost difficulty for a complete surgical excision due to their intimate anatomical and functional relationships with the hypothalamus. An accurate definition of the topographical relationships between intraventricular CPs and the functional hypothalamus is essential prior to planning the most appropriate surgical approach and degree of excision, a judicious decision that should take into account the age of the patient and the preoperative presence of symptoms of hypothalamic derangement.

In 2004, we developed a topographical classification system for intraventricular CPs based on a meticulous analysis of the tumour-third ventricle relationships observed on autopsies, surgical procedures and neuroradiological computed tomography (CT) or magnetic resonance imaging (MRI) studies of individual well-described lesions considered as “truly” or “purely” intraventricular [106]. Considering the integrity of the third ventricle floor, in addition to the location of the whole mass within the third ventricle, as the decisive factor proving the strictly intraventricular location of the CP, we were able to reclassify a majority of the previously considered purely intraventricular CPs as not strictly intraventricular lesions. CPs with such topography had originally developed within the neural tissue of the third ventricle floor and had then progressively replaced the floor while growing into the third ventricle cavity [107, 108]. Not strictly intraventricular CPs differ from the classical suprasellar CP as well as from the rare strictly intraventricular type in the wide and circumferential tight adhesion to the hypothalamus they present [46, 78, 99, 136, 143]. Very recently, Qi et al. [115] have reviewed the microsurgical meningeal relationships of 195 CPs operated on in their Department and classified 104 lesions as infundibulo-tuberal CPs, a topography characterized by its subarachnoidal position at the junction of the pituitary stalk with the floor of the third ventricle. A subset of 17 CPs belonging to this topography had a pure or strict third ventricle development, with a variable type of attachment to the floor of the third ventricle [104]. Such a high rate of the infundibulo-tuberal topography is surprising and apparently contradictory with the classical view of CPs as the paradigmatic example of a lesion with a suprasellar location. Given the considerable predominance of infundibulo-tuberal or not strictly intraventricular CPs among the well-described intraventricular CPs included in our previous review, a result parallel to the findings in the work by Qi et al. [115], we decided to investigate all the existing evidence for the infundibulo-tuberal topography of CPs provided since the original categorization of these lesions. In this work, a systematic and comprehensive account of the clinical, pathological, neuroradiological and

surgical evidence for the infundibulo-tuberal topography of CPs is presented. The purpose of this survey is to provide a comprehensive synthesis of the accumulated knowledge regarding the specific characteristics and risks associated with this topographical category and help neurosurgeons to properly diagnose and plan the surgical treatment to prevent any undue damage to the hypothalamus.

Methods

A thorough search of embryological, clinical, pathological, neuroradiological and/or surgical studies of CPs providing evidence for the infundibulo-tuberal origin and/or location of the lesion was carried out. The critical morphological finding taken into consideration to categorize a CP within the tubero-infundibular topography was the replacement of the floor of the third ventricle by a lesion with a predominant intraventricular growth. These are the same criteria that define the not strictly intraventricular category of intraventricular CPs as it is differentiated in the classification system of intraventricular CPs by Pascual et al. [106].

This survey comprises CPs presented in both large series of patients and well-detailed individual cases in medical journals obtained from the PubMed, Medline and Scopus databases after introducing the keyword craniopharyngioma. Reference lists of the selected articles as well as CPs displayed in specialized texts and monographs focused on the fields of Neurosurgery, Neurology, Neuroradiology, Neuroophthalmology, Neuroendocrinology, Neurooncology and Neuropathology were also scrutinized. Scientific reports and monographs of interest from the nineteenth and the first half of the twentieth centuries referenced in the articles selected from the previous databases were all retrieved and reviewed from the following medical libraries: The National Library of Medicine, NIH, Bethesda, Maryland, USA; The Francis Countway Library, Harvard School of Medicine, Boston, MA, USA; The Tompkins McCaw Library, Medical College Virginia, Richmond, VA, USA; The New York Academy of Medicine Library, New York, NY, USA; The Harvey Cushing/John Hay Whitney Medical Library, Yale University, New Haven, Connecticut, USA; The Welch Medical Library, Johns Hopkins University, Baltimore, MD, USA; The British Library, London, UK; The Complutense Medical School Library, Madrid, Spain and The Medical libraries of La Paz University Hospital, Ramón y Cajal University Hospital and Gregorio Marañón University Hospital, Madrid, Spain.

A final set of 1,232 scientific documents—articles, monographs and textbooks—including CPs either categorized within the infundibulo-tuberal or not strictly intraventricular topography or providing anatomical, pathological,

neuroradiological or surgical evidence for such topography were finally selected and analysed. The database of evidence for the infundibulo-tuberal topography for CPs includes a total of 3,449 CPs reported in 67 surgical, pathological and neuroradiological series and 122 CPs displayed in necropsy studies.

Results

Table 1 presents the number and relative rate of CPs classified within the infundibulo-tuberal or not strictly intraventricular category in the 36 surgical series of CPs providing evidence of such topography published in the scientific literature [3, 24, 30, 31, 35–39, 41, 42, 46, 48, 51, 53, 56, 74, 79, 87, 88, 96, 99, 104, 112, 115, 116, 119, 120, 125, 127, 131, 136, 137, 143, 149, 151, 152, 154, 158–161, 164]. Table 2 presents the list of infundibulo-tuberal CPs found in autopsy studies and included in the corresponding surgical or pathological series from the literature [5, 7, 12, 15, 17, 19, 20, 24, 25, 32, 34–36, 39, 40, 44, 47, 49, 52, 56, 60, 61, 65, 67, 69, 70, 76, 78, 81, 83, 85, 93, 100, 126, 136, 137, 141, 146, 147, 154, 165, 166]. Figures 1, 2, 3, 4, 5, 6, 7 show, respectively, a pictorial collection of anatomical (Fig. 1), embryological (Figs. 2 and 3), histological (Fig. 4), neuroradiological (Fig. 5), surgical (Fig. 6) and radiosurgical (Fig. 7) evidence supporting the concept of the infundibulo-tuberal topography as a separate category of CPs. In addition, remarkable examples of individual cases of CPs providing noteworthy evidence for the infundibulo-tuberal topography from autopsies, MRI studies, surgical procedures or radiosurgical treatments selected from a collection of 2,100 intraventricular CPs published in the literature are included in Figs. 1, 4, 6 and 7.

The infundibulo-tuberal or not strictly intraventricular topographical category of CPs was substantiated by the following six kinds of evidence:

1. *Pathological*: the tubero-infundibular topography has been confirmed in whole non-operated specimens of CPs obtained from necropsies. Table 2 presents a list of 122 non-operated or biopsed CPs disclosed during autopsy studies. Some additional examples of necropsy specimens showing intraventricular CPs developed at the floor of the third ventricle are presented in Figs. 1 and 4. In these necropsy brain specimens tubero-infundibular CPs are characterized as lesions that replace the floor of the third ventricle, above an identifiable, almost intact pituitary stalk, and whose mass bulk is occupying the lower half or the whole third ventricle chamber. Although the lesion expands predominantly within the third ventricle, its lower pole protrudes into the chiasmatic cistern; therefore, this

type of CP corresponds to the not strictly intraventricular category. The walls of the third ventricle containing the hypothalamic nuclei are separated from each other by the mass and identifiable remnants of the hypothalamus are found around the equator or lower pole of the lesion. Nearly all lesions were smoothly rounded or elliptic, lacking the multilobulated pattern of typical suprasellar lesions. This shape pattern is modelled by the expansion of the mass within the boundaries of third ventricle. Three major tumour consistency patterns were observed: pure solid, pure cystic or basal solid/upper cystic. In mixed lesions, the solid component was placed at the floor of the third ventricle, whereas the cystic component occupied the cavity of the ventricle. In both pure solid and pure cystic lesions, the lower pole of the mass had a retrochiasmatic position, within the chiasmatic cistern.

2. *Histological*: the basal, solid component of tubero-infundibular CPs is usually tightly adhered to the remnants of the infundibulum and tuber cinereum, the neural structures forming the floor of the third ventricle (Table 2). In most histological studies this area of the tumor was surrounded by a circumferential, non-functional layer of rective gliosis of variable thickness, ranging from 0.1 to 1.5 mm. The reactive gliosis can be identified by glial fibrillary acidic protein (GFAP) immunostaining at the boundaries of the lesion in histological samples taken from wholly removed lesions. However, in some cases a direct contact between peripheral finger-like tumour protrusions and the viable hypothalamic nuclei was observed in autopsy specimens. (Fig. 4g-i) A thin layer of neural tissue corresponding to the stretched remnants of the third ventricle floor was identified on the outer border of the lesion in some macroscopic specimens (Fig. 4b). Although the gliotic plane seems to represent an appropriate cleavage plane for tumour dissection, no studies have analysed the relationship between the presence of a gliotic layer around infundibulo-tuberal CPs and the easiness of dissection. The distribution of histologic types in the 85 infundibulo-tuberal CPs diagnosed at autopsy providing this information was 59 adamantinomatous (69.4%) and 26 squamous-papillary (30.6%) lesions, a result that confirms the predominance of the adamantinomatous variety for this topography.
3. *Surgical*: a tubero-infundibular topography for CPs has been explicitly addressed or described according to intraoperative findings in 1,372 cases from 36 surgical or neuroradiological series in the literature including a total of 2,907 CPs (Table 1). This figure represents 47.2% of CPs. Considering the age distribution of cases, the infundibulo-tuberal topography corresponds

Table 1 Infundibulo-tuberal or not strictly third-ventricle CPs observed in large surgical and neuroradiological series of the literature

First author, year [ref.]	No. of patients ^a	Infundibulo-tuberal/ not strictly IIIv CPs ^a	Strictly IIIv CPs	Surgical approach (no. of patients)	Degree of removal	Histology/adhesion/ outcome/complications
Cushing 1912–1932 [30, 31, 35–39]	92 patients (43 Ch<20, 49 A>20)	7 cases (1 Ch, 6 A)	2 cases	FTV (3 c), subfrontal ± TLT (3 c)	Subtotal or partial	5 adamant, 2 postop deaths due to HD
Frazier 1931 [51]	14 patients (9 Ch<18, 5 A >24)	6 cases (2 Ch, 4 A)	No	Subfrontal, STDC	Not found or STDC or partial	5 adamant/1 papillary, 4 postop deaths due to HD
Dott 1938 [46]	28 patients (?)	4 cases (1 Ch, 3 A)	2 cases	Subfrontal ± optic nerve section	Total	1 op death (tight adherence), 2 transitory HD
Globus 1945 [56]	14 patients (8 Ch<18, 6 A>20)	7 cases (3 Ch, 4 A)	No	Subfrontal	STDC or partial	6 adamant/1 mixed, 3 postop deaths due to HD
Williams 1954 [154]	32 patients (13 Ch<20, 19 A>20)	21 cases (7 Ch, 14 A)	No	?	?	?
Nothfield 1957 [99]	49 patients (23 Ch<20, 26 A>20)	31 cases (8 Ch, 23 A)	No	Subfrontal (16 c), FTV (5 c)	Total in 21	9 op deaths—all FTV, only 4 survivals
Grekhov 1959 [159]	90 patients (?)	50 cases ?	?	?	?	17% papillary histology
Rougerie 1962 [119]	26 patients (14 Ch<19, 12 A>19)	12 cases (7 Ch<19, 5 A>19)	No	FTV (6 c), pterional-TLT (6 c)	Total in 7	1 op death
Rougerie 1979 [120]	140 patients (92 Ch<17, 48 A>17)	33 cases (Ch<20)	No	Subfrontal + FTV or pterional + FTV	Total in 2	1 op death, 4 memory or behaviour deficits
Aiba 1980 [3]	22 patients (A >16)	12 cases (A >16)	1 case	Bifrontal + TLT	Total in 4, partial in 8	DI and severe mental disorder in all totally removed
Steno 1985 [136]	30 patients (10 Ch<15, 20 A>15)	14 cases (?)	8 cases	?	Partial in 19, 11 not operated	Circumferential tight adhesion to hypothalamus
Raybaud 1991 [116]	23 patients (Ch<17)	6 cases (Ch<17)	2 cases	?	?	?
Sweet 1988 [143]	43 patients (21 Ch<17, 22 A>17)	23 cases (?)	2 cases	TLT	Total in 32	2 op deaths, 3 postop hyperphagic obesity
Pierre-Kahn 1988 [112]	50 patients (Ch<16)	13 cases (Ch<16)	1 case	Subtemporal	Total in 22	5 postop deaths
Fukushima 1989–91 [24, 53]	38 patients (10 Ch<15, 28 A >15)	13 cases (?)	No	TC (7 c), TLT (4 c)	Total in 16, subtotal in 21	80% postop drowsiness or mental confusion
Konovalov 1992 [79]	198 patients (139 Ch, 59 A)	198 cases (139 Ch, 59 A)	?	Subfrontal ± TLT	Total in 127 (92 Ch, 59 A)	42% op death in A, 40% op death in Ch
Weiner 1994 [152]	56 patients (26 Ch<21, 30 A>21)	32 cases (?)	?	Pterional	Total in 30	3 deaths due to HD, 16 with brain invasion
Eldevik 1996 [48]	27 patients (13 Ch, 14 A)	7 cases (?)	No	Pterional	Partial + RXT	?
De Vile 1996 [42]	75 patients (Ch<16)	58 cases (Ch<16)	?	Subfrontal (40 c), pterional (28 c)	Total in 39	21 HD and 56 postop obesity, 17 tight hypothalamus adherence
Yasargil 1996 [158]	162 patients (80 Ch<15, 82 A>15)	69 cases (?)	7 cases	TC + TLT (31 c), Pt + TLT (38 c)	Total in 130	10 postop deaths due to HD, 25 tight hypothalamus adherence
Sartoretti-Shaefer 1997 [127]	42 patients (?)	25 cases (?)	1 case	?	?	16 adamant, 5 papillary
Zhang 2002 [160]	189 patients (Ch<15)	121 cases (Ch<15)	2 cases	TC	?	?
Wang 2002 [151]	25 patients (Ch<15)	11 cases (Ch<15)	No	Pt + TLT	Total in 10	1 op hypothalamus bleeding, 4 postop HD
Van Efferente 2002 [149]	122 patients (29 Ch<16, 93 A>16)	21 cases (?)	3 cases	Pt + TLT	Total in 72	24 mental or behaviour disturbances, 3 deaths due to ischemic HD

Table 1 (continued)

First author, year [ref.]	No. of patients ^a	Infundibulo-tuberal/ not strictly IIIv CPs ^a	Strictly IIIv CPs	Surgical approach (no. of patients)	Degree of removal	Histology/adhesion/ outcome/complications
Steno 2004 [137]	76 patients (?)	25 cases (?)	1 case	TC (11 c), TLT (14 c)	Total in 87%	4 postop deaths due to HD
Tomita 2005 [147]	54 patients (Ch<16)	22 cases (Ch<16)	9 cases	Pt + TLT (29 c), TC (2 c)	Total in 80%	15 hypothalamic obesity
Saint Rose 2005 [125]	103 patients (Ch mean age 7)	43 cases (Ch)	?	?	Total in 50%	30% preop HD, 38% postop breached IIIv floor
Zuccaro 2005 [164]	153 patients (Ch<21)	94 cases Ch<21	2 cases	Pt + TLT	Total in 57%	3 postop deaths due to HD
Lena 2005 [88]	47 patients (Ch<18)	25 cases (Ch<18)	1 case	Pt + TLT	Total in 65%	1 postop death due to stroke
Shi 2006 [131]	284 patients (58 Ch<15, 226 A >15)	92 cases (?)	23 cases	Pterional (191 c), TLT (53 c)	Total in 220 c	12 postop deaths, 4 due to HD
De Divitis 2007 [41]	10 patients (A>18)	6 cases (A>18)	1 case	Extended TSS	?	1 brainstem hemorrhage, 1 CSF leak
Lee 2008 [87]	66 patients (Ch<18)	39 cases (Ch<18)	No	?	?	33% hyperphagic obesity
Zhang 2008 [161]	202 patients (Ch<15)	89 cases (Ch<15)	5 cases	TC	Total in 27%, subtotal in 65%	2 postop deaths, 23 postop obesity, 75% transitory HD
Mortini 2011 [96]	112 patients (34 Ch<18, 78 A>19)	31 cases (13 Ch, 18 A>18)	No	Pt + TLT	Total in 71%	3 HD
Kim 2011 [74]	18 patients (2 Ch<18, 16 A>19)	8 cases (8 A>25)	No	Extended TSS	Total in 100%	PS preservation in only 1 c, postop CSF fistula in 1 c
Qi/Pan 2011 [104, 115]	195 patients (81 Ch, 114 A)	104 cases (38 Ch, 66 A)	9 cases	Subfrontal/Pt + TLT	?	2 postop deaths among 8 c in the study by Pan
Total 36 series	2,907 patients (1,365 Ch<21, 418 A) ^b	1,372 cases (773 Ch<21, 228 A)	82 cases			

A adults, *adamant* adamantinomatous histology, *c* cases, *Ch* children, *DI* diabetes insipidus, *CSF* cerebrospinal fluid, *FTV* frontal transventricular surgical approach, *HD* hypothalamus dysfunction, *op death* operative death, *papillary* squamous-papillary histology, *preop* preoperative, *postop* postoperative, *Pt* pterional approach, *PS* pituitary stalk, *retroch* retrochiasmatic location, *STDC* subtemporal decompressive craniectomy, *TC* transcallosal approach, *TLT* translamina terminalis approach, *TSS* transsphenoidal surgery, *IIIv* third ventricle

^a The number of children or adults and their ages in years are given in *parentheses*

^b Not included the series in which the age distribution of infundibulo-tuberal CPs was not provided

to 56% and 54.5% of paediatric and adult CPs, respectively. These lesions are usually hidden at a retrochiasmatic position within the anteroinferior portion of the third ventricle, causing the ballooning of the lamina terminalis. With an apparently tumour-free suprasellar space, the lower pole of the CP was the only part observable under the optic chiasm or through the optic-carotid triangle using a basal pterional or subfrontal approach. Tubero-infundibular CPs have been defined in some of the series included in Table 1 with diverse terms such as retrochiasmatic-intraventricular [112, 120, 149, 151, 160, 164], suprasellar-intraventricular [41, 48, 53, 125, 147, 158], or extra-intraventricular [136, 137], following alternative anatomical criteria for classification. Nevertheless, the anatomical relationships of such lesions confirmed during surgery or at necropsy, with replacement of the third ventricle floor by a mass that expands

predominantly into the third ventricle, allowed their unequivocal ascription to the infundibulo-tuberal topography. Checking a breach or defect in the third floor after removing the lesion through a translamina-terminalis or transcallosal transventricular approach was the surgical finding allowing the neurosurgeon to confirm the removal of a tubero-infundibular CP (Fig. 6). With the introduction of the extended transphenoidal approach, a direct view of the CP's lower pole, replacing the infundibulo-tuberal area, is possible during the initial stages of surgery (Fig. 6b,c). Following tumour removal through this approach, the same defect in the third ventricle floor is observed from the chiasmatic cistern, allowing illumination of the third ventricle chamber and identification of its inner structures with the aid of the endoscope.

4. *Neuroradiological*: tubero-infundibular CPs can hardly be differentiated from strictly intraventricular lesions

Table 2 Infundibulo-tuberal or not strictly intraventricular CPs diagnosed at autopsy in surgical/pathological case series

First author, year [ref.]	No. of CPs included in surgical/necropsy series ^a	No. of tuberal-third ventricle CPs autopsied ^a	Histological distribution	Treatment/complications outcome
Langer 1892 [85]	2 necropsies	2 cases (2 A)	2 papillary	Not operated
Erdheim 1904 [49]	12 necropsies	4 cases (3 A>21, 1 Ch 16)	2 adamant, 2 papillary	Not operated
Cushing 1912–1932 [35, 36, 39]	92 CP patients (43 Ch<20, 49 A>20)	6 cases (1 Ch 16, 5 A>25)	3 adamant, 3 papillary	4 deaths due to HD, 2 failed surgeries
Duffy 1920 [47]	3 patients (1 Ch 11, 2 A >20)	1 case (A 20)	1 adamant	Death due to HD
Bailey 1924 [12]	2 necropsies after failed surgery	2 cases (2 Ch<15)	2 adamant	1 death due to HD, 2 failed surgeries
Armstrong 1924 [7]	3 necropsies	3 cases (2 Ch<18, 1 A 35y)	3 adamant	3 deaths due to HD
Critchley 1926 [32]	7 patients (3 Ch<18, 4 A >20)	2 cases (1 F 35, 1 M 11)	2 adamant	1 death due to HD
Beckmann 1929 [15]	21 patients (6 Ch<15, 15 A >16)	6 cases (3 Ch<12, 3 A>25)	4 adamant, 2 papillary	1 death due to hyperthermia, 1 postop death due to HD
Frazier 1931–1936 [52]	14 patients (Ch 9<20, A 4 >21)	5 cases (1 Ch 12, 4 A>25)	3 adamant, 2 papillary	1 death due to hyperthermia, 3 failed surgery
Harbitz 1935 [61]	6 patients (4 Ch<18, 2 A>18)	3 cases (2 Ch<18, 1 A 67)	2 adamant, 1 papillary	1 death due to HI, 1 death due to pneumonia
Globus 1945 [56]	14 patients (8 Ch<18, 6 A>20)	6 cases (3 Ch<12, 3 A,>33)	4 adamant, 2 papillary	2 death due to hyperthermia, 1 op death due to HI
Ingraham 1946 [69]	16 patients (Ch<18)	2 cases (Ch<14)	1 adamant, 1 papillary	1 death due to cachexia
Davison 1946 [40]	17 third ventricle lesions (15 A)	1 case (A 45)	1 adamant	Death due to hyperthermia
Biggart 1949–1961 [17]	Neuropath texts	2 cases	1 adamant, 1 papillary	Not operated
Cuneo 1952 [34]	Neurosurg text	2 cases	2 adamant	Not operated
Williams 1954 [154]	21 patients, all infun-tuberal CPs	2 cases (A>21)	2 adamant	1 death due to hyperthermia
Khan 1955 [70]	51 patients (29 Ch <20, 22 A>20)	3 cases (A>33)	2 adamant	1 death in coma, 2 postop deaths due to HI
Northfield 1950–73 [100]	49 patients (23 Ch<20, 26 A>20)	4 cases (1 Ch 4, 1 A 45)	1 papillary	1 death due to HI
Grekhov 1959 [60]	90 patients (?)	3 cases	?	Not operated
Hirsch 1959 [65]	23 patients (11 Ch<20, 12 A>20)	3 cases (A>21)	2 adamant	1 death due to HI
Del Vivo 1962 [44]	30 patients (11 Ch<17, 19 A>18)	1 case (A 59)	1 papillary	1 postop death due to PE
Malamud 1967 [93]	7 patients (A>23)	3 cases (A>23y)	1 adamant	1 postop death due to HD, 3 with psychiatric symptoms
Svolos 1969 [141]	108 patients (42 Ch<18, 66 A>19)	2 cases (1 Ch 7, 1 A 40)	2 adamant	1 death due to HI
Zulch 1975–86 [165, 166]	185 patients, 8 autopsies	5 cases	1 papillary	Not operated
Kubota 1980 [83]	6 autopsies (2 Ch<15, 4 A>30)	6 cases (2 Ch<15, 4 A>30)	4 pdamant, 2 papillary	1 death due to HI
Kobayashi 1981 [76]	21 cases (5 Ch<20, 16 A>21)	7 cases (3 Ch<20, 4 A>20)	5 adamant, 2 papillary	3 deaths due to HD, 4 postop deaths by infection
Hoffman 1977–92 [66, 67]	48 patients (Ch<18)	3 cases (Ch<18)	?	2 not operated, 1 death due to HI
Steno 1985–2004 [136, 137]	30 autopsies and 44 patients (18 Ch<16, 26 A>16)	4 cases 2004, 14 cases 1985	?	?
Konovalov 1981–98 [78, 80, 81]	Neurosurgical text	2 cases	1 adamant	1 postop death due to HI
Burger 1994–2002 [19, 20]	Neuropathology text	4 cases (1 Ch 11)	2 adamant, 2 papillary	Not operated
Samii 1995 [126]	Neurosurgical text	2 cases	2 adamant	Not operated
Allegranza 1995 [5]	Neuropathology study	2 cases (2 A>30)	2 adamant	Not operated
Choux 1991–1998 [24, 25]	Neurosurgical text	2 cases	2 adamant	Not operated
Thapar 1998 [146]	Neuropathology text	2 cases	1 adamant, 1 papillary	Not operated
Tomita 2005 [147]	54 patients (Ch<18)	1 case	?	Not operated
TOTAL	664 patients	122 cases	59 adamant, 26 papillary	31 deaths due to HI/HD

A adult patients, *adamant* adamantinomatous histology, *papillary* squamous-papillary histology, *Ch* children, *CPs* craniopharyngiomas, *HD* hypothalamus dysfunction, *HI* hypothalamic injury, *y* years old, *PE* pulmonary embolism

^a The number of children or adults and their ages in years are given *in parentheses*

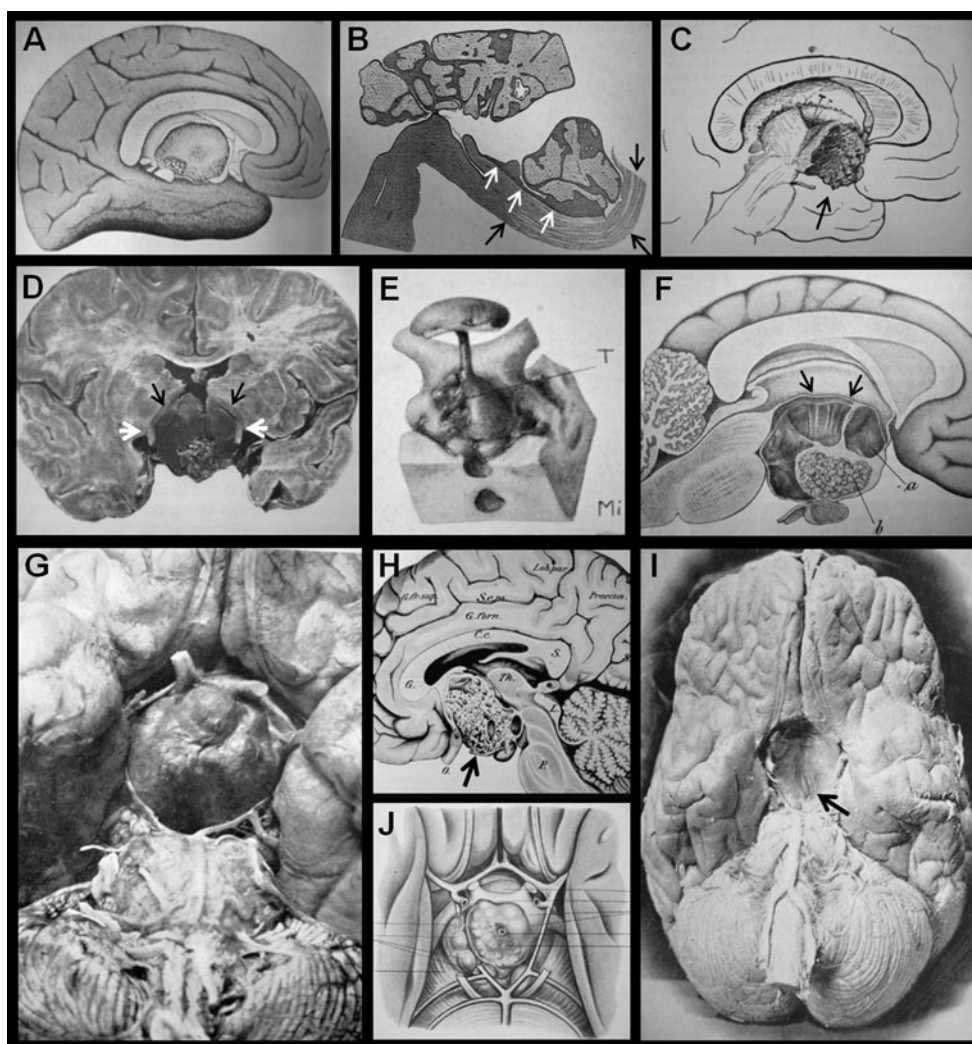
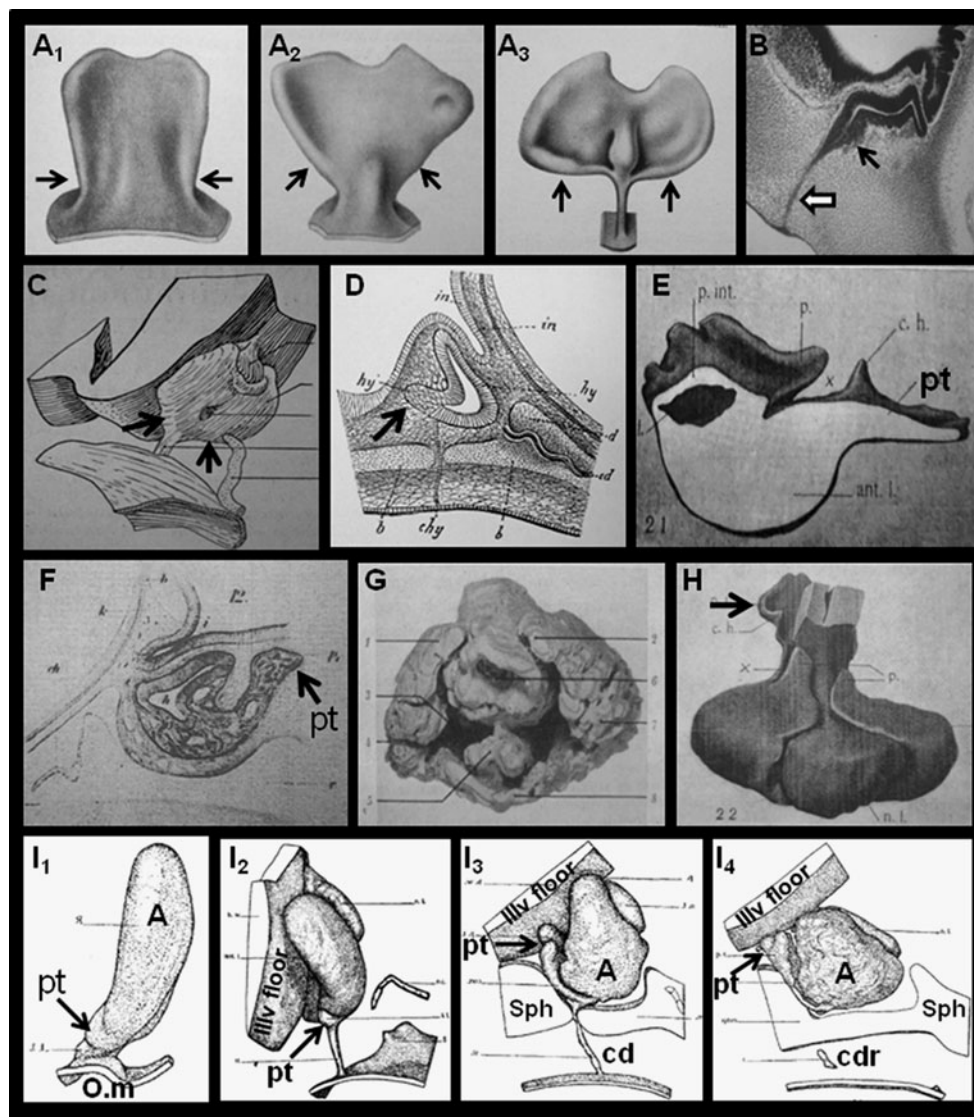


Fig. 1 Topographical classification of CPs involving the third ventricle: differentiation of the infundibulo-tuberal or not strictly intraventricular category in necropsy specimens. **a, b** Strictly or truly third ventricular CP of the squamous-papillary type (Mott and Barrat, 1899 [97]); **a** midsagittal brain section showing a rounded cystic/basal solid papillary epithelial lesion confined to the third ventricle; **b** Histological detail from the same case showing the morphologically intact floor of the third ventricle (*black arrows*) and the basal tumour area of attachment to the ependymal lining of the third ventricle floor (*white arrows*); **c** Artistic illustration showing a solid epithelial mass replacing the floor of the third ventricle (*black arrow*) and expanding into the third ventricle cavity (Babinski, 1900 [11]). **d-i** The three major topographical categories of intraventricular CPs according to the type of involvement of the third ventricle floor: strictly intraventricular (**d, g**), infundibulo-tuberal or not strictly intraventricular (**e, h, j**) and pseudointraventricular (**f, i**). **d, g** Strictly intraventricular CP located within the third ventricle above a morphologically intact tuber cinereum and infundibulum as observed on coronal (**d**) and brain undersurface (**g**) views of the necropsy specimen (Schilder, 1927 [129]). Notice the position of both optic tracts (*white arrows*) and the cleavage plane for dissection between the CP's upper pole and the walls of the third ventricle (*black arrows*). The lesion is not observable from the brain undersurface yet it can be presumed because of the belly-like protrusion of the tuber cinereum

(**g**). **e** Basal view of a solid CP (*T*) developed within the neural tissue of the infundibulum and tuber cinereum. Notice the intact pituitary stalk and gland and the lack of tumour expansion into the chiasmatic cistern (Cushing, 1932 [39]). **h** Artistic reproduction of the sagittal view of a tubero-infundibular, adamantinomatous CP which had replaced the floor of the third ventricle (*black arrow*) and expanded predominantly within the third ventricle. Notice the intact pituitary stalk below the lesion and the cystic infiltration of the mamillary body (Kaufmann, 1929 [73]). **j** Undersurface brain view of an infundibulo-tuberal CP diagnosed in a 16-year-old man who died after a 4-year history of severe headache, progressive visual deficit, recurrent seizures and obtundation followed by bradycardia and respiratory arrest. This solid, adamantinomatous CP was confined into the third ventricle and separated from the suprasellar cistern by a layer of pia mater (Erdheim, 1904 [49]). Note the tumoral papillary protrusions through the tuber cinereum. **f** Pseudointraventricular type of CP. The heterogeneous solid-cystic mass developed from the pituitary stalk is pressing on a morphologically intact third ventricle floor (*black arrows*) masquerading a truly intraventricular position (Strada, 1911 [138]). **i** Undersurface brain view showing the concave deformation of the intact third ventricle floor (*black arrow*) caused by a suprasellar expanding mass mimicking an intraventricular position (Blackburn, 1903 [18])



preoperatively because of the the impossibility of a proper identification of the limits of the third ventricle in most MRI studies. Gadolinium administration usually obscures the delimitation of the neural structures from the tumour capsule. The use of T2-weighted, heavily T2-weighted and/or 3D-FIESTA MRI sequences has proved useful for the identification and differentiation of the remnants of the third ventricle floor, pituitary stalk and tumour capsule [124]. Postoperative MRI studies after total removal of the lesion show a characteristic breached or defective floor of the third ventricle without evidence of injury extending into the hypothalamus (Fig. 5). This defect in the floor, easily observed in midsagittal and coronal MRI sequences, corresponds to the area of neural tissue that becomes replaced by the expansion of the CP and not to an iatrogenic injury.

5. *Radiosurgical*: the use of stereotactic radiosurgery in the treatment of intraventricular CPs shows a progressive shrinkage of the tumour mass accompanied by normalization of the third ventricle's shape. A small solid tumour remnant occupying the infundibulum and/or the tuber cinereum is displayed on long-term follow-up MRI studies following the application of this therapeutic modality, which presumably represents the epithelial nests' original growth site within the third ventricle floor (Fig. 7). A sequence of regressive changes in the lesion induced by radiation might reverse the CP growth stages, allowing identification of the tumour's original area of development.
6. *Embryological*: tubero-infundibular CPs are presumably originated from nests of epithelial cells incorporated or derived from metaplastic transformation of glandular cells of the pars tuberalis of the pituitary

◀ **Fig. 2** Embryological basis for the development of infundibulo-tuberal craniopharyngiomas I: embryology of the pars tuberalis of the pituitary gland. **a₁–a₃** Early stages of development of Rathke's pouch. Rathke's pouch is developed as a pouch of cube epithelial cells evaginated from the dorsal surface of the primitive mouth. From early stages of embryo development Rathke's pouch presents two inferolateral thickenings of epithelial tissue (*black arrows*) close to the craniopharyngeal duct which become fused as the flattened disc-shaped pouch bends forward upon itself to transform into a vesicle. **a₁** Carnegie stage 17 (6th week of development, embryo about 8 mm long). **a₃** Carnegie stage 19 (7th week of development, embryo about 16 mm long) (Henke, 1926 [64]) **b** Sagittal section of Rathke's pouch connected by the solid remnant of the craniopharyngeal duct (*white arrow*) to the roof of the primitive mouth (Carnegie stage 18, 6 and half weeks of development). The *black arrow* points to the primordia of the pars tuberalis (O'Rahilly, 2001 [102]). **c** Artistic illustration showing the disc of Rathke's pouch closely apposed to the floor of the diencephalic evagination at a similar Carnegie stage as shown in **b** (Rouvière, 1947 [122]). *Black arrows* point to the inferolateral thickenings adjacent to the craniopharyngeal duct which will transform into the pars tuberalis. **d** Initial rotation of the pars tuberalis: the lower edge of the Rathke's pouch is now closed and the pouch transforms into an epithelial vesicle which progressively folds upon itself and becomes apposed against the third ventricle floor. Such rotation could presumably transfer cell remnants of the craniopharyngeal duct or, alternatively, either epithelial cells from the primitive oral mucosa or dental ridge cells, into the third ventricle floor (Dialti, 1910 [45]). **e–g** Rathke's pouch vesicle stage. **e** The pars tuberalis (*pt*) is observed at the most anterior position after the rotation of Rathke's pouch (Attwell, 1926 [10]). **f** Original artistic illustration by von Mihalkovics showing the upward and forward bending of the parts tuberalis (*pt*) towards the floor of the diencephalon in a dog embryo (von Mihalkovics, 1875 [150]). **g** Genital view of Rathke's pouch as a hollow vesicle (Rouvière, 1947 [122]). **h** Final embryological stage of Rathke's pouch development; the pars tuberalis is holding the upper pituitary stalk and extends as a sheet upon the anterolateral infundibulum and the tuber cinereum (Attwell, 1926 [10]). **i₁–i₄** Stages of development of the pars tuberalis in a rabbit embryo; **i₁** Rathke's pouch attached to the primitive mouth (12-day rabbit embryo); **i₂** initial stage of migration of Rathke's pouch toward the floor of the third ventricle. The primordia of the pars tuberalis (*pt*) is still attached to the remnant of the craniopharyngeal duct (15-day rabbit embryo); **i₃** Rathke's pouch transforms into a vesicle by upward migration of the pars tuberalis to the floor of the third ventricle (17-day rabbit embryo); **i₄** The sphenoid bone and sella turcica are formed by organization of the mesenchymal tissue and the craniopharyngeal duct (*cdr*) is disconnected from the vesicle. The pars tuberalis has completed its rotation toward the diencephalic vesicle and may become embedded within the third ventricle floor. *A* adenohypophysis, *cd* craniopharyngeal duct, *cdr* craniopharyngeal duct remnant, *pt* pars tuberalis, *IIIv* floor third ventricle floor, *O.m.* oral mucosa, *Sph* sphenoid bone (Attwell, 1918 [9])

gland [10, 49, 123, 159]. The body of evidence for this hypothesis is presented in Figs. 2 and 3. The inferolateral thickenings of Rathke's pouch, precursors of the pars tuberalis, are adjacent to the area of the primitive mouth from which the craniopharyngeal duct is evaginated [10]. These paired primordia of the pars tuberalis rotate and move upwards into the primitive meningeal layer covering the floor of the diencephalic vesicle. Such an embryological course might move epithelial cells from the primitive dental ridge, the oral

mucosa or the craniopharyngeal duct into a subpial position, within the floor of the third ventricle [9, 27, 49, 150]. Nests of epithelial cells, presumably originated from a metaplastic transformation of glandular cells of the adenohypophysis, have been found predominantly within the uppermost area of the pars tuberalis, which covers the infundibulum and tuber cinereum [23, 49, 68, 92].

Discussion

The concept of the infundibulo-tuberal topography for CPs: historical background

The original description of hypophyseal duct tumours or CPs was made by the Austrian pathologist Jakob Erdheim in 1904 on the basis of the analysis of a collection of suprapituitary lesions in autopsy brain specimens, proving unequivocally their intimate relationship to the substance of the third ventricle floor and the hypothalamus (Fig. 1j) [49]. Such overlooked evidence is contrary to the classical prevailing notion of a general, extra-axial suprasellar location for CPs. Many of the earliest reports on CPs displayed accurate artistic depictions of the anatomical situation of these lesions as they were observed on a view of the undersurface of the brain and on midsagittal and coronal sections made through the third ventricle. Most of these illustrations show brain specimens whose neural tissue constituting the basal components of the hypothalamus—the infundibulum and the tuber cinereum—had been replaced or had become encroached by the CP to a degree incompatible with life [11, 40, 49, 58, 73, 85, 98, 163]. This category of CPs respected the anatomical integrity of the pituitary gland and the pituitary stalk, structures easily identifiable under the lesion (Fig. 1e,h and Table 2). Many of these lesions were diagnosed in adults showing unequivocal symptoms of hypothalamic derangement, such as drowsiness, apathy, behaviour alterations, severe memory defects and gait disturbances [11, 46, 49, 85, 154]. Aware of this kind of tumour expansion within the diencephalus, some neurosurgeons considered in the following decades that these CPs should be topographically classified as hypothalamic lesions rather than as suprasellar ones (Figs. 1, 4) [13, 14, 46, 70, 99, 143]. J.H. Biggart and Norman Dott were the first authors to consider typical epidermoid suprasellar tumours—actual CPs—as lesions developing at the junction of the optic chiasm and the infundibular recess (Fig. 3g) [16]. Although hypothalamus-centered CPs were considered inoperable or not amenable to surgical dissection with the methods and techniques employed at that time, Norman Dott reported the successful removal of four such lesions placed in the substance of the third ventricle

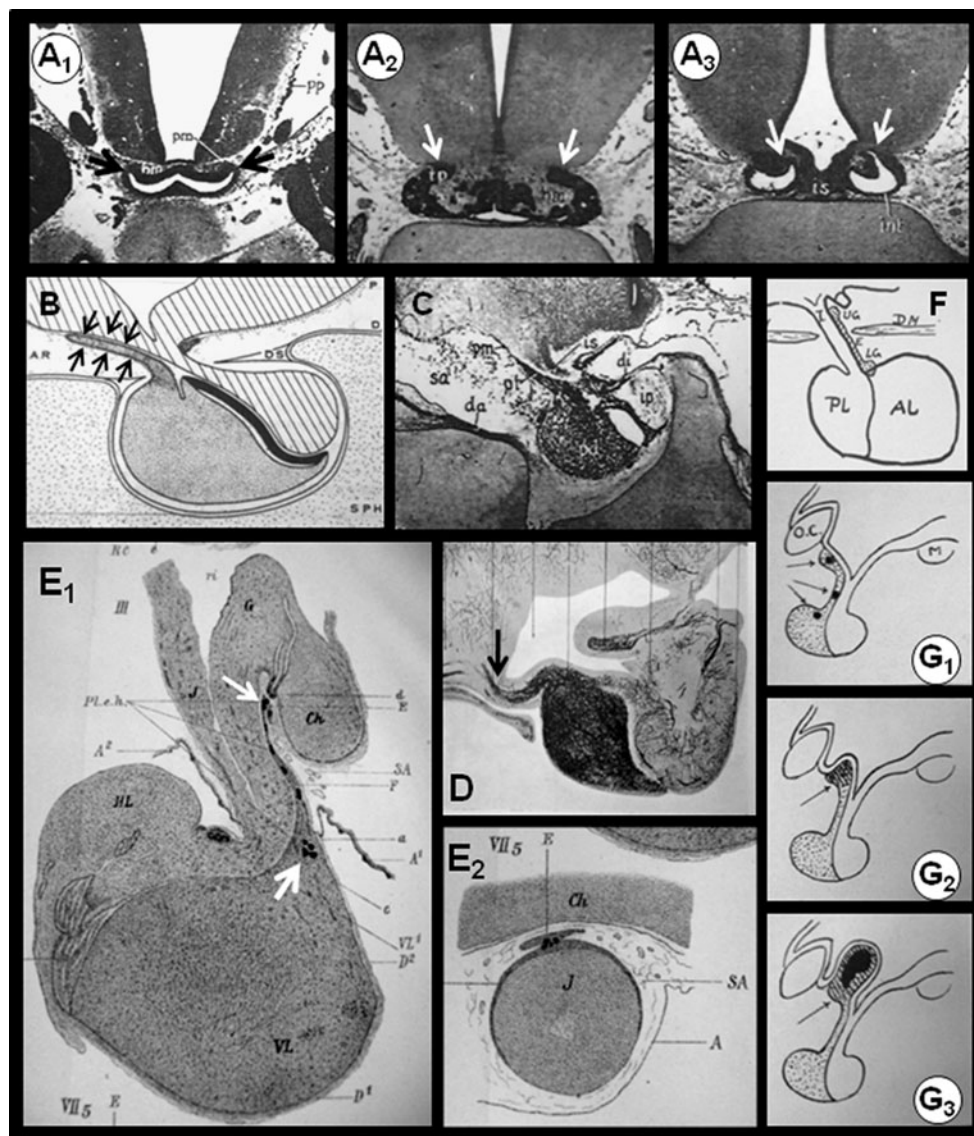


Fig. 3 Embryological basis for the development of infundibulo-tuberal CPs II: meningeal relationships of the pars tuberalis and epithelial cell nests within this structure. **a₁–a₃** Coronal sections of human embryos at the level of the third ventricle showing the fusion of the upper edges of the pars tuberalis with the neural tissue of the third ventricle floor. **a₁** The primordia of the pars tuberalis undergo a movement towards the floor of the diencephalic evagination and become embedded into the primitive meningeal layer covering the floor (*black arrows*) (18.2 mm embryo); **a₂** Rathke's pouch has become a vesicle whose antero-superior edges are in close contact with the floor of the third ventricle (*white arrows*) (36 mm fetus); **a₃** the pars tuberalis has invaded the neural tissue of the third ventricle floor by trespassing the barrier of the pia mater (*white arrows*) (36 mm fetus) (Wislocki, 1937 [156]). **b** Illustrative scheme showing the meningeal relationships of the pars tuberalis. This structure is enclosed between two layers of pia mater, one antero-ventral, covering its outer aspect together with the arachnoidal layer (*lower row of black arrows*), and one postero-dorsal, corresponding to the pia mater formed from the primitive meningeal layer that covers the neural tube (*upper row of black arrows*) (Attwell, 1926 [10]); **c** Sagittal section of the pituitary in a human fetus (16 cm sitting height), showing the pars tuberalis

ensheated by the two layers of pia mater (Wislocki, 1936 [155]); **d** Medial sagittal section of the pituitary body of a cat embryo showing the pars tuberalis embedded within the neural tissue of the third ventricle floor (*black arrow*) (Schäfer, 1922 [128]). **e₁** Midsagittal section through the infundibulum and pituitary gland of a 49-year-old man showing the presence of squamous-epithelial cell nests within the pars tuberalis (*white arrows*) (Erdheim, 1904 [49]). Notice the accumulation of squamous cells at the junction between the infundibulum and the optic chiasm, where perforant hypothalamic vessels penetrate the floor of the third ventricle. **e₂** Axial section through the infundibulo-chiasmatic junction in the same patient, showing the nests of squamous epithelial cells at this level (*E*) (Erdheim, 1904 [49]). **f** Areas of the pars tuberalis where nests of epithelial cells are most frequently observed: at the upper edge (*UG*) in close contact with the floor of the third ventricle immediately posterior to the optic chiasm and at the junction between the gland and the pituitary stalk (*LG*) (Simonds, 1922 [133]). **g₁–g₃** Theoretical development of infundibulo-tuberal CPs from tumoural growth of epithelial cell nests at the junctional area between the infundibulum and the optic chiasm (Dott, 1938 [46])

floor for which he devised specific surgical strategies to minimize the risk of hypothalamic injury [46]. The tight attachment of CPs to the hypothalamus was considered the major cause for incomplete resection and poor patient outcomes before the use of corticoid therapy and microsurgical techniques [70, 120].

Douglas Northfield in the UK and V. Grekhov in the USSR were the first authors to explicitly propose the topographical category of tuberal CPs as the subgroup of tumours with an intrapial origin which had replaced the floor and/or anterior walls of the third ventricle [59, 99]. Northfield considered CPs as epitheliomas originated from small nests of squamous cells commonly found in the pars tuberalis of the pituitary. Biggart's concepts about CPs agreed with Northfield's by employing the term "epidermoid tumors of the pars tuberalis" to define the lesions presumably originated from the pars tuberalis that developed a cauliflower-like papillary solid excrescence at the floor of the third ventricle [17]. This concept, scarcely mentioned in the literature, was substituted in the following decades by the categorization of infundibulo-tuberal CPs as retrochiasmatic lesions in classical classification schemes based on the position of the tumour with respect to the optic chiasm [67, 110]. In fact, these lesions were hardly visible through the standard basal approaches—subfrontal/pterional—which led to a high rate of failed surgical procedures following these surgical routes (Table 2). William Sweet was the pioneer neurosurgeon who advocated the use of the translamina terminalis approach (TLT) to remove most adult CPs with an infundibulotuberal or predominant intraventricular location [142, 143]. He observed that the breach left in the floor of the third ventricle after total removal of these lesions did not necessarily mean that injury to the hypothalamus occurred but rather the logical consequence of removing the circumferential plane of reactive gliosis developed around the lesion's origin at the base of the third ventricle.

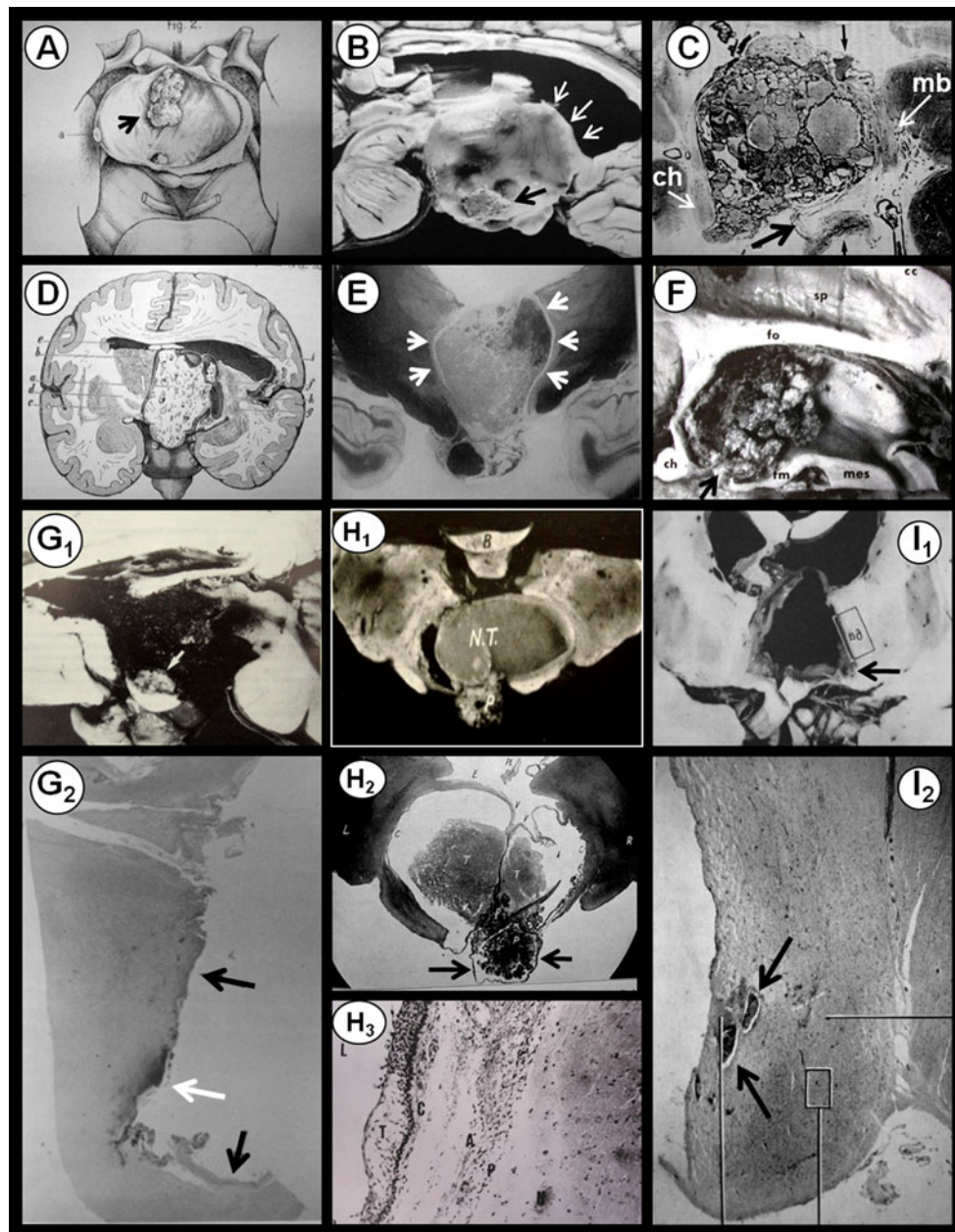
In the most conclusive pathological investigation on the microscopic topographical relationships of CPs performed on necropsy specimens, Juraj Steno confirmed the whole replacement of the third ventricle floor by a majority of CPs, which were classified as extra-intraventricular lesions and presented a tight band of adherence to the hypothalamus around their equators [136]. According to Steno's observations, the central area of the tuber cinereum is usually absent and the infundibulum is usually substituted by this kind of CP [137]. Alexander Konovalov confirmed the findings reported by J. Steno and W. Sweet to further highlight the differentiation of intraventricular CPs developed from the infundibulo-tuberal area—whose total removal usually left a wide opening at the floor of the ventricle—from the much rare type of purely intraventricular lesions [78]. The category of infundibulo-tuberal or

intra-third ventricle floor CPs has been confirmed in the recent CP surgical series published by Tomita et al. [147], Shi et al. [131] and Qi et al. [115]. In light of this astounding evidence, it is surprising that the classical view of CPs as lesions located in the sellar/suprasellar regions has dominated the literature.

Topographical classification of CPs involving the third ventricle: the infundibulo-tuberal or not strictly intraventricular category

A majority of CPs involve the third ventricle at the time of diagnosis; however, different manners of third ventricle involvement must be distinguished. Of special importance is differentiating between the morphological distortions of the hypothalamus caused by compression by an extra-axial lesion and the intrinsic damage to the hypothalamus caused by invasion of this region by an intraparenchymal lesion (Fig. 1) [6]. In 2004, a topographical classification scheme for CPs with a predominant or whole intraventricular position was designed according to the tumour-third ventricle relationships described in individual case reports since 1955 [106]. The objective of such a classification was to highlight the existence of two categories of CPs within the ill-defined term "intraventricular", the strictly and the not strictly intraventricular topographies, the latter associated with a lower total excision rate and a higher poor postoperative outcome rate because of its closer anatomical relationship to the hypothalamus. Although the anatomical criteria for segregation in these two categories rested primarily on the intactness or disruption of the third ventricle floor, the essential fact supporting the usefulness of such a differentiation is the tumour's tighter attachment to the neural tissue and worse patient outcomes observable in the group of not strictly intraventricular CPs, which represents approximately 75% of lesions developing within the third ventricle. The tight tumoural adherence is related to the lack of a leptomeningeal layer separating the neural tissue from the tumour wall, because of the subpial expansion of the lesion within the neural layer of the third ventricle floor [104, 106, 115]. The progressive growth of a CP originating within the floor of the third ventricle would cause the stretching and atrophy of this neural tissue as the infundibulo-tuberal area is progressively replaced by the mass, as has been very elegantly proved in the histological studies by Qi et al. [115] and Pan et al. [106]. At the same time, a reactive gliotic layer will develop between the mass and the hypothalamic nuclei.

The concepts of not-strictly intraventricular and infundibulo-tuberal topographical categories for CPs with a major third ventricle component can be used as equivalent, interchangeable terms. Strictly intraventricular lesions, whether pathologically or intraoperatively proven,



should be considered as the special and rare subgroup of infundibulo-tuberal lesions presenting a dissectable attachment to the inner surface of the third ventricle floor [104, 106, 136]. Numerous surgical series of CPs reported in the literature consider a topographical category of lesions involving specifically the infundibulo-tuberal area of the hypothalamus (Table 1). Multiple examples of lesions disclosed at autopsies of non-operated patients are displayed in many other studies even when their authors did not consider such specific topography and defined a retrochiasmatic or a general suprasellar position for these CPs (Table 2) [66, 110]. The infundibulo-tuberal category is predominant in the most recent series of CPs diagnosed at autopsy [60, 76, 83, 136, 165]. On the basis of such a body

of evidence the differentiation of a category of infundibulo-tuberal or not strictly intraventricular CP seems to be conclusive.

Embryological basis for the development of infundibulo-tuberal CPs

CP was initially considered a benign, epithelial type of lesion developed from embryologic remnants of the hypophyseal duct [49, 97]. This concept was established by the prominent Austrian pathologist Jakob Erdheim, who observed the predominant location of CPs in the pars tuberalis, precisely the region of the pituitary gland where scattered nests of squamous-epithelial cells were known to

Fig. 4 Histopathological relationships between infundibulo-tuberal CPs and the hypothalamus. **a** One of the earliest depictions of a cystic, infundibulo-tuberal CP of the squamous-papillary type. Notice the basal papillary nodule in the infundibulum (*black arrow*) and the cyst capsule replacing the floor of the third ventricle (Langer, 1892 [85]). **b** Sagittal section of a CP similar to that reported by Langer found in an autopsy study. Observe the infundibulo-tuberal origin of the basal papillary nodule (*black arrow*) and the thin layer of neural tissue surrounding the intraventricular cystic component corresponding to the stretched remnant of the third ventricle floor, as proved by Pan et al. [104] (*white arrows*) (reproduced with kind permission from Springer Science+Business media from Zülch KJ, Atlas of Gross Neurosurgical Pathology, 1975, figure 267 [165]). **c** Histological tumor-third ventricle relationships of an infundibulo-tuberal or not strictly intraventricular CP of the adamantinomatous type. The lesion has developed at the infundibulum-chiasm junction and replaced most of the tuber cinereum while expanding into the third ventricle. The arachnoid of the chiasmatic cistern is intact below the basal aspect of the lesion (*black arrow*); *ch* optic chiasm, *mb* mamillary body (Reproduced from: Wheatley et al., 1986 [153], with permission from BMJ Publishing Group Ltd.). **d** Artistic picture of an infundibulo-tuberal CP of adamantinomatous type whose lower pole is protruding into the suprasellar area (Ziegler, 1902 [163]). **e** Histological coronal section of an infundibulo-tuberal CP whose intraventricular component shows no infiltration of the ventricle walls. A clear plane of dissection of the lesion is observed between the tumor capsule and the walls of the third ventricle (*white arrows*) (Newmark, 1917 [98]). **f** Midsagittal brain section showing the autopsy specimen of a strictly intraventricular papillary CP attached to the third ventricle floor by a short gliovascular pedicle (*black arrow*). In contrast to the previously shown lesions, an intact third ventricle floor is observed beneath the lesion (reproduced with permission from Schmidt P et al, Craniopharyngiome pédiculé du troisième ventricule. Revue Neurologique, 1984, vol 140, pp 281-283, Copyright © 1984 Elsevier Masson SAS. All rights reserved. [130]). **g₁-g₂** Macroscopic midsagittal section (**g₁**) and microscopic coronal section of an intraventricular CP in a 30-year-old man who died postoperatively due to hypothalamic haemorrhage. Basal solid portions of the tumour were tightly adhered to the third ventricle floor and walls (*black arrows*) with areas of haemorrhagic infiltration of the hypothalamus (*white arrow*) (Reproduced with permission from Kubota et al., 1980 [83], with the kind permission of the Japan Neurosurgical Society). **h₁-h₃** Coronal macroscopic and microscopic sections of a solid-cystic infundibulo-tuberal CP showing the whole obliteration of the third ventricle. The basal solid portion of the lesion which replaces the infundibulo-tuberal area is surrounded by the arachnoid-pia mater (*black arrows*); its cystic intraventricular portion is separated from the hypothalamus by a three-layered wall formed by a connective tissue layer (*C*), the arachnoid (*A*) and the pia mater (*P*) (Goldstein, 1928 [58]). **i₁-i₂** Coronal macroscopic and microscopic sections of a cystic third ventricle CP showing the infiltration of the hypothalamus by epithelial finger-like protrusions (*black arrows*) (Orthner and Rettinger, Fortschr Neurol Psychiatr Grenzgeb 33:299–331 1965 [103]. Reproduced with permission from Thieme Medical Publishers.)

occur with the highest frequency (Fig. 3e) [49, 133]. The pars tuberalis is the slender, tongue-like upward extension of pituitary glandular tissue covering the anterolateral surface of the pituitary stalk, the infundibulum and the tuber cinereum (Fig. 2h) [10, 95]. It is constituted by a functionally distinct population of cells which have receptors for melatonin, plus a small population of gonadotrophs and other fibrous cells [63]. In 1875, von Mihalkovics described, in seminal studies on the embryolo-

logical development of the pituitary gland of dogs, how the lowest edge of Rathke's pouch, in contact with the vanishing hypophyseal duct, underwent an antero-superior rotation to become the segment of the pars tuberalis that spreads beneath the infundibulum and the tuber cinereum (Fig. 2f) [150]. According to Erdheim, this embryological rotation would account for the presence of epithelial nests within the pars tuberalis, as well as for the development of epithelial growths with a structure similar to the oral mucosa within the tubero-infundibular area, as a consequence of tumoral transformation of these epithelial cell remnants [49]. Modern embryological studies on hypophyseal development have shown that the pars tuberalis joins the diencephalic floor during the 7th week of embryo development (Carnegie stage 20, 18-22 mm) and that the hypophyseal duct is vanished at the end of the 8th week (Carnegie stages 21–23, 20-25 mm) [101, 102, 134]. For its part, the undifferentiated mesenchyma situated between the hollow vesicle derived from rotation of the Rathke's pouch and the floor of the diencephalon, undergoes transformation into the leptomeninges surrounding the pars tuberalis and the infundibulum at later stages of development, in embryos from about 25 mm on (Fig. 3 a₁-a₃) [156]. Therefore, epithelial cells derived from the craniopharyngeal duct or transferred from the primitive mouth with the rotation of the Rathke's pouch may become embedded within the neural tissue of the diencephalic floor and give rise to the development of infundibulo-tuberal CPs [27].

The identification of epithelial cell nests at the pars tuberalis of fetus and infants by Goldberg et al. [57] and of some cases of CPs developed during the embryonic period [157], besides the high rate of CPs occurring in the infundibulo-tuberal area in the studies by Tomita and Bowman [147], Shi et al. [131] and Qi et al. [115], constitute additional sources of evidence supporting the embryological theory for the origin of infundibular-tuberal lesions (Table 1). Alternatively, a metaplastic squamous transformation of glandular cells of the pars tuberalis has been considered as a plausible process for the development of CPs at adult age, given the increasing number of squamous cell nests found in the pars tuberalis with age, and the predominant histological papillary structure among adult CPs involving the infundibulum and the third ventricle [23, 33, 68, 92]. Further support for this theory came from immunochemical studies demonstrating the double-labelling of CP cells for keratin and hormones [8, 139] and the presence of glandular cells within CPs [144, 145].

Ciric and Cozzens [28] proposed that the development of CPs within the tuberal area and the third ventricle could be explained if cell remnants of the craniopharyngeal duct become embedded within the neural tissue of the third ventricle floor before the formation of the leptomeningeal layer of arachnoid-pia mater (Fig. 3a). In fact, the accurate

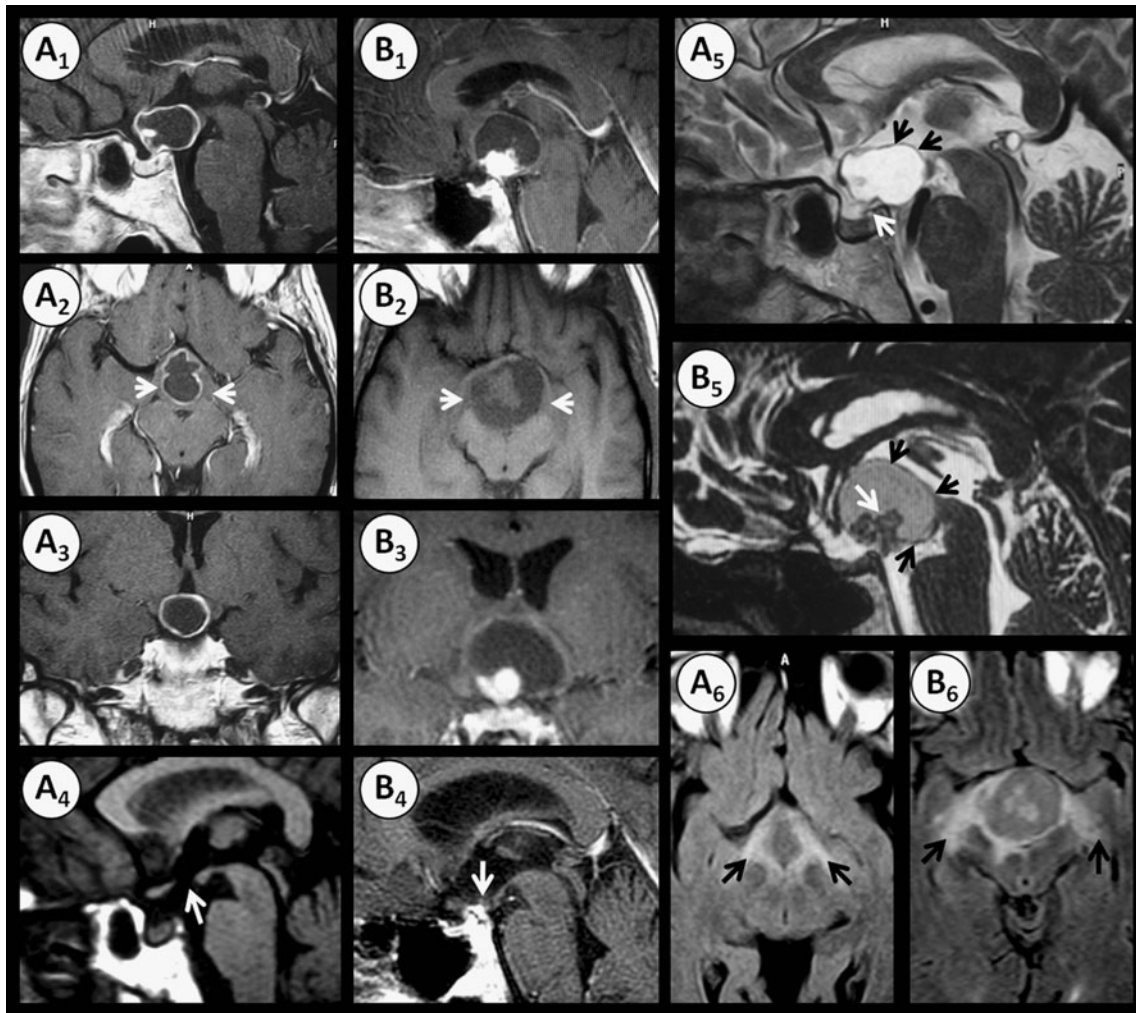


Fig. 5 Neuroradiological differentiation of the infundibulo-tuberal or not strictly intraventricular topographical category of CPs. **a**₁–**a**₃ Preoperative midsagittal (**a**₁), axial (**a**₂) and coronal (**a**₃) T1-weighted MRI sections after gadolinium administration of an infundibulo-tuberal cystic CP diagnosed in a 49-year-old woman with a history of headache, anorexy, left hemianopsy and loss of libido for the last 2 years. The third ventricle floor is apparently replaced by the lesion, which obliterates both the suprachiasmatic and infundibular recesses of the third ventricle, above a normal pituitary gland. Irregular tumour protrusions are observed expanding within the hypothalamic issue on the axial section (*white arrows*). **a**₄ Postoperative midsagittal T1-weighted MRI study after total removal of the lesion. The defective third ventricle floor allows the free CSF flow into the chiasmatic cistern (*white arrow*). **a**₅ Preoperative midsagittal T2-weighted MRI section of the same lesion showing the integrity of both the pituitary gland and pituitary stalk (*white arrow*); a thin layer of neural tissue around the intraventricular portion of the lesion, between the optic chiasm and the compressed mamillary bodies can be observed (*black arrows*). **b**₁–**b**₃ Preoperative midsagittal (**b**₁), axial (**b**₂) and coronal (**b**₃) T1-weighted MRI sections of an infundibulo-tuberal basal solid/

upper cystic craniopharyngioma diagnosed in a 48-year-old man with a history of headache, short memory defect and behaviour disturbance for the last few months. A normal, free-of-tumour pituitary gland, pituitary stalk and chiasmatic cistern are observed on these sections. The third ventricle floor is apparently replaced by the lesion that fills almost the whole third ventricle. The stretched thin walls of the third ventricle containing the hypothalamic nuclei are observed on the axial section (*white arrows*). **b**₄ Postoperative midsagittal T1-weighted MRI study after total removal of the lesion. A defect in the third ventricle floor caused by the mass can be observed (*white arrow*). **b**₅ Preoperative midsagittal 3D FIESTA (fast imaging employing steady-state acquisition) MRI image showing the basal, cauliflower-like portion of the lesion replacing the infundibulum and tuber cinereum (*white arrow*) and the thin layer of neural tissue surrounding its intraventricular cystic portion, between the optic chiasm and the compressed mamillary bodies (*black arrows*). **a**₆–**b**₆ Proton density-weighted axial MRI sections of both CPs shown above; a marked symmetrical hyperintense signal corresponding to edema along the optic tracts (*black arrows*) is characteristically caused by infundibulo-tuberal or not strictly intraventricular CPs

relationships of the pia mater and the pars tuberalis remains as one of the most intriguing issues not well addressed in embryological studies focused on the development of meningeal layers around the pituitary gland. Attwell [10]

considered that the pars tuberalis was ensheated between two layers of pia mater: (1) the inner layer, interposed between the dorsal aspect of the pars tuberalis and the tuber cinereum, which is derived from the primitive pia mater covering the

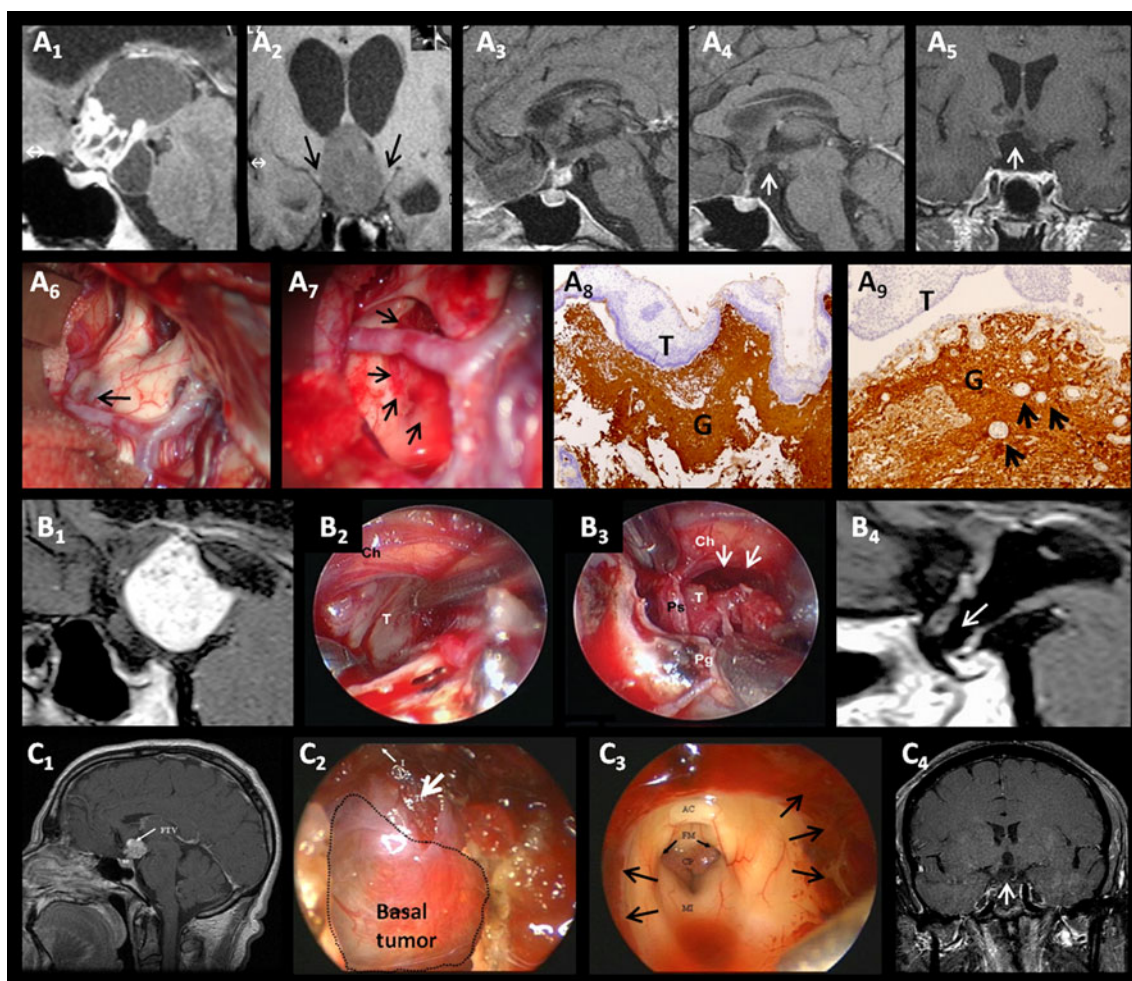


Fig. 6 Surgical evidence of the infundibulo-tuberal or not strictly intraventricular topographical category of CPs. **a₁–a₉** Giant mixed solid-cystic infundibulo-tuberal CP diagnosed and surgically removed in a 33-year-old man with a history of headache, visual deficit and hyperphagic obesity disorder. **a₁** Preoperative midsagittal T1-weighted MRI study after gadolinium administration showing the elliptical lesion filling the whole third ventricle. **a₂** Coronal T1-weighted MRI section showing the position of both hypothalami around the equator of the lesion (*black arrows*). **a₃** Postoperative midsagittal T1-weighted MRI study showing a tumor remnant at the level of the infundibulum. **a₄, a₅** Postoperative midsagittal and coronal T1-weighted MRI sections showing the defect in the floor of the third ventricle after total removal of the infundibular CP remnant. **a₆** Intraoperative photograph of the initial surgical procedure. The chiasm and optic nerves are exposed through a pterional right approach. Notice the bulged lamina terminalis beneath the A-1 segment of the anterior cerebral artery due to the mass effect of the intraventricular component of the lesion (*black arrow*). **a₇** Intraoperative view of the third ventricle obtained in the second surgical procedure after removing the infundibular CP remnant through the same pterional approach. The inner aspect of the third ventricle left wall is observed, in addition to the bloody rim of attachment of the lesion (*black arrows*). **a₈–a₉** Histological specimens of the tumor-brain interface showing a functionless band of reactive

gliosis (*G*) around the adamantinomatous CP at the level of the third ventricle floor in the initial (**a₈**) and recurrent (**a₉**) lesions. The thickness of this band ranged from 50 to 600 μm and was similar in both tumour specimens, although it showed a significantly more prominent vascular proliferation in the recurrent CP (*black arrows*). **b₁–b₄** Intraventricular solid CP originated in the infundibulum and removed through an endoscopically assisted extended transphenoidal approach (de Divitiis, 2007 [41]. Reproduced with permission from Lippincott Williams & Wilkins Publishing group.). **b₂, b₃** Intraoperative endoscopic views of the basal aspect of the lesion which expands at the chiasmatic-infundibular junction. The border of the breach in the third ventricle floor left by the lesion can be observed in the surgical field after removal of the tumor (*T*) (*white arrows*) and on the postoperative midsagittal MRI study (**b₄**, *white arrow*). **c₁–c₄** Infundibulo-tuberal CP removed through an endoscopically assisted extended transphenoidal approach (Kassam, 2008 [72]. Reproduced with permission from JNS Publishing group). The basal aspect of the solid lesion replaces the tuber cinereum with the remnants of the third ventricle floor being visible adjacent to the anteroinferior tumour border (**c₂**, *white arrow*). A wide defect in the tuber cinereum is left after total removal of the CP allowing a view of the inside of the ventricle which presents a rim of blood infiltration (**c₃**, *black arrows*). The breach in the third ventricle floor is observed on postoperative coronal MRI (**c₄**)

neural tube, and (2) the outer layer, which, together with the arachnoid, covers the ventral aspect of the pars tuberalis (Fig. 3b). This concept of a double pia mater covering for the

pars tuberalis was initially proposed by Roussy and Mosinger in 1917 [121], then it was confirmed by Suderland [140] on human fetuses. Ultrastructural studies of the pia

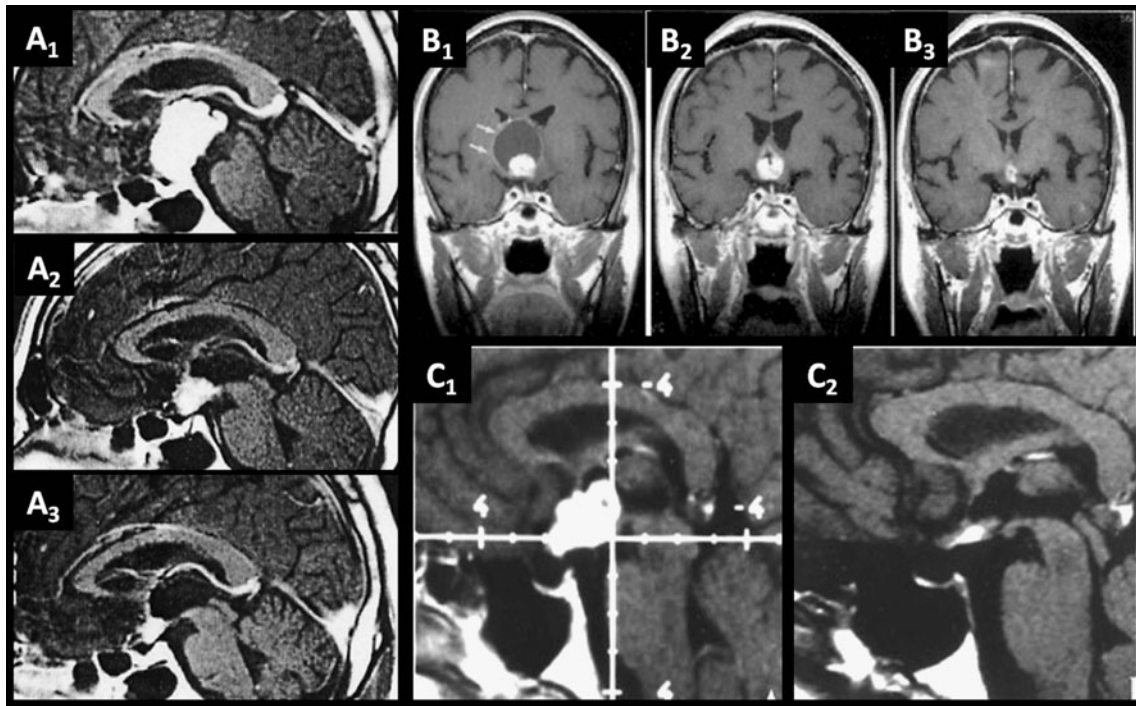


Fig. 7 Radiosurgical evidence of the infundibulo-tuberal or not strictly intraventricular topographical category of CPs. **a₁a₂–a₃** Infundibulo-tuberal solid CP treated with gamma knife (Kobayashi et al., 1994 [77]. Reproduced with the kind permission by S. Karger AG, Basel.). The sequential follow-up MRI studies obtained 6 months and 1 year after the treatment show the progressive shrinkage of the lesion which last remnant remains at the infundibulo-tuberal area, the probable site of origin of this CP. **b₁, b₂** Similar long-term evolution of a basal-solid/upper cystic intraventricular CP following gamma knife radiosurgery showing the progressive shrinkage of the residual solid mass in the floor of the third ventricle, above an intact pituitary stalk

(Chung et al., 2000 [26]. Reproduced with permission from the JNS Publishing group.). **c₁, c₂** Elliptic solid CP treated by stereotactic radiosurgery which last remnant is observed embedded within the floor of the third ventricle 4 months following application of the therapy (This figure was published by Steiner L et al: Gamma surgery in cerebral vascular lesions, malformations, tumors and functional disorders of the nervous system, in Schmidek HH & Sweet WH (eds): Operative Neurosurgical Techniques, indications, methods and results, fourth edition, WB Saunders Company, Vol 1 pp 670–706, Copyright Elsevier, 2000. [135])

matter have shown that it does not represent a continuous water-tight layer isolating the cerebral surface, a role played by the interdigitated processes of the glia limitans [91]. On the other hand, the pars tuberalis is perforated by subarachnoid channels, allowing the tuberal cells to be bathed by soluble factors in the cerebrospinal fluid such as melatonin [2]. These structural properties favour the subpial expansion of epithelial nests located at the dorsal surface of the pars tuberalis into the neural tissue of the third ventricle floor.

Growing evidence for the existence of overlapping histological features within epithelial lesions of the pituitary-hypothalamic axis, supports the concept of a common origin of CPs, Rathke's pouch cysts and suprasellar epidermoid/dermoid lesions, from remnants of the primitive mouth incorporated into Rathke's pouch [62, 159]. Depending on the original position and type of cell that gives origin to an epithelial parasellar lesion, either from embryonic cells of the dental ridge/primitive oral mucosa or from metaplastic transformation of cells of Rathke's pouch, different types of lesions may develop [159]. Independently of the mechanism involved, CPs developing at the floor of the third ventricle should be

considered as lesions of definite origin from primitive or metaplastic squamous cells placed within the pars tuberalis.

Hypothalamus impairment by infundibulo-tuberal CPs

CPs involving the third ventricle and the hypothalamus frequently associate symptoms of obesity or emaciation, sexual dystrophy and diabetes insipidus (DI). In 1929, John F. Fulton and Percival Bailey described a specific clinical picture consisting of drowsiness, mental disturbances and reduced awareness caused by tumours affecting the hypothalamus and the third ventricle [54]. As early as 1930, Cushing noticed that those CPs situated at the tuber cinereum and expanding into the third ventricle caused specific metabolic and behavioural disturbances such as hypersomnia, hyperphagia with marked adiposity, personality changes and polyuria (Fig. 1e) [37–39]. By analysis of human patients and experimental hypothalamic lesions induced in animals, it was shown that many of these symptoms had a hypothalamic origin [4, 17, 21, 46, 100, 154]. For example, the isolated bilateral destruction of the

ventromedial nuclear complex of the hypothalamus led to marked hyperphagia, obesity, and associated rage behaviour [117]. Other symptoms of hypothalamic damage are severe hyperthermia, marked peripheral vasoconstriction, sleep-like coma and electrolyte imbalances [22, 29]. In addition, remarkable evidence of a Korsakoff's dementia-like disorder associated with intraventricular CPs was accumulated. Mental impairment was recorded in one-third of tuberal CPs reported by Northfield, with variable symptomatology from dullness and moderate impaired memory to frank dementia [99, 100]. Williams and Pennybacker [154] drew attention to the memory defect found in 75% of cases of CPs involving the third ventricle. In the surgical series reported by Aiba et al. [3], CPs with a tuberal involvement were also characterized by apparition of mental disturbances associated with DI after surgery. The existence of psychiatric symptoms was significantly correlated with death or a poor postoperative outcome in the clinical study by Kobayashi et al. [76]. In the series of 45 papillary CPs by Crotty et al. [33], most of them involving the third ventricle and its floor, changes in mentation occurred in 22% of patients.

In the long term, the development of progressive obesity, Froelich syndrome or dystrophia adiposogenitalis are the principal syndromes associated with radical excision of infundibulo-tuberal CPs [100, 113]. In contrast, lateral hypothalamic lesions cause syndromes characterized by hypophagia and emaciation [22]. A positive correlation between a greater hypothalamic damage on postoperative MRI studies after surgical removal of CPs and a superior postoperative patient's body mass index (BMI) has been demonstrated by DeVile et al. [43]. Severe postoperative obesity occurs predominantly in patients who have sustained bilateral hypothalamic damage. In particular, all the subjects with marked postoperative obesity in the study by DeVile et al. [43], showed evidence of significant disruption of the normal hypothalamus anatomy, with either a complete deficiency or extensive destruction of the third ventricle floor [42, 43]. In a recent clinical study, Meuric et al. [94] observed significant behaviour disturbances, including uncontrollable hyperphagia, in the group of CPs in which the hypothalamus became unrecognizable on the preoperative MRI.

Histopathological relationships between infundibulo-tuberal CPs and the hypothalamus

The major difference between CPs developing within the third ventricle floor in comparison with other topographies is the presence, in the former category, of a layer of neural tissue and reactive gliosis around the tumour [76, 83, 99, 106, 115, 143]. In 1926, Critchley and Ironside [32] were the first authors to describe the “glial reaction in the structures surrounding the tumor” as a consistent third element found adjacent to CPs, along with the epithelial

lesion and the connective tissue. This glial proliferation forms a sort of capsule composed externally of neuroglia and internally of fibrous tissue. Bailey et al. [14] emphasized that the extreme adhesiveness of the glial layer was a sign indicating that the plane of cleavage was positioned in the normal hypothalamus. Such a statement correlated well with the fact that CPs expanding within the hypothalamus usually present a wide, circumferential band of attachment to the neural structures of the base of the third ventricle—the optic chiasm, the infundibulum and the hypothalamic walls—contrary to strictly intraventricular CPs that usually show a pedicular attachment to the third ventricle floor, without accompanying reactive gliosis [46, 106]. This histological difference was demonstrated by Steno [136] in his superb autopsy study that included 14 lesions showing disruption of the third ventricle floor, and very recently it has been confirmed intraoperatively by Pan et al. [104] in a large series of intraventricular CPs. The histological arrangement of the interface between the CP and the viable hypothalamus is a feature of paramount importance for neurosurgeons, because it predicts that the cleavage gliotic plane of dissection will be circumferential, just between the equator/lower half of the lesion and the walls of the third ventricle [104, 106, 136].

Theoretical discussions about the functionality of the neural layer covering the dome of CPs growing within the third ventricle were present in the works by Pertuiset et al. [109] and Van den Bergh et al. [148], with contradictory views between those authors warning about the risks of trespassing this still viable layer through a transventricular or a translamina terminalis (TLT) approach [6], and those affirming the non-functional gliotic nature of such tissue [78, 142]. Poor outcomes in patients with CPs implanted in the floor of the third ventricle who were operated upon by Long and Chou [90] and others through a transventricular approach seemed to validate such a warning [99]. Observation of isolated islands of epithelium at the border of infundibulo-tuberal CPs, which give rise to an intense gliosis within the proper hypothalamus, corroborated Northfield's opinion that a true fusion of the tumour and the brain render impracticable a safe, complete surgical removal of infundibulo-tuberal CPs [99]. Against that opinion was Sweet's claim that the finger-like epithelial streamers described by some pathologists were embedded within a gliotic non-functional layer which provides a safe cleavage plane for surgical dissection of the lesion (Fig. 6a₈–a₉) [142, 143]. Nearly every researcher analysing the boundaries of infundibulo-tuberal CPs have observed “fingers” or “islands” of the tumour invading the brain that were considered the cause of early recurrence after gross total resection [1, 16, 71, 76, 83, 89, 111, 132, 142]. Some authors have regarded these epithelial elements penetrating the neural tissue as the major obstacle to total surgical removal [6, 55, 71, 78, 132, 158]. Others considered that the areas of

apparent CP invasion into adjacent brain probably did not represent a true tumor invasion but rather the original site of CP growth within the nervous substance of the third ventricle floor [78].

In an attempt to answer the question of brain invasiveness by CPs, thorough microscopic studies of the tumor-brain interface of CPs involving the third ventricle were performed by Kubota et al. [83] and Kobayashi et al. [76]. Kubota et al. [83] described a double-layer structure in the capsule of the intraventricular, cystic component of retrochiasmatic CPs, formed by a thin inner layer of adamantinomatous or squamous epithelium and an outer layer of reactive gliosis. Although the solid, basal portion of these lesions situated at the tubero-infundibular area was usually surrounded by a thick layer of gliosis that separated the tumor 0.5–2.5 mm from the hypothalamus, at some areas no effective distance for a safe dissection occurred between the CP and the viable hypothalamic nuclei (Fig. 4g). In addition, a hypervascular layer of brain parenchyma was observed around the peritumoural gliotic tissue, with vessels of 20–200 μm in diameter that increased the risk of hypothalamic bleeding with surgical dissection. The histological analysis by Kobayashi et al. [76] of the brain-tumor interface of predominantly intraventricular CPs confirmed that the basal portion of such lesions, located within the tissue of the third ventricle floor, showed finger-shaped protrusions of solid epithelial cords invading the adjacent brain. The electron microscopy study performed by Landolt [84] on the boundaries of CPs found that in general the basal membranes of epithelial cells and reactive glia were separated by a few collagen fibres, this interface helping the surgeon to find the safe cleavage plane of dissection. However, the gliotic boundary zone was not present in all cases. Therefore, two not mutually exclusive possibilities can occur, the presence of a functionless interface of reactive gliosis or a direct contact between the tumor and the hypothalamic nuclei, even in the same lesion. Overall, these findings highlight the high risk associated with the indiscriminate attempt of total removal of tubero-infundibular CPs.

Neuroradiological differentiation of infundibulo-tuberal CPs

Limitations of neuroradiological methods used before the introduction of MRI, led authors to use the term intraventricular for many CPs actually developed within the infundibulo-tuberal area of the third ventricle floor [108]. Definition of the infundibulo-tuberal topography for CPs on the basis of the tumour-third ventricle relationships observed on MRI scans was first proposed in the classification by Raybaud et al. [116]. This location has also been considered as a separate category in the recent seminal neuroradiological work made at the Burdenko Neurosurgery Institute in Moscow [82]. Rossi et al. [118] proposed a similar MRI-based vertical classification

system differentiating the classical suprasellar type of CP, originating at the pituitary stalk, and the suprasellar type of CP originating in the tuber cinereum, which typically extend upwards into the hypothalamus and the third ventricle. In the latter scheme, as well as in other topographical classification systems, pure intraventricular lesions are mistakenly considered as a separate ectopic category of CPs [118, 162], but in view of the previous body of evidence, the strictly intraventricular location represents the upper position across the spectrum of anatomical locations of CPs along the hypothalamic-pituitary axis [99, 106, 136].

An accurate preoperative definition of the degree of hypothalamic involvement by a CP is of crucial importance to determine whether the lesion is amenable to surgical excision. In recent years there has been a renewed interest in the assessment of the degree of hypothalamic impairment by CPs and several clinico-radiological studies have been conducted showing a positive correlation between a greater morphological distortion of the hypothalamus on preoperative MRI and worse patient outcomes after surgery [43, 125]. Saint Rose et al. [125] differentiated between suprasellar lesions pushing the floor of the third ventricle upward without gross invasion of the hypothalamus and suprasellar/intraventricular lesions which replaced the third ventricle floor, making the hypothalamic area no longer recognizable. A breach or anatomical defect in the floor of the third ventricle was observed after complete removal of CPs in the latter group, corresponding to 42% of CPs (Figs. 5a₄, b₄ and 6a₄, b₄, c₄) [125]. This defect, which is invariably present after total excision of infundibulo-tuberal CPs tightly attached to the third ventricle floor, is not usually related to iatrogenic injury caused by the neurosurgeon but rather to the elimination of the tumoural mass which had replaced the floor of the third ventricle (Fig. 6). De Vile et al. [43] have proposed a postoperative MRI-based five-grade scoring system for the degree of hypothalamic involvement by CPs, from the third ventricle floor occupation with tumour remnants (grade I) to a thinned or distorted intact floor (grade II) or a breached floor with a small (grade III), large (grade IV) or wholly deficient third ventricle floor (grade V). The major conclusion of these works has been that patients with neuroradiological signs of hypothalamic involvement by the CP, and especially those with preoperative symptoms of hypothalamus dysfunction are at high risk of suffering from long-term hypothalamic sequelae such as progressive obesity due to intractable hyperphagia, and emotional and behavioural changes [114].

Surgical approach and complications associated with infundibulo-tuberal CPs

Surgery of intraventricular CPs associates morbidity and mortality rates three-times higher than for endosellar or

suprasellar CPs [106]. Direct surgical injury to the hypothalamus remains the major cause of long-term morbidity and mortality after radical excision of infundibulo-tuberal CPs, as revealed by post-mortem necropsy findings [70, 100]. Invasion of the hypothalamus represents the main limiting factor against total removal of the lesion because of the lack of an identifiable safe, non-functional cleavage plane of dissection. According to Frank et al. [50], this fact is related to the absence of a meningeal layer interposed between the lesion and the diencephalic neural structures. Only extrapial CPs would be amenable to safe and complete surgical removal in most cases [27, 28]. Unfortunately, preoperative MRI is unable to accurately define the extrapial or subpial involvement of the third ventricle floor by the CP. When the CP causes a severe distortion of the hypothalamus—type 2 and 3 in Saint Rose and Meuric MRI classification schemes—subtotal tumor resection combined with local radiation therapy seems to represent the best therapeutic option [94, 125].

Prevention of hypothalamic injury remains as the neurosurgeon's principal concern during removal of infundibulo-tuberal CPs. Preservation of the anteroinferior walls of the third ventricle as well as the tiny hypothalamic perforating arteries is critical to avoid delayed fatal diencephalic disturbances [42, 81, 131, 137, 143, 147]. Apart from direct mechanical injury to the hypothalamus due to inadequate surgical manipulation, disturbances of regional blood flow in the hypothalamus are one of the major causes of postoperative morbidity and mortality [81]. It is likely that traumatic and/or ischemic hypothalamic damage results from the “blind” pulling of infundibulo-tuberal, tightly adhered portions of the tumour [90]. This problem can be overcome only when the infundibulo-tuberal and intraventricular portions of a CP are sufficiently exposed to be manipulated under direct view during all phases of the surgical procedure. No single supratentorial surgical approach provides a good view of the whole hypothalamus. In the case of infundibulo-tuberal CPs extending into the third ventricle the classical pterional approach would provide insufficient exposure of the anteroinfero-lateral walls of the third ventricle and the perforant vessels of the hypothalamus surrounding the tumour capsule [161]. This setback led Yasargil [158] and Steno et al. [137] to employ successfully the combined transcassal-pterional approach to have direct control of the areas of tumour adhesion to the hypothalamus during the whole procedure. Alternatively, William Sweet was the pioneer author advocating the use of the TLT approach for removal of tubero-infundibular and purely intraventricular CPs [142, 143]. This approach provides a good access to the area of hypothalamic attachment of the lesion and yields excellent results after total removal of large infundibulo-tuberal CPs [75, 104, 106, 115, 131, 137,

143, 147]. A small hole, corresponding to the area of infiltration of the lesion, is left behind the chiasm at the floor of the third ventricle, as the surgical confirmation of the intratuberal location of the CP [143]. The major disadvantage of the TLT approach is the fact that tumour remnants attached at the undersurface of optic chiasm can hardly be seen and reached.

The combination of extended transsphenoidal approaches to the suprasellar region with the use of endoscopically assisted techniques has allowed a much more reliable assessment of the anatomical relationships between infundibulo-tuberal CPs and the diencephalic structures (Fig. 6b,c) [41, 50, 72, 74, 86]. Probably this kind of approach is the only suitable procedure to perform a sharp dissection of the lesion from the hypothalamus with direct control of the perforating vessels from the beginning to the end of tumour excision. Recent series of CPs including retrochiasmatic and intraventricular cases operated upon using this approach have demonstrated the replacement of the floor of the third ventricle by CPs with an infundibulo-tuberal or not strictly intraventricular topography (Fig. 6) [41, 50, 72, 74, 86]. A wide breach at the floor of the third ventricle was left after total removal of such lesions, allowing for the direct inspection of the third ventricle with an endoscope, confirming the not-strictly intraventricular location of the mass as well as its original position within the neural tissue of the tuber cinereum [41, 72, 74, 86].

Conclusions

The concept of a general suprasellar position for cranio-pharyngiomas is insufficient to define the accurate relationships between the vital diencephalic structures and the tumour, and to plan the most appropriate surgical route accordingly. A large body of evidence supports the differentiation of the primary infundibulo-tuberal or not strictly intraventricular type of CP which is characterized by its primary subpial development above an identifiable pituitary stalk and a predominant expansion into the third ventricle. This topographical category of CPs is highly prevalent in both the adult and child populations, although it can hardly be differentiated from the strictly or purely intraventricular topography on preoperative MRI studies. Infundibulo-tuberal CPs usually present a basal, circumferential band of tight adhesion to the hypothalamus and remnants of the third ventricle floor. This band is formed by a non-functional layer of reactive gliosis without leptomeningeal or conjunctive tissue and can be used in many cases as a safe plane of dissection, although in some lesions finger-like epithelial protrusions extending directly into the viable hypothalamus preclude any attempt of radical excision. After total removal of the lesion, a defective or

breached third ventricle floor can be observed both intraoperatively and on postoperative MRI brain scans. A deficient third ventricle floor does not invariably mean an iatrogenic injury, but rather a consequence of removal of a lesion which replaced the floor itself. The endoscopic extended transsphenoidal approach allows an accurate anatomical definition of infundibulo-tuberal CPs and a non-traumatic, sharp dissection of these lesions off the hypothalamus.

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Conflict of interest None.

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Comment

This substantial piece of work makes a compelling case for a new classification of craniopharyngiomas. Whereas the “Not strictly intraventricular” name does not quite slip off the tongue, the concept will give those working in the field, particularly those adept in the extended endoscopic transsphenoidal procedure, some help in decid-

ing on the radicality of their resection. Also to add a word of caution, as things stand, radiation techniques do continue to have a very major place in the management of these tumours. There is little mention of the role of this therapy here.

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