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Clinical Article

Intraventricular craniopharyngiomas: topographical classification and surgical approach selection based on an extensive overview

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Summary

Background. This retrospective study analyzes the clinical, neuroradiological, pathological and surgical characteristics of well-described intraventricular craniopharyngiomas with the aims of: (i) critically to review the criteria used to affirm the diagnosis of an intraventricular location (ii) defining more accurately this topographical diagnosis preoperatively, and (iii) to investigate factors influencing the surgical outcome.

Method. Clinical, neuroradiological, pathological and surgical objective data of 104 well-described intraventricular craniopharyngiomas (IVC) reported in the literature, in addition to a new case, were analyzed. On the basis of the proofs provided for third ventricle intactness, a new topographical classification for IVC was developed, distinguishing between: (i) strict IVC, with a proved third ventricle floor integrity and (ii) non-strict IVC, without any reliable proof confirming the intactness of the third ventricle floor. Following this classification, clinical features, pathology and surgical outcome for strictly and non-strictly IVC were compared.

Findings. For 105 IVC compiled, 36 belonged to the strictly group and 69 to the non-strictly group. Two pathological features were associated with the non-strictly IVC group: a preferentially adamantinomatous pattern ($p = 0.106$) and wider and tighter adherences to third ventricle margins ($p = 0.01$). The non-strict topography was also associated with a worse postoperative outcome ($p = 0.046$). There was a significant relationship between the surgical approach and the final outcome ($p = 0.05$), being the translamina terminalis approach associated with the best outcome.

Conclusions. Two different topographies might be considered among IVC: strict and non-strict intraventricular location. Non-strictly IVC have wider and tighter adhesions to third ventricle boundaries and this subtype is associated with a worse outcome.

Keywords: Craniopharyngioma; third ventricle; intraventricular; lamina terminalis.

Introduction

Since 1953, when Dobos described a craniopharyngioma wholly located in the third ventricle for the first time [19], there have been a few additional cases which were diagnosed at necropsy, proving the undoubted existence of this particular and rare location. In these necropsy brain specimens the tumor was hidden from outside view, and the third ventricle floor was intact [7, 8, 13, 14, 19, 33, 34, 45–47, 57]. They were named intraventricular craniopharyngiomas (IVC). Their topographical location challenged the embryological theory about craniopharyngioma development, since there was no obvious pathway ascent of Rathke's pouch-derived epithelial cells to the third ventricle cavity. Correct preoperative topographical diagnosis is mandatory in these lesions in order to choose a more appropriate surgical approach to the third ventricle than the classic basal approaches to the suprasellar area.

So far, an increasing number of craniopharyngiomas have been diagnosed, treated and reported as intraventricular, but the term can lead to confusion since, in many cases, a part of a large suprasellar craniopharyngioma can also invade the third ventricle region. It is very difficult, even with modern diagnostic tools, to decide whether a tumour is primarily intraventricular or has secondarily occupied the third ventricle region.

Historically, many of the reported IVC belong to the pre-MRI era and the diagnostic proofs given for their intraventricular location do not also reliably confirm the intactness of the third ventricle. In fact, in some cases, the topographical misdiagnosis of the craniopharyngioma has lead to a mistaken surgical approach being taken [7, 18, 22, 29, 32, 36, 44, 49, 70, 73, 74]. In these cases the tumour was either erroneously considered as primarily intraventricular, when it was suprasellar, or it was considered as suprasellar with secondary involvement of the third ventricle, when it was actually purely intraventricular. Some of these misdiagnoses were even made with MR images [22, 32, 36, 73].

Our interest in this subject began in 1997, with the treatment of a craniopharyngioma which was originally diagnosed as suprasellar and, consequently, approached via a pterional route. However, we could not find the tumour at the suprasellar level because it was wholly intraventricular. An extensive retrospective review of well-described IVC was then undertaken with the aim of: (i) analyzing the criteria used to affirm the diagnosis of an intraventricular location; (ii) classifying these data according to their reliability. Then a comparison of the main demographical, clinical, neuroradiological, histological and surgical features was carried out between those IVC which provided proof of third ventricle intactness and those which did not clearly prove an intraventricular location. We must remark that the well-described IVC cases have been reported for a long period of time and we are concerned for the subjectivity and incompleteness of the data recorded in many of the articles analyzed in this extensive review. However we think that to gather all the information on IVC's topography provided by the literature might be the most useful way to help make a correct diagnosis and decide the appropriate surgical approach to these lesions. This is the main objective of the present study.

Materials and methods

Topographical classification hypothesis

Intraventricular craniopharyngioma should be considered to be just those tumours located exclusively within the third ventricle. This restrictive definition sharply separates this kind of tumour from those that arise in the suprasellar region and have secondarily occupied the third ventricle cavity [2, 11, 31]. The main problem with the term *intraventricular* is that by the time of diagnosis, most craniopharyngiomas are quite large and have expanded into the third ventricle area, so that clearly differentiating the anatomical relationships between the tumour and the third ventricle margins, which are extremely thin, is usually not possible, even with the use of MRI [51, 73]. Once those suprasellar tumours secondarily involving the third ventricle cavity have been excluded from the term intraventricular, one should differentiate between those few cases in which all the third ventricle margins, including the floor, are completely intact, and the remaining cases (the majority), in which third ventricle floor integrity can not be demonstrated. For the first case, we employed the term strictly intraventricular craniopharyngioma and for the second, non-strictly intraventricular craniopharyngioma.

Following these concepts, diagnostic proof, evidenced by illustrations or surgical descriptions in the reported well-detailed IVC [4–8, 13–15, 18, 19, 21–23, 25–27, 29, 30, 33–38, 40, 42–45, 47–50, 52, 53, 57, 58, 61, 62, 64, 65, 67–70, 73, 74], were meticulously evaluated with an aim to assessing the integrity of the third ventricle floor. On the basis of the diagnostic evidence provided by the different studies a topographical classification was elaborated and the tumours were grouped as strictly or non-strictly intraventricular (Table 1). Thus, grade I, II and III corresponded to cases in which an intact third ventricle floor had been demonstrated by different diagnostic methods (with a decreasing grade of reliability) and were assigned to the strictly IVC category. By contrast, grade IV and grade V corresponded to those cases in whom diagnostic tools had not been able to demonstrate third ventricle floor integrity, so they were assigned to the non-strictly IVC category.

Description of variables included in the study

Descriptive characteristics of well-described IVC found in an extensive Index Medicus and computer-assisted Medline searches are exposed in Table 2. Variables recorded in our study include demographic (age

Table 1. *Grade of diagnostic reliability score system used to classify an intraventricular craniopharyngioma as a strictly or non-strictly intraventricularly located case on the basis of the proof provided by the different diagnostic tools*

Grade of reliability	Definition
I	an intact third ventricle floor can be seen in a necropsy specimen or in the preoperative MRI scans.
II	an intact third ventricle floor can be seen both in sagittal and coronal postoperative MRI after total surgical excision.
III	an intact third ventricle floor is observed and reported by the surgeon after total tumour removal.
IV	either an intact pituitary stalk and/or a patent chiasmatic cistern that is visible on preoperative MRI but without identifying the integrity of the third ventricle floor or surgical description of a tumoural mass restricted to the third ventricle but with a disrupted third ventricle floor.
V	tumour mainly restricted to the third ventricle but with extension into the chiasmatic cistern was assessed either on preoperative coronal CT scans or by the air/metrizamide suprasellar occupation observed on preoperative pneumoencephalography/ventriculography.
Vb	necropsy study proving a tumoural mass within the third ventricle but without integrity of the third ventricle floor.

Grades I, II and III correspond, hierarchically, to a proven strictly intraventricular location (strictly intraventricular craniopharyngioma) and Grades IV and V to an unproven strictly intraventricular location (non-strictly intraventricular craniopharyngioma).

Table 2. *Characteristics of well-described cases of intraventricular craniopharyngioma (IVC) reported in the literature*

No.	Author (ref.)	Year	Sex-age	Clinical history	Histological type	Diagnosis methodology	Surgical route	Extent of excision	Outcome[a]	Type of IVC and grade of reliability[b]
1	Dobos *et al.* [19]	1953	M – 53	H, S, P, M, G, V.	papillary	necropsy	FTV	partial	death (2w)	strict I
2	Cashion [14]	1962	M – 47	H, S, P.	papillary	necropsy	not operated	–	death (1y)	strict I
3	Pecker *et al.* [49]	1966	M – 43	H, S, M, V, E.		air-encephalogr.	FTV	?	death (1m)	non-strict V
4	”	”	M – 29	H.		ventriculography	FTV	?	good	non-strict V
5	”	”	F – 38	H, P, V, E.		ventriculography	FTV	?	death (11d)	non-strict V
6	”	”	F – 32	H, S, P, M.		air-encephalogr.	FTV	?	death (5d)	non-strict V
7	”	”	F – 53	H, P, M, E.	3 papillary	air-encephalogr.	FTV	partial	death (5d)	non-strict V
8	”	”	F – 59	H, S, P, G.	and	ventric + necropsy	TC	total	death (3d)	non-strict V
9	”	”	M – 12	H.	7 adamant.*	ventric + necropsy	TC	total	death (2m)	non-strict V
10	”	”	M – 44	H, M, V, E.		air-encephalogr.	FTV	?	fair (1y)	non-strict V
11	”	”	M – 43	P, M, E.		ventriculography	FTV	?	good (2y)	non-strict V
12	”	”	F – 37	H, S, P.		air-encephalogr.	FTV	?	good (6y)	non-strict V
13	Van den Bergh *et al.* [70]	1970	M – 1	H, S, G, E.	adamant.	ventric + necropsy	FTV	subtotal	death (5w)	non-strict Vb
14	”	”	F – 27	H, S, E.	papillary	ventriculography	FTV	subtotal	good	non-strict V
15	”	”	F – 31	H, S, E.	adamant.	ventric + necropsy	FTV	subtotal	death (6w)	non-strict Vb
16	”	”	F – 6	H, S.	adamant.	ventriculography	FTV	subtotal	good	non-strict V
17	Cashion *et al.* [15]	1971	M – 46	H.	papillary	necropsy	not operated	–	death	strict I
18	”	”	M – 26	H, S.	adamant.	necropsy	biopsy	–	death	strict I
19	Long *et al.* [38]	1973	? – ?	H.	?	air-encephalogr.	FTV	total	death (1w)	non-strict V
20	”	”	? – ?	H.	?	air-encephalogr.	FTV	total	death (1w)	non-strict V
21	”	”	? – ?	H.	?	air-encephalogr.	TC	total	death	non-strict V
22	”	”	? – ?	H.	?	air-encephalogr.	TC	total	? (survive)	non-strict V
23	Northfield [47]	1973	F – 45	P, S, G, V, E.	?	necropsy	not operated	–	death	strict I
24	Bollati *et al.* [7]	1974	M – 30	H, S, P, G.	adamant.	necropsy	FTV	subtotal	death (1m)	strict I
25	Rush *et al.* [52]	1975	M – 48	H, S, P, M.	papillary	air-encephalogr.	FTV	partial	fair	non-strict V
26	Ignelzi *et al.* [25]	1976	M – 51	H, S, P, M, V, E.	?	airenceph + necropsy	biopsy + subfrontal	subtotal	death	non-strict Vb
27	Namba *et al.* [45]	1977	M – 47	H, S, P.	papillary	necropsy	FTV	partial	death (2m)	strict I
28	King [29]	1979	F – 68	S, M, V.	papillary	air-encephalogr.	TLT	subtotal	good	non-strict V
29	”	”	M – 10	H, V, E.	adamant.	air-encephalogr.	TLT	subtotal	fair	non-strict V
30	”	”	M – 47	H, V, E.	adamant.	air-encephal + CT	TLT	subtotal	fair	non-strict V
31	Asari *et al.* [4]	1980	M – 53	H, P.	adamant.	CT	TC	partial	death (4m)	non-strict V
32	Kubota *et al.* [33]	1980	M – 30	H, S.	papillary	CT + necropsy	FTV	partial	death	strict I
33	Mori *et al.* [44]	1980	M – 54	S, P, M, V.	?	CT	TC	subtotal	?	non-strict V
34	”	”	M – 11	H, V.	?	ventriculography	TLT	partial	?	non-strict V
35	Papo *et al.* [48]	1980	M – 47	H, P, M, G, V.	papillary	CT	FTV	total	poor	strict III
36	”	”	M – 49	H, P, M, G.	papillary	CT + necropsy	FTV	total	death (19d)	strict I
37	Goldstein *et al.* [23]	1983	F – 57	H.	papillary	CT	TLT	subtotal	good	non-strict V
38	Matthews *et al.* [42]	1983	F – 65	P, S.	papillary	CT	FTV	total	fair	non-strict V
39	Chin *et al.* [15]	1983	F – 57	H.	papillary	CT	?	partial	moderate	non-strict V
40	Solé Llenas *et al.* [62]	1983	F – 33	H, S, P.	mixed	CT + necropsy	FTV	total	death	non-strict V

(*continued*)

Table 2 (*continued*)

No.	Author (ref.)	Year	Sex-age	Clinical history	Histological type	Diagnosis methodology	Surgical route	Extent of excision	Outcome[a]	Type of IVC and grade of reliability[b]
41	Schmidt *et al.* [57]	1984	M – 62	H, G, V.	mixed	necropsy	not operated	–	death	strict I
42	Baudrillard *et al.* [5]	1984	M – 45	H, S, P, M.	?	CT	FTV	total	moderate	non-strict V
43	”	”	M – 27	H, P, M, V, E.	?	CT	FTV	partial	good	non-strict V
44	Suzuki *et al.* [64]	1984	M – 4	H, S.	?	CT	TLT	total	moderate	non-strict V
45	Bose *et al.* [8]	1985	M – 65	M, G.	mixed	CT + necropsy	TC	subtotal	good	strict I
46	”	”	M – 47	H, M, V.	adamant.	CT	TC	total	moderate	non-strict V
47	Lanzieri *et al.* [35]	1985	F – 54	H, M, G.	?	CT	TC	total	?	non-strict V
48	”	”	M – 43	M, G.	?	CT	TC	total	?	non-strict V
49	”	”	F – 60	H, M.	?	CT	TC	?	?	non-strict V
50	”	”	M – 50	H, M.	?	CT	TC	?	?	non-strict V
51	Kunishio *et al.* [34]	1987	M – 47	P, M.	papillary	CT + necropsy	TC	partial	death (20d)	strict I
52	Suzuki [65]	1987	M – 24	H, S.	?	CT + MRI	TLT	?	?	non-strict IV
53	Urasaki *et al.* [68]	1988	F – 55	H.	adamant.	CT	TLT	total	moderate	non-strict V
54	Klein *et al.* [30]	1989	F – 15	H, V.	?	CT	TLT	total	moderate	strict III
55	”	”	M – 14	H, V.	?	CT	TLT	total	moderate	strict III
56	”	”	M – 11	P, E.	?	CT	TLT	total	moderate	strict III
57	Ferrara *et al.* [21]	1989	F – 50	H, P.	adamant.	CT	TC	subtotal	fair	non-strict V
58	”	”	M – 26	H, S, P.	?	CT	TC	subtotal	good	non-strict V
59	Linden *et al.* [37]	1989	M – 65	S.	papillary	CT + MRI	TC	?	?	non-strict IV
60	Ikezaki *et al.* [26]	1989	F – 70	H, P, M.	papillary	CT + MRI	TLT	partial	good	non-strict IV
61	Sacher *et al.* [53]	1990	M – 34	H.	adamant.	CT + MRI	TC	total	?	non-strict IV
62	Fukushima *et al.* [22]	1990	M – 28	H, S, V.	papillary	CT + MRI	1st TLT 2nd TLT	partial total	good good	strict II
63	Tada *et al.* [67]	1992	M – 45	H. (IC).	papillary	CT + MRI	TC	total	good	strict II
64	Migliori *et al.* [43]	1992	F – 11	H, S, P.	adamant.	CT	TC	total	good	strict II
65	Iwasaki *et al.* [27]	1992	M – 39	H.	papillary	MRI	FTV	total	good	strict II
66	”	”	M – 49	H.	papillary	MRI	FTV	total	good	strict II
67	Yasargil [73]	1994	M – 48	H, G, E.	?	MRI	combined	total	moderate	non-strict IV
68	Sharma *et al.* [54]	1994	M – 48	H, S, P, G.	papillary	CT	biopsy	–	good	non-strict V
69	Yasargil [74]	1996	F – 38	H, G, E.	?	MRI	TC	total	good	strict II
70	Sipos *et al.* [61]	1997	M – 57	H, M, G.	adamant.	MRI	TC	total	good	strict I
71	Davies *et al.* [18]**	1997	F – 60	V.	papillary	CT	TLT	partial	good	non-strict IV
72	”	”	M – 39	H, V.	papillary	MRI	TLT	total	poor	strict III
73	”	”	F – 36	H, S, M, V, E.	adamant.	CT	1st TLT 2nd FTV	biopsy subtotal	fair	non-strict V
74	Urbach *et al.* [69]	1998	M – 54	H, V.	papillary	CT + MRI	TC	total	death (2d)	non-strict IV
75	Perneczky [50]	1999	F – 48	H, P, M, V, E.	?	MRI	FTVe	total	death (4w)	non-strict IV
76	”	”	F – 41	V, E.	?	MRI	TCe	total	poor	non-strict IV
77	Lejeune *et al.* [36]	2000	F – 65	P, M, V.	?	CT + MRI + necrop	FTV	partial	death (1m)	non-strict IV
78	”	”	M – 37	H, V, E.	?	CT + MRI	FTV	total	moderate	non-strict IV
79	”	”	M – 51	H, M.	?	CT	TC	total	death (3m)	non-strict IV
80	”	”	M – 2	H.	?	CT	TC	total	good	strict III

81	”	”	F – 55	H, P, M.	?	CT	FTV	total	death (1m)	non-strict Vb
82	”	”	M – 55	P, M.	?	CT + MRI	biopsy	–	moderate	strict I
83	”	”	M – 40	H, P, M, V.	?	CT	FTV	subtotal	death (3m)	non-strict IV
84	”	”	M – 8	H.	?	CT + MRI	TLT	total	fair	strict III
85	”	”	M – 76	H, P, M, G, E.	?	CT + MRI	FTV	subtotal	moderate	non-strict IV
86	”	”	M – 39	H, G, V.	?	CT	FTV	subtotal	moderate	non-strict IV
87	”	”	M – 35	H.	?	CT + MRI	FTV	subtotal	good	non-strict IV
88	”	”	F – 30	H, M, P.	?	CT + MRI	FTV	total	moderate	strict III
89	”	”	M – 40	H, P, M.	?	CT + MRI	combined	total	fair	strict III
90	”	”	M – 61	H, P, M.	?	CT + MRI	FTV	subtotal	poor	non-strict IV
91	Maira *et al.* [40]	2000	F – 33	E.		CT	TLT	total	moderate	strict III
92	”	”	F – 45	P, E.		MRI	TLT	partial	fair (death after 1 year)	non-strict IV
93	”	”	F – 17	E.		MRI	TLT	total	moderate	strict II
94	”	”	M – 45	H.	2 papillary	MRI	TLT	total	good	strict III
95	”	”	F – 25	H, E.	and	MRI	TLT	total	moderate	strict II
96	”	”	M – 28	H, E.	6 adamant.*	MRI	TLT	total	good	strict III
97	”	”	F – 51	H, E.		MRI	TLT	total	good	strict II
98	”	”	M – 25	P, E.		MRI	TLT	total	fair (death after 2 years)	non-strict IV
99	Behari *et al.* [6]	2003	M – 60	H, V.	?	CT + MRI	TLT	subtotal	moderate	non-strict IV
100	”	”	M – 16	H, 6th nerve palsy	?	CT + MRI	TC	subtotal	moderate	non-strict IV
101	”	”	F – 56	H, P, G.	?	CT + MRI	TC	total	good	non-strict IV
102	”	”	M – 32	S, P, V, E.	?	CT	TLT	subtotal	fair	non-strict V
103	”	”	F – 30	H.	?	CT + MRI	TC	total	death	non-strict IV
104	”	”	M – 11	H.	?	CT + MRI	TLT	total	good	strict II
105	Pascual *et al.*	2004	M – 47	H, P, M.	adamant.	CT + MRI	TLT	partial	good	non-strict IV

No case number; *Ref* reference number; *M* male; *F* female; *H* headache; *S* somnolence; *P* psychiatric disturbances; *M* memory deficit; *G* gait disturbance; *V* visual deficit; *E* endocrine disturbance; *Adamant*: adamantinomatous histological type; *Papillary* squamous-papillary histological type; ? unknown; *Air-encephalogr* air-encephalography; *Ventric* ventriculography; *CT* computed tomography; *MRI* Magnetic Resonance Image; *FTV* Frontal Transcortical-Transventricular approach; *TC* Transcallosal approach; *TLT* Translamina Terminalis approach (pterional or subfrontal); *FTVe* Frontal-Transcortical-Transventricular approach endoscopically assisted; *Comb* Combined approach (TC + TLT); *IVC* intraventricular craniopharyngioma; *Strict* strictly third ventricle located craniopharyngioma (with a proven intact third ventricle floor). *Non-Strict*: non-strictly third ventricle located craniopharyngioma (within the third ventricle but without a proven intact third ventricle floor).

[a] Postoperative survival is indicated between brackets; d: days; w: weeks; m: months; y: years.

[b] The strict or non-strict category, together with its grade of reliability, was ascribed to each case according to the conditions defined in Table 1.

* Individual patients' histological types not designated.

** Six cases are reported in this paper but 3 of them corresponded to the cases previously reported by King *et al.* (cases number 28 to 30).

and sex), clinical characteristics, topographical and histological diagnosis, surgical approach with extent of excision and postoperative outcome.

The seven most representative variables included in the clinical history were analyzed: headache, somnolence, dementia-like symptoms (any combination of the following: disorientation; confusion; apathy; delirium; sphincter disturbances and/or mood swings), gait dysfunction, and memory, visual or endocrine disturbances.

Approximately half of the revised articles defined the histological tumour type as adamantinomatous, squamous-papillary or mixed. Other articles gave no definition of the histological type but did supply a detailed histological description that allowed us, following the criteria of Burger and Scheithauer [10] and Crotty *et al*. [17], to assign the tumour to one of the three previously-mentioned types. More than one-third of the tumours could not be histologically classified.

Surgical details could not be determined in some cases who had been reported in radiological or pathological journals, in which the surgical treatment is usually not mentioned or detailed. The surgical analysis only considered those cases in whom there was a description of the three objective surgical variables: approach, extent of excision and postoperative outcome. The different surgical approaches used have been: frontal transcortical-transventricular, transcallosal, translamina terminalis and combined. Following authors' descriptions, the extent of excision was classified in one of three degrees: total (the entire visible tumour was extirpated), subtotal (a small remnant of adherent tumour capsule was left) and partial removal (a significant tumour fragment was not removed).

The postoperative neurological, neuropsychological and endocrine disturbances, were used to classify postoperative outcome as one of five grades, following, with slight modifications, the classification used by Fahlbusch *et al.* [20]: good (without any new permanent neurological, neuropsychological or endocrine deficit); moderate (with new endocrine deficits requiring permanent replacement therapy); fair (with neurological or neuropsychological deficits but with autonomy); poor (severe neurological and/or hypothalamic disturbances with total dependency) or death. Surgical mortality included cases deceased within a six-month postoperative period.

Additionally, the degree of tumoural adherence to the third ventricle walls, when noted by the surgeon or the pathologist, was also recorded. To simplify the question, the degree of tumoural attachment to the walls and/or floor of the third ventricle was classified in one of the following categories: 1) non-adherence, with the tumor freely floating in the third ventricle cavity; 2) pedicle attachment; 3) adherence easily dissectible; 4) narrow tight attachment; and 5) wide tight attachment.

Statistical analysis

Two different frequency table formats: rxc (rows $\times$ columns) and $2 \times c$ ($2 \times$ columns), were employed for statistical analysis. The statistical procedure used to resolve the hypothetical differences either among the different surgical approaches, or between the strictly and non-strictly IVC groups, were the asymptotic Pearson's chi-square test and the Monte Carlo exact test for Chi-square in those frequency tables containing cells with 0 elements or those in which more than 20% of cells had less than five elements [3]. Significance was assumed at $p \leq 0.05$. Statistical computation was done using the SPSS 10.0 program (Windows system; Marketing Department SPSS Inc., 444 North Michigan Av., Chicago, Il 60611).

New case report included as example of topographical misdiagnosis

A 47-year-old man was admitted following a one week history of headache and mental disturbances. Close relatives had noticed abrupt changes in behaviour with transient episodes of disorientation and repeated memory loss episodes for recent events. On admission the patient was euphoric and unable to express himself coherently. He was disoriented as to time and place. General physical examination was unremarkable. Neurological examination revealed an anterograde memory defect but no other abnormalities. He had no motor or sensory deficits. There was no evidence of defect in the visual fields or visual acuity. Routine blood studies and endocrinology work-up were both within normal limits.

Plain skull roentgenograms were normal without erosion or pathological calcification of the sella turcica. Cranial CT scan revealed a hypodense suprasellar mass occupying the third ventricle and causing obstructive hydrocephalus. The capsule displayed linear egg shell calcifications and there was no enhancement after contrast administration. Brain MRI confirmed the presence of a cystic tumour that seemed to be occupying the suprasellar and third ventricle regions, but not invading the sella turcica. The lesion was lightly hypo-intense on T1- and hyperintense on T2-weighted images. There was no enhancement after gadolinium-DTPA contrast administration. Dilation of the lateral ventricles and obstruction of the foramina of monro was evident (Fig. 1).

With the diagnosis of a suprasellar craniopharyngioma, a right pterional approach was taken to examine the suprasellar region with the aid of an operating microscope. No tumour could be found despite a meticulous search through the interoptic-carotid and carotid tentorial

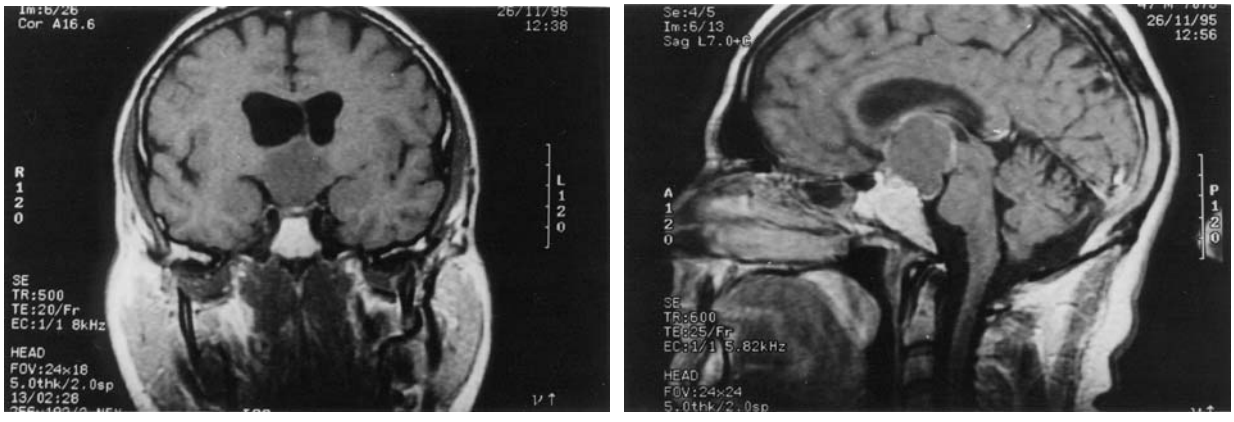

Fig. 1. T1-weighted magnetic resonance image showing a suprasellar-third ventricle hypo-intense lesion. *Left:* coronal section demonstrating preservation of the lateral wings of the suprasellar cistern (TR 500 msec, TE 20 msec); *Right:* sagittal section after gadolinium administration showing ring enhancement and a pot belly expansion reaching the prepontine cistern; pituitary gland is intact. (TR 600 msec, TE 25 msec)

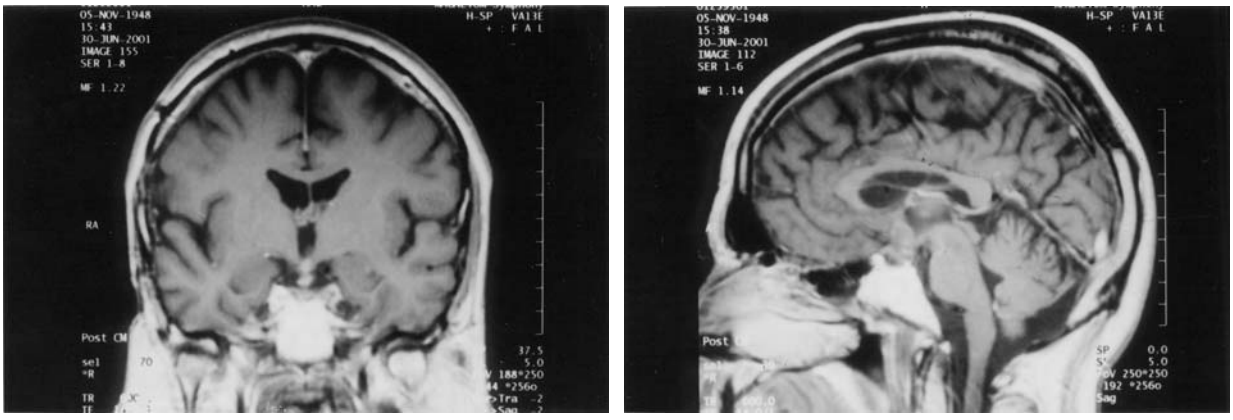

Fig. 2. Follow-up T1-weighted magnetic resonance image with contrast administration (six years after operation) displaying a small remnant of the tumour in the floor of the third ventricle with a patent chiasmatic cistern and intact pituitary gland. *Left:* coronal section; *Right:* sagittal section. (TR 600 msec, TE 20 msec)

triangles. At that point, a bulging lamina terminalis was opened and a spotted grey-white tumoural capsule appeared. It was opened and a motor oil-like liquid appeared within the field. The cyst was emptied and the capsule only partially removed, due to its tight adherence to the third ventricle floor. Histological examination of the excised tissue showed it to be a craniopharyngioma with an adamantinomatous pattern.

Postoperatively, the patient did well with complete recovery and normal neurological examination. Radiotherapy was given and he was able to resume his previous professional activity. At six years post-surgery, the MRI shows a small remainder of the tumour (Fig. 2a, b), and the patient is still doing well.

Results

Descriptive analysis of cases

Demography

There is a clear male predominance among IVC (64.3% vs. 35.6%), which contrasts with the similar sex distribution observed in craniopharyngiomas as a whole [12]. Age distribution shows only 14.8% of the cases in the first two decades of life and 64.3% of the cases between the third and the fifth decades, contrasting with the two incidence peaks for general craniopharyngiomas [12].

Clinical findings

Headache is the most frequent symptom (90%). It is noteworthy that visual symptoms and signs (28.5%) and endocrine dysfunctions (27.5%), usually present in suprasellar craniopharyngiomas, are not that frequent in IVC, whereas other symptoms such as mental disturbances (40%), memory dysfunction (33.3%), somnolence (29.5%), and gait disturbances (17%), usually not present in craniopharyngiomas in general, are commonly reported among IVC.

Diagnosis and neuroradiological findings

Nineteen cases were studied by necropsy. Air-encephalography and ventriculography were the main diagnostic tools in the pre-CT scan era (23 cases). Thirty-eight cases were diagnosed with only a CT scan and thirty-seven with MRI studies with or without CT. Coronal CT scan and MRI slices displayed a round-shaped tumour occupying the third ventricle cavity and a free chiasmatic cistern. In addition, the configuration of the pituitary stalk can be demonstrated on sagittal MRI. However, the integrity and location of the third ventricle floor, the crucial landmark for distinguishing whether the tumour is strictly or non-strictly intraventricular, could not be accomplished by preoperative MRI, except in only three exceptional intraventricular craniopharyngiomas that were surrounded by a layer of cerebrospinal fluid signal, with an identifiable intactness of the third ventricle walls and floor [36, 55, 61]. This is the only sign that to our knowledge permitted an exact preoperative topographical diagnosis. Conversely, postoperative MRI, once the tumour was debulked or removed, did delineate the integrity of the third ventricle floor in some, but not all, cases.

Pathology

The adamantinomatous and the squamous-papillary types are equally distributed among the 61 IVC cases with a defined histological type or with a description of histological features [3, 4, 6–8, 14, 15, 18, 19, 21–23, 26, 27, 29, 33, 34, 37, 40, 42, 43, 45, 48, 49, 52–54, 57, 61, 62, 67–70]. Macroscopic tumour consistency (solid, cystic or mixed) was reported in 90 cases. Macroscopically, the solid pattern predominates (62.2%) over the cystic (18.8%) and mixed solid-cystic ones (19%).

Surgical treatment

No surgical operation was performed in four cases and only a stereotactic biopsy was done in another three cases. The surgical approach was not mentioned in one case. The three most commonly used surgical approaches to the tumour were: a frontal transcortical-transventricular approach, carried out in 38 cases (39.5%), a transcallosal-transventricular approach in 27 cases (28%) and a translamina terminalis approach in 29 cases (30%). Two cases employed a combined approach (2.3%): one employed transcallosal and pterional translamina terminalis approaches [73] and the other a frontal transcortical-transventricular and pterional approach [36]. Lastly, another two cases were initially biopsied and operated on later via a non-specified subfrontal route [25] and a frontal transventricular approach [18] respectively. The extent of excision was mentioned in most cases (88.7%) and has been classified in three degrees, according to the surgical descriptions provided in the revised articles: macroscopically total (49 cases), subtotal (23 cases) and partial (15 cases).

Outcome

Outcome was not reported in ten cases and the remaining were classified according to the criteria detailed in Material and Methods. The four cases not operated on died as well as the three cases who were only biopsied. There were twenty-seven deaths among the surgical cases, yielding a 27.5% mortality rate. In the latter group, sixteen patients died within the first month after surgery and most within the first three months. Overall mortality, including ''operated'' and ''non-operated'' patients, was 32.3%.

Relation of the selected surgical approach with the extent of excision and the final outcome

Table 3 correlates simultaneously the postoperative outcome to the selected surgical approach and the extent of excision in each of the 78 cases that provide all the required data. In both the total and partial excision subgroups the analysis showed a clear, very close to statistical significance association between the surgical approach chosen and the postoperative outcome ($p_{\text{total}} = 0.054$ and $p_{\text{partial}} = 0.057$). The best outcome was obtained with a translamina terminalis approach. In contrast, the frontal transcortical approach was associated with the worst outcome, especially in the partial excision subgroup.

Figure 3 separately correlates: A) type of approach to extent of excision, B) type of approach to outcome; and C) extent of excision to outcome, with no significance reached in the first and third analysis, but with a significant relationship obtained between the type of approach and outcome ($p = 0.01$; Exact test for Chi-square). The frontal transcortical-transventricular approach was associated

Table 3. *Relationship between surgical approach and postoperative outcome for extent of each excision in 78 intraventricular craniopharyngiomas***

Extent of excision	Postoperative outcome	Type of surgical approach (no. and percentage by each extent of excision)		
		Frontal transcortical-transventricular approach	Transcallosal approach	Translamina-terminalis approach
TOTAL	good/moderate	6 (42.9%)	7 (50%)	12 (80%)*
$p_{total} = 0.054$	fair/poor	2 (14.3%)	1 (7.1%)	3 (20%)
	death	6 (42.9%)	6 (42.9%)	0
		14 (100%)	*14 (100%)*	*15 (100%)*
SUBTOTAL	good/moderate	5 (45.5%)	3 (75%)	3 (50%)
$p_{subtotal} = 0.251$	fair/poor	2 (18.2%)	1 (25%)	3 (50%)
	death	4 (36.4%)	0	0
		11 (100%)	*4 (100%)*	*6 (100%)*
PARTIAL	good/moderate	1 (14.3%)	0	4 (80%)
$p_{partial} = 0.057$	fair/poor	1 (14.3%)	0	1 (25%)
	death	5 (71.4%)#	2 (100%)	0
		7 (100%)	*2 (100%)*	*5 (100%)*

p: *p* Value calculated by Exact test for Chi square for each extent of excision.

* Best postoperative outcome was obtained with this type of approach and extent of excision.

\# Worst postoperative outcome was obtained with this type of approach and extent of excision.

** The references of the cases included in this analysis are (the number of cases is indicated between brackets when it exceeds the figure of one case): 4, 5 (2c), 6 (6c), 7, 8 (2c), 18 (3c), 19, 21 (2c), 22 (2c), 23, 26, 27 (2c), 29 (3c), 30 (3c), 33, 34, 36 (12c), 38 (4c), 40 (8c), 42, 43, 45, 48 (2c), 49 (3c), 50 (2c), 52, 61, 62, 64, 67, 68, 69, 70 (4c), 74 and our own case.

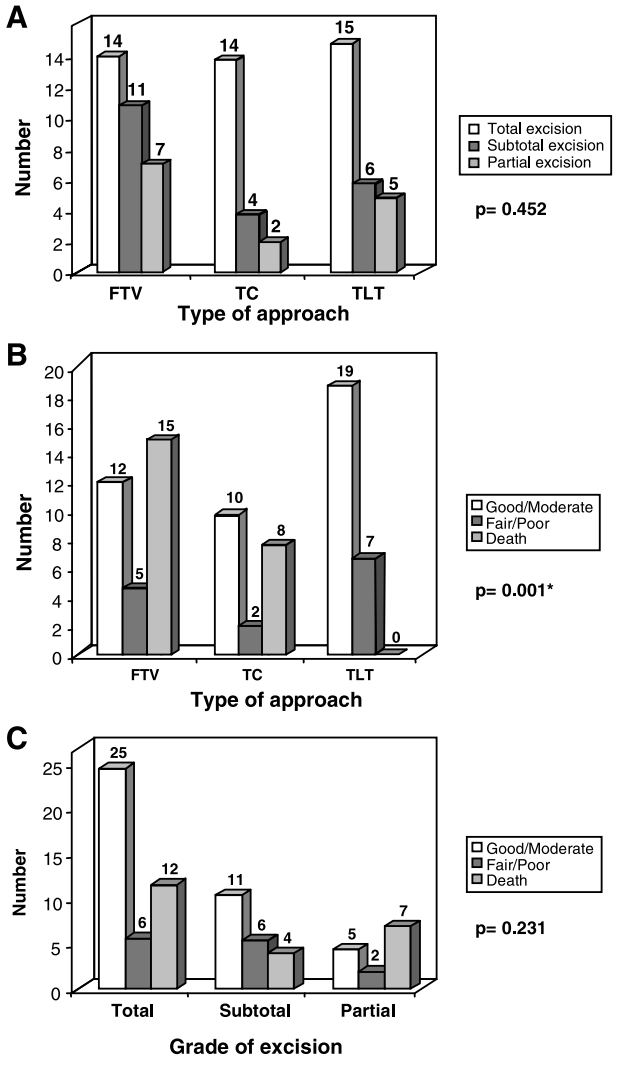

Fig. 3. Bar graphs showing relationships between: (A) surgical approach and extent of excision; (B) surgical approach and outcome; (C) grade of excision and outcome. *FTV* frontal transcortical transventricular approach; *TC* transcallosal approach; *TLT* translamina terminalis approach. $^{*}p$ Value proving a statistically significant relationship between the chosen type of approach and surgical outcome

with the highest number of deaths, regardless of the degree of excision achieved. The best final outcome was achieved when the translamina terminalis approach was taken; very importantly, no surgical death was observed with this approach. The transcallosal-transventricular approach also produced a similar final outcome, in so far as morbidity was concerned, but there were eight deaths (within the six-month postoperative period) among the twenty "operated" patients.

Relation of the studied variables to the topographical classification of the tumours in strictly and non-strictly intraventricular craniopharyngiomas

Following the criteria of diagnostic reliability defined in the material and methods section, there were fourteen grade I, ten grade II and twelve grade III cases respectively, making a total of 36 strictly IVC. There were 28 grade IV cases and 41 grade V cases, yielding a total of 69 non-strictly IVC. A correlation between IVC topographical classification and each one of the studied variables was performed:

Clinical picture

Table 4 compares the seven most frequent clinical features between strictly and non-strictly IVC. No clinical variable was associated with either one and not the other topographical category, although there was a tendency toward memory loss being associated with the non-strictly IVC group ($p = 0.275$) and unsteady gait with the strictly IVC group ($p = 0.172$). When the number of clinical features for each individual patient was related to the IVC topographical category, the presence of three or more symptoms tended to be associated with the non-strictly IVC group ($p = 0.122$, asymptotic significance obtained with a linear by linear association test).

Pathology

While the papillary pattern was equally frequent in both groups, the adamantinomatous pattern was much more frequent in the non-strictly IVC group, although

Table 4. *Comparative clinical features between strictly and not strictly intraventricular craniopharyngiomas*

Signs/symptoms	Total number and rate (n = 105)	Strictly intraventricular location (n = 36)	Not strictly intraventricular location (n = 69)	p value
Headache ± vomiting	86 (90.3%)	29 (80.5%)	57 (82.6%)	0.795
Drowsiness	31 (29.5%)	9 (25%)	22 (31.8%)	0.507
Mental disturbances	42 (40%)	13 (36.1%)	29 (42%)	0.676
Memory loss	35 (33.3%)	9 (25%)	26 (37.6%)	0.275
Unsteady gate	18 (17.1%)	9 (25%)	9 (13%)	0.172
Visual field and/or acuity loss	29 (27.6%)	8 (22.2%)	21 (30.4%)	0.366
Hormonal disorders	29 (27.6%)	8 (22.2%)	21 (30.4%)	0.491

not significantly so ($p = 0.106$, Fisher's exact test). The predominance of the adamantinomatous pattern in the non-strictly IVC group agrees with the idea that the topographical level of origin of the craniopharyngioma would influence the histological pattern; thus the higher the level of origin of the tumour, the more frequent the squamous-papillary pattern, and conversely, the lower the level, the more frequent the adamantinomatous type. In addition, a significant relationship between patient's age and histological type was found ($p = 001$, Fisher's exact test), with 100% of cases under twenty years old showing an adamantinomatous pattern, while 100% over sixth decade presenting a squamous-papillary one.

Pattern of tumoural adherence

Table 5 shows the degree of tumoural attachment to the third ventricle margins, as described in 45 IVC cases by surgical or necropsy protocols. Only three cases showed no adherence at all -grade 1-, and they obviously belonged to the strictly IVC group. There was a clear and significant difference between the two groups: the strictly IVC preferentially had a pedunculated attachment -grade 2-, whereas most of the non-strictly IVC had a tight attachment -grades 4 and 5-, ($p = 0.012$, Exact test for Chi-square). This observation correlates well with the fact that the adamantinomatous pattern, more frequently observed in the non-strictly IVC group, tends to adhere tighter to neural tissue than the squamous-papillary one.

Surgical excision and prognosis

Table 6 compares the postoperative outcome of the 88 IVC cases who were operated on. Compared to the strictly intraventricular group the non-strictly IVC group

Table 5. *Patterns of adherence between tumoural capsule and internal surface of the third ventricle walls and floor in 45 intraventricular craniopharyngiomas*

Pattern of adherence (Ref)	Strictly intraventricular location (n = 23)	Non-strictly intraventricular location (n = 22)	Total number and rate of the pattern (n = 45)
No visible tumour attachment to the third ventricle floor/walls is identified either on preoperative MRI or in the surgical field. [36, 43, 61]	3 (100%)	0 (0%)	3 (6.8%)
Tumour is pedunculated, attached to the third ventricle floor by a narrow vascular-gliotic pedicle. [8, 15, 21, 27, 33, 34, 42, 44, 48, 50, 57, 67]	11 (78.6%)	3 (21.4%)	14 (31.8%)
Tumour is adhered to third ventricle floor/walls, but easily dissectable by blunt dissection. [13, 22, 38, 50]	3 (28.6%)	5 (71.4%)	8 (15.9%)
Tumour adhered to third ventricle floor/walls by a small tight attachment that required sharp dissection. [6, 7, 22, 26, 33, 35]	4 (40%)	6 (60%)	10 (22.7%)
Tumour is adhered to third ventricle floor/walls by a wide tight attachment, preventing a safe dissection. [14, 35, 48, 52, 53, 70]	2 (20%)	8 (80%)	10 (22.7%)

p Value = 0.012 (Exact test for Chi-square).

Table 6. *Comparative outcome between strictly and not strictly intraventricular craniopharyngiomas in 88 "surgical" cases*[*]

Topographical category (number and rate)			
Outcome	Strictly intraventricular (n = 30)	Not strictly intraventricular (n = 58)	Total number and rate
Good/Moderate	20 (44.4%)	25 (43%)	45 (100%)
Fair/Poor	4 (25%)	12 (75%)	16 (100%)
Death	6 (22.2%)	21 (77.8%)	27 (100%)

p Value = 0.109 (Asymptotic chi-square test). The difference in the postoperative outcome between the strict and non-strict groups became statistically significant when a supplementary test of linear by linear association was applied ($p = 0.046$).

[*] The references of the cases included in this analysis are (the number of cases is indicated between brackets when it exceeds the figure of one case): 4, 5 (2c), 6 (6c), 7, 8 (2c), 15, 18 (3c), 19, 21 (2c), 22 (2c), 23, 25, 26, 27 (2c), 29 (3c), 30 (3c), 33, 34, 36 (13c), 38 (4c), 40 (8c), 42, 43, 45, 48 (2c), 49 (10c), 50 (2c), 52, 61, 62, 64, 67, 68, 69, 70 (4c), 73, 74 and our own case.

shows a clearly higher morbi-mortality, probably reflecting their higher frequency of tight attachment to the third ventricle margins, including the hypothalamic nuclei, observed in the former. Statistical significance was at the limit ($p = 0.109$, asymptotic Chi-square test), but when a supplementary test of linear trend was performed, the difference became significant ($p = 0.046$, linear-by-linear association test).

Discussion

Intraventricular craniopharyngiomas: importance and limitations of a retrospective review

IVC constitute a neurosurgical challenge due to their complex topographical relationships with vital neurovascular structures. They need to be diagnosed accurately and approached correctly in order to achieve a good outcome. A retrospective review of well-detailed cases would be useful with the aim of defining the criteria that could reliably distinguish this topography. As an extremely infrequent tumour subtype (approximately 5% of craniopharyngiomas) with a wide-spread distribution, there is scant material with which perform a prospective multicentric study of these tumours. In specific cases like this one a systematic review of only the fully well-reported cases may be the best way to obtain some useful clues for arriving at a correct diagnosis and in taking management decisions.

We are aware of this retrospective study has some important disadvantages which probably prevent definitive conclusions. The major limitation would be the long time period spanned by this study, since the older case reports would presumably introduce biases in terms of both diagnosis and surgical results. Before the MRI era it was difficult to perform tests that could unequivocally support the diagnosis of intraventricular topography and many of well-described IVC belong to this period. In addition, almost every case was operated on by different surgeons with different skills, experience and technology, again undermining the complete reliability of our conclusions. The improvement in surgical outcome for these lesions in the last three decades has been outstanding, as result of better microsurgical technique and postoperative care. In fact the outcome for IVC operated on since the advent of MRI is much more favourable than for similar cases operated on previously (there was only a 10% of death rate among cases operated on in the MRI period, whilst it was 50% in the preCT era). Despite these drawbacks we think this retrospective analysis somewhat counteracts the influence arising from differences in surgical skills and technique on IVC's final outcome.

Topographical classification of intraventricular craniopharyngiomas

Several topographical classifications have been developed for the group of craniopharyngiomas placed behind the chiasm, which usually involve the third ventricle area (classically considered as retrochiasmatic tumours) [24]. Some of the most remarkable ones are reported by Yasargil *et al.* [72]; Samii *et al.* [54] and Steno [63], all sharing the common feature of taking into account the relationships between the tumour and the third ventricle margins. Yasargil *et al.* found 7 craniopharyngiomas with a pure third ventricle location among his 162 ''surgical operated'' cases [74]. Steno reported a necropsic series with an unexpectedly high frequency of strict third ventricle craniopharyngiomas in which the inferior pole was completely covered by an intact third ventricle floor (8 out of 30 cases) [63]. In this study the topographical relationship between the tumor capsule and the third ventricle walls and floor was analyzed in both strict and non-strict intraventricular cases. As a major difference, it was observed that in non-strict intraventricular craniopharyngiomas the remnants of third ventricle walls, containing hypothalamic nuclei, were tightly attached to the equator of the tumour, suggesting a higher risk associated with its removal [63].

Using the information provided by the different diagnostic studies (including necropsies) and by surgical descriptions taken from reports of craniopharyngiomas involving the third ventricle area [2, 11, 14, 16, 24, 31, 32, 47, 51, 54, 56, 63, 65, 66, 70, 72], it is possible to distinguish among four theoretical topographical relationships between the tumour and the third ventricle floor, that should be considered preoperatively: 1) suprasellar tumor pushing the intact third ventricle floor upwards (pseudo-intraventricular craniopharyngioma; Fig. 4A); 2) suprasellar mass breaking through the third ventricle floor and invading the third ventricle cavity (secondarily intraventricular craniopharyngioma; Fig. 4B); 3) intraventricular mass within the third ventricle cavity and floor, the latter being replaced by the tumor (non-strictly IVC; Fig. 4C); and 4) intraventricular mass completely located within the third ventricle cavity and with the intact floor lying below its inferior surface (strictly IVC; Fig. 5).

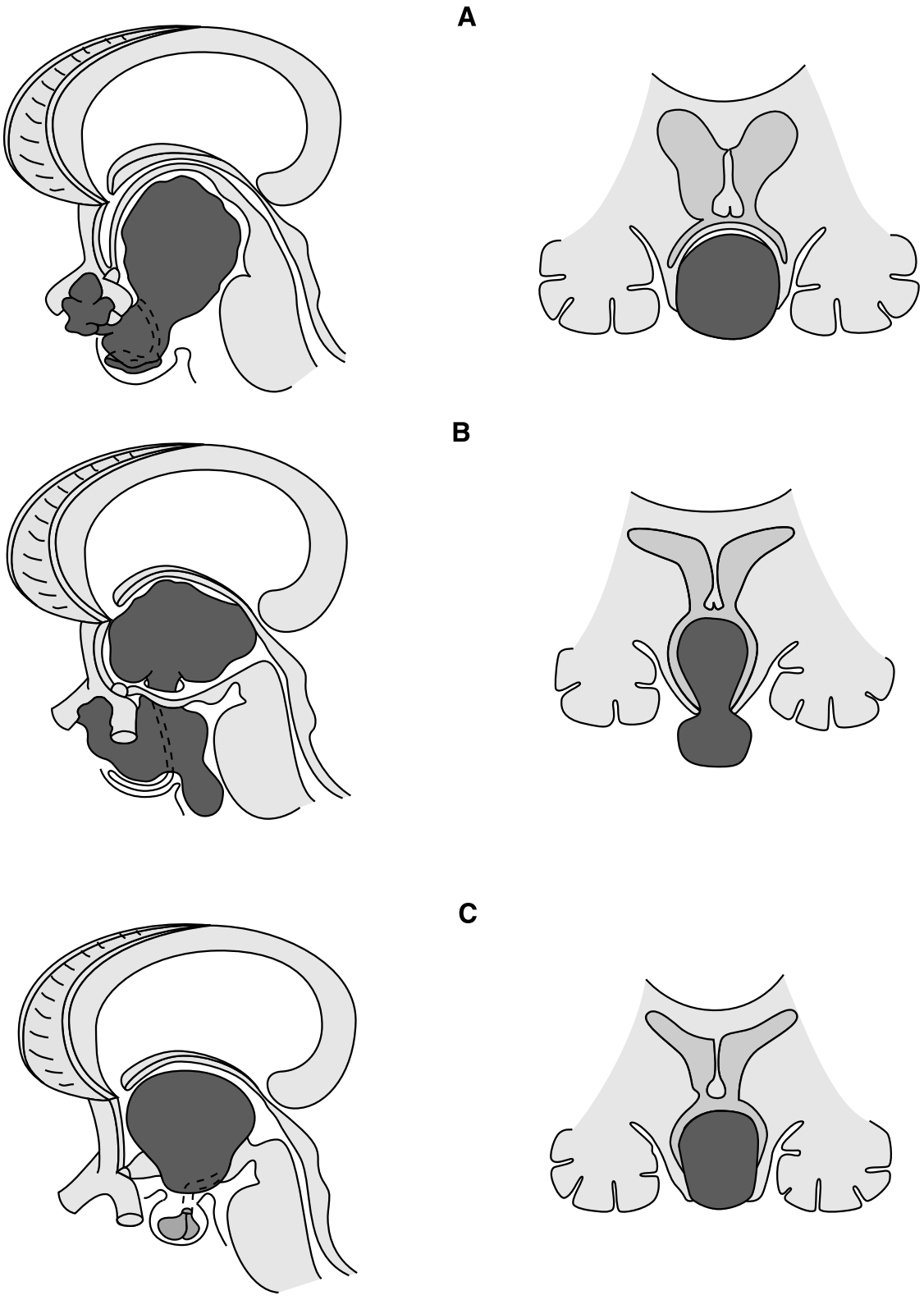

Fig. 4. Illustrative drawing representing in both sagittal and coronal sections, three possible alternative topographies for craniopharyngiomas involving the third ventricle area, to be considered in the differential diagnosis. (A) Suprasellar tumour which invaginates the third ventricle (pseudo-intraventricular); (B) Suprasellar tumour which invades the third ventricle (secondarily intraventricular); and (C) Intrinsic third ventricle floor tumour that during its growth has expanded the floor of the third ventricle, leaving an opening in it (non-strictly intraventricular); this type of tumor mainly fills up the third ventricle cavity but it also may extend to the suprasellar space

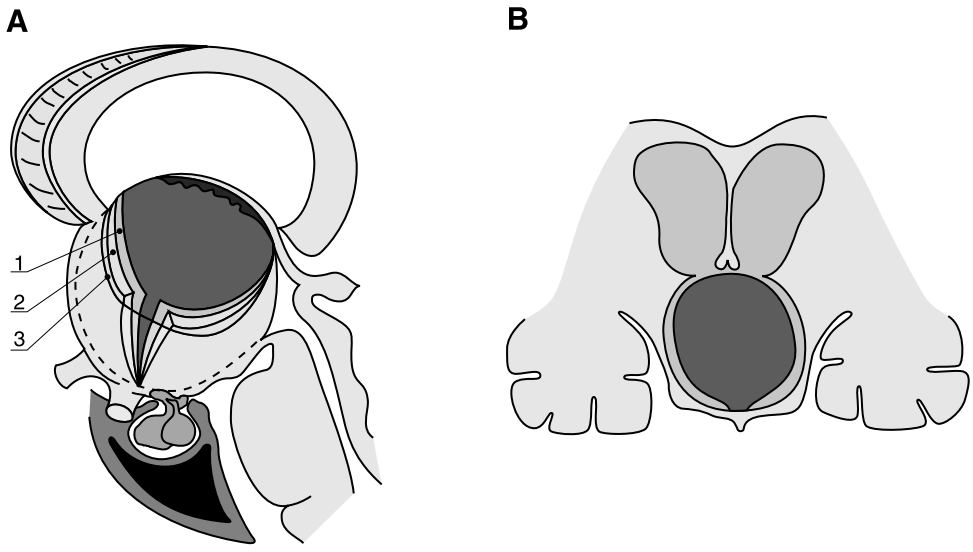

Fig. 5. Illustrative drawing representing the topographical relationship between a strict intraventricular craniopharyngioma and the third ventricle margins in both sagittal (A) and coronal (B) sections. (*1*) ependymal layer; (*2*) neural tissue wall including the hypothalamic nuclei; (*3*) pia mater layer. Note the intact third ventricle floor

IVC's clinical features

In comparison with the high prevalence of visual and endocrine disturbances usually observed in suprasellar craniopharyngiomas (between 70 and 90% of cases, both in adults and children), and their low prevalence of psychiatric symptoms (less than 15%) [12, 16], IVC have a much lower frequency of endocrine (27%) and visual (28%) disturbances and a higher presence of psychiatric abnormalities (40%) and memory dysfunction (33%). These differences must be related to the different position of the tumor, which is located above the suprasellar area and involves the third ventricle floor, including the mamillary bodies, and the hypothalamus.

Histological type's distribution

Two main clinical-pathological variants of craniopharyngioma have been distinguished so far: the adamantinomatous type which occurs in both adults and children, and the squamous-papillary type which appears almost exclusively in adults [1, 10, 28]. The histological differences between both types have been meticulously outlined in the recent work by Crotty *et al.* [17], who emphasize the tendency of the papillary type to specifically involve the third ventricle area (40% of squamous-papillary cases). A previous IVC review [27] also reported a clear predominance of the squamous-papillary type in this topography, but our study shows an equal distribution between adamantinomatous and papillary cases in IVC.

When IVC' histological type was analyzed according to its distribution between the strictly or non-strictly intraventricular subtypes, the adamantinomatous pattern was more strongly associated with the non strictly IVC group (72.4%), a difference close to statistical significance ($p = 0.106$, Fisher's exact test). This suggests the existence of a relationship between the development of the adamantinomatous type and a lower position of the original remnant of epithelial cells on the hypothalamic-pituitary complex. In addition the adamantinomatous pattern was the only one shown in the lowest age group. The facts that IVC are exceptional in the childhood [16] and that most childhood craniopharyngiomas correspond to the adamantinomatous type and have a lower location at the suprasellar and sellar spaces, supports this idea [24, 41].

Topographical misdiagnosis leading to wrong surgical approach

A meticulous survey of the literature has reveal several cases of craniopharyngioma, apparently located at the suprasellar region, which had been approached via a standard basal route with the result that no tumour tissue could be found, since the tumour was actually located inside the third ventricle [7, 18, 22, 29, 32, 36, 44, 49, 70, 73, 74]. One might think that this topographical

misdiagnosis would be due to a lack of sensitivity of neuroradiological tools in previous decades, but this is not so, since several of the cases, including ours, had well-detailed preoperative MRI studies [22, 36, 63]. Obviously, even with modern neuroradiological techniques, the correct topographical diagnosis can not be made in all cases, as other authors have also remarked [21, 32, 51, 70, 73], and this point is also true of any other lesion involving the suprasellar-third ventricle region [59]. Our retrospective review of the available preoperative MRI studies of IVC could not distinguish the position of the third ventricle floor and could not define its integrity nor its relation to the margins of the tumour, except in the three cases mentioned above who showed a thin layer of cerebrospinal fluid separating the inferior tumour margin from the third ventricle floor [36, 55, 61]. However, an examination of the published postoperative MRI studies did show the anatomical situation of the third ventricle floor and its integrity, allowing criteria for a diagnosis of strictly IVC [22, 27].

Although the integrity of the third ventricle floor cannot always be determined on a postoperative MRI, requiring dye studies or cine-CSF (MRI) studies, coronal-postoperative MRI sections clearly show the disruptions of the third ventricle floor in those cases ascribed to the non-strict category. In addition, we have observed that a rounded tumour shape, whether solid or cystic, and of homogeneous signal intensity, are signs that help to suggest an intraventricular position and should lead to the suspicion of an IVC [56]. The introduction of new technologies, like the recently reported use of intraoperative high field MRI with microscope-based neuronavigation [46], might constitute the best advance for implementing the topographical diagnostic accuracy of intraventricular craniopharyngiomas.

IVC's adherence patterns

Although craniopharyngiomas are histologically benign tumours, they tend to invade the adjacent brain, sometimes with finger-like epithelial projections [1, 9] and they can cause a reactive and adherent gliosis layer. For some authors this gliosis, which would be non-functional, provides a safe cleavage plane along which to achieve total excision [9, 24, 41, 66] whereas for others it constitutes a dangerous barrier, extremely narrow in some cases, that can not be crossed without causing significant damage in the viable neural tissue [47, 60, 64]. Since IVC develop close to the hypothalamic area, the pattern of tumour adherence is quite important. Description of tumoural adherences has only been addressed by a few authors whose assessment was necessarily somewhat subjective (see Table 4). However we think this characteristic requires analysis since, in many cases, it guides the surgeon's decision as to what extent the tumoural resection must be performed. It is noteworthy that many of the strictly IVC showed a narrow attachment by a pedunculated, vascular-gliotic stalk to the third ventricle floor (48% of cases). Conversely, the non-strictly IVC were mostly associated with a tight and wide adhesion to the third ventricle floor and walls (64% of cases) that correlates well to its preferential growth within these structures. The present study suggests a significant association between the adherence pattern and the topographical type of IVC.

Surgical treatment and outcome

The election of the proper surgical approach and extent of excision for craniopharyngiomas continues to challenge neurosurgeons. Further difficulties are added in the case of IVC, because access to the third ventricle cavity requires penetrating healthy neural structures. Up to the present time, there has been no agreement as to which of the three possible approaches used by the different authors, frontal-transcortical, transcallosal or translamina terminalis, is best for this kind of surgery. In the present retrospective review each type of approach was evaluated taking into consideration two parameters: extent of excision and outcome. According to this analysis the translamina terminalis approach, although providing a lower rate of total removal, resulted in no mortality. It is not surprising that a superior approach to the third ventricle would have a poorer outcome since one would need to somehow work through foramina of Monro and fornices. However definite conclusions about the approach to be chosen cannot be elicited because many unaddressed variables might have influenced the outcome in each case.

Comparative results of the surgical outcome between the strict and non-strict groups showed a statistical tendency toward a worse outcome in the latter location. Recently, Maira *et al.* [38] have also reported a worse outcome in two of six operated ICs that showed an open third ventricle floor after total tumour excision (and thereby corresponded to the non-strictly group). Wide and tight adhesions to the third ventricle walls and floor, usually present in the non-strictly IVC group, should council us to avoid radical tumour excision in order to prevent hypothalamic damage.

Conclusions

Intraventricular craniopharyngiomas (IVC) represent a specific topographical location that should be distinguished from suprasellar craniopharyngiomas which secondarily invade the third ventricular cavity. They are a rarity and two different categories of diagnostic certainty have been distinguished by a review of well-described single cases reported in the literature: strictly IVC, which grow exclusively in the third ventricle cavity above an intact third ventricle floor, and non-strictly IVC, in which expansion of the tumor has breached the floor of the third ventricle. At the present time and with the current neuroradiological tools, it is not possible to differentiate these two topographical types of tumours preoperatively in almost any case. However, some differences help differentiate one type from the other: preferentially adamantinomatous pattern, wider and tighter adhesions to the third ventricle margins and a worse surgical outcome in the non-strictly IVC group.

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Comments

The authors have performed a literature review of intraventricular craniopharyngiomas and described a case of their own. The object of the review was to establish criteria to define the intraventricular location, and to investigate factors which influence the surgical outcome. They categorise the craniopharyngiomas into those tumours wholly within the third ventricle (strict) and those with secondary third ventricular involvement (non-strictly) based upon integrity of the third ventricular floor. They did note a trend towards specific pathology in relation to tumour location – the more superior the level of origin, the more frequent the squamous-papillary pattern, and more inferiorly located tumour were more frequently adamantinomatous.

The study suffers from the usual problems of a literature review, in that complete information, including surgical details and histology, are not available for all the cases. It is also difficult to define the exact location with respect to the third ventricle given that they have included cases spanning from the pre-CT era.

The authors have attempted a difficult task given the location of these lesions and the difficulty in defining them. The outcome data is less reliable given the wide variety of approaches used, and different surgical techniques spanning several decades. The pathological correlates with location are of interest.

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Pascual *et al*. take the opportunity to offer an own observation in which they suppose a pure intraventricular craniopharyngioma to contribute with an extensive overview about the topographical classification and selection of surgical approaches. This paper arises again much more the question where the third ventricle can be located preoperatively as well as intraoperatively and where the bilateral hypothalamus is located – than the question if the tumor is located purely intraventricularly or not. This question is not easy to be answered since even in their own case Pascual *et al*. couldn't resect the supposed intraventricular tumor totally and the Figure 3 demonstrates tumor remnants in the anterior basal area of the third ventricle. When the lamina terminalis has been approached, this does not mean that the surgeon is directly in the third ventricle. The third ventricle is – even in the lamina terminalis approaches – displaced and can be visualised intraoperatively in the majority of cases not earlier than after total tumor removal.

In summary the question arises: Was the major part of the tumor (Fig. 1) really in the third ventricle and was the smaller remnant outside, below and lateral from it. From this point of view the complete literature especially from the time before the MRI-era has to be regarded very critically. In my own experience I didn't realize a pure intraventricular craniopharyngioma, all these larger tumors had extrinsic parts.

2/3 of the quoted modern literature with intraventricular participation had similar tumor growth. These are the more severe cases to be diagnosed before surgery respectively intraoperatively, because in case of total resection hypothalamic damages and high morbidity and mortality can occur. There have been repeated efforts in the literature for example by Yasargil, Samii and Steno to classify craniopharyngiomas in relation to the third ventricle, without real help during surgery. In the majority of the giant craniopharyngiomas cases the third ventricle is compressed and displaced in a way that it cannot be identified in the MRI. A new chance of intraoperative identification offers intraoperative MRI with low field [1] and meanwhile high field MRI.

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Authors' Reply

As initial comment I would like to remark my complete agreement with the doubts and criticisms raised by the reviewer about the weaknesses that any study of this type, based on the analysis of data gathered from anecdotal operated cases, does have. Although the results obtained by reviewing retrospectively case reports are very far from the offered by Class I evidence-based medicine studies, we believe that once the sum of isolated well-described cases of any rare entity reaches a considerable figure, it's a useful exercise try to find out the characteristics shared by the different cases as well as their diffferences. Regarding intraventricular craniopharyngiomas, knowledge spans more than fifty years and, of course, dramatic neuroradiological and surgical advances have improved the outcome of these lesions. The definition of a pure intraventricular location was established initially on the basis of necropsy findings. Since then, this topography has been presumed more than demonstrated, because of the limitations in resolution of the neuroradiological tools available before the introduction of high field MRI. Even today, using this methodology most of the cases cannot be diagnosed preoperatively with enough certainty.

Regarding the first question raised by the reviewer, we share his critical opinion about the reliability of the diagnosis of many of the intraventricular craniopharyngiomas reported in the literature, and our manuscript has been an attempt to introduce a methodology for critically analyzes the topographical diagnosis of this kind of craniopharyngiomas. Like the reviewer, we thought that many of the cases taken as truly intraventricular did not prove this location preoperatively, even with the use of MRI. With the analysis offered by our study, we just try to define more accurately the concept of a pure intraventricular location for a craniopharyngioma. We share the opinion of the reviewer that this concept has been employed too much superficially along the history, mainly due to the low sensibility of the available neuroradiological tools before the introduction of high field MRI. In this sense many of the craniopharyngiomas considered truly intraventricular were in fact suprasellar cases that had occupy secondarily the third ventricle area, either after invading the third ventricle cavity or just by pushing and elevating progressively the third ventricle floor. However the real existence of pure third ventricle craniopharyngiomas cannot be denied, so this rare topographical location has been demonstrated undoubtedly by many necropsy brain samples. We agree with the reviewer that our case cannot be considered as purely intraventricular, neither by the preoperative MRI scans nor by their postoperative counterparts on which small, hyperintense tumour remnants can be observed at the infundibular-tuberal area. That's the reason why this case was categorized as a non-strict intraventricular craniopharyngioma, like 66% of the previously reported cases that could not provide reliable proofs of an exclusive tumour location in the third ventricle.

The strong point to be emphasized from our study is to make the difference between those intraventricular craniopharyngiomas that can be delimited from the third ventricle floor and walls (strict cases) and those that are imbedded in the floor and/or walls of the third ventricle (non-strict cases). The last group usually shows tight adhesions to neural tissue and, as a consequence, it associates a higher risk in case of a total tumour removal is attempted, a fact that may be related to the adjacent position of hypothalamic neclei to the tumoural capsule. The preferential adamantinomatous histological pattern showed by non-strict intraventricular craniopharyngiomas compared to the much more frequent squamous-papillary pattern observed among strictly located third ventricle cases suggests that the initial level of tumoural growth might influence the future histological development. In this sense, the observation registered by Russel and Rubinstein of two rare intra- and suprasellar dumbbell shaped craniopharyngiomas characterized by an abrupt histological transition at the level of the diaphragma sellae, supports this finding [1]. In these cases, the intrasellar tumoural portion showed a single lined cuboidal/ciliated epithelium while the suprasellar one, displayed the usual squamous pattern. We think that the different initial position of the tumour cells that will originate an intraventricular craniopharyngioma might determine the histological development of these lesions.

Regarding the question about the anatomical position reached by the surgeon after the opening of the lamina terminalis, we agree with the reviewer that this approach does not imply a direct access to the third ventricle in all cases. In the case of a suprasellar tumour which has pushed the third ventricle floor during its growth, the floor may become

apposed against the lamina terminalis as a gliotic-non functional layer, a concept firstly addressed by Van den Bergh *et al.* [2], or it may even be displaced to a higher situation, so the opening of the lamina terminalis would let the surgeon to remove an extraventricular part of a suprasellar tumour which simulates to be intraventricular. We think that this distinction is of paramount importance in the surgical field, but it has not been clearly addressed by all experts. For example, if we look it up in the classic Apuzzo's work "Surgery of the Third Ventricle" (Williams & Wilkins, 1987), Jiro Suzuki considers that most craniopharyngiomas elevates the floor of the third ventricle, allowing the floor to lie against the lamina terminalis and consequently "the incision of the lamina terminalis will sever both the superior and inferior wall of the third ventricle" [3], while Russel H. Patterson illustrates the translamina terminalis approach as a way to gain access to a suprasellar-extraventricular tumour that has displaced the third ventricle floor above an stretched and thinned lamina terminalis [4].

In our survey we have studied meticulously the morphological alterations that are shown on preoperative and postoperative MRI studies of the reported intraventricular craniopharyngiomas, comparing their differences before and after the removal of the tumour, not only among the well-described cases included in the analysis of the manuscript, but also in many other anecdotal cases which illustrations were included in other large series (not included in this manuscript in order to make it short). We have realized that in the cases of craniopharyngiomas that had invaded secondarily the third ventricle or had grown at the level of the third ventricle floor (tubero-infundibular tumours) a clear breach of the third ventricle floor or even its absence could be observed on postoperative MRI scans when the tumour had been removed totally. Conversely, the normal morphology of third ventricle floor is preserved after the removal of a pure third ventricle craniopharyngioma on postoperative MRI studies. If this normal morphology is equally preserved after removing an extraventricular craniopharyngioma that was compressing the third ventricle, we cannot give an answer. Unfortunately, the identifications of the third ventricle floor and its actual relationship with the tumour capsule could not be established preoperatively in most cases on the MRI studies. We have found only four preoperative MRI images of third ventricle craniopharyngiomas on which the third ventricle floor is clearly differentiated from the tumour capsule, being both structures separated by a layer of cerebrospinal fluid [5–8]. We think the use of intraoperative high field MRI in combination with microscope-based neuronavigation proposed by Fahlbusch *et al.* [9] might be the best method for making the correct topographical diagnosis. Likewise, this technology would be also the most reliable for the surgeon when dealing with so complex lesions as giant craniopharyngiomas. We regret that the high costs associated to this technological implementation cannot be afforded by most departments of neurosurgery in our public health system by now.

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