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Craniopharyngioma: Radiologic and Histologic Findings and Recurrence

O. Petter Eldevik, Mila Blaivas, Trygve O. Gabrielsen, John K. Hald, and William F. Chandler

PURPOSE: To identify the CT and MR characteristics of craniopharyngiomas, to evaluate the histologic types of craniopharyngioma, and to compare the radiologic/histologic appearance and type of therapy with tumor recurrence. **METHODS:** We reviewed the records of 45 patients with craniopharyngiomas for which surgical specimens ($n = 45$), preoperative MR or CT studies ($n = 27$), or other MR or CT studies or reports ($n = 18$) were available. Radiologic appearance, histologic morphology, treatment, and tumor recurrence were studied. **RESULTS:** Adamantinomatous epithelium was found in 40 of 45 surgical specimens, keratin in 34 of 45, and squamous epithelium in 11 of 45. A continuum of mixed morphology rather than distinct subtypes of tumors was found. The radiologic appearance did not correlate with the histologic features. No statistically significant difference was found between children and adults with respect to tumor size, calcification, histology, or tumor recurrence. Patients treated with radiation after subtotal resection had far fewer tumor recurrences ($n = 3$) than patients treated with surgery alone ($n = 18$). **CONCLUSION:** Craniopharyngiomas could not be divided into distinct histologic types. No differentiating radiologic or histologic characteristics could be established for craniopharyngiomas in children versus adults. Radiation treatment was strongly associated with tumor regression or lack of recurrence.

Index terms: Craniopharyngioma; Efficacy studies; Sella turcica, neoplasms

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Craniopharyngiomas account for about 3% of all primary intracranial tumors (1). Two types of craniopharyngiomas have been described in the literature: a childhood type, with frequent occurrence of cyst formation and calcifications, an adamantinomatous microscopic pattern, and generally poor prognosis; and an adult type, generally without calcifications or cyst formation, with papillary squamous epithelium, and generally a good prognosis (2-5). Marked differences in clinical presentation, frequency of calcification, and postoperative outcome be-

tween the two types of craniopharyngioma have been reported (2, 4, 6). The purpose of this study was to identify the magnetic resonance (MR) imaging and computed tomographic (CT) characteristics that might be associated with craniopharyngiomas that have distinctly different histologic features, which might in turn predict tumor recurrence and guide therapy.

Materials and Methods

Of the 56 patients with craniopharyngioma who had been seen in our institution from January 1984 to March 1995, surgical specimens and CT or MR studies or reports were available for review in 45 cases (Table 1). Ten of these patients had been treated initially at other institutions between 1966 and 1986 before coming to our institution for treatment of recurrent craniopharyngioma. Histologic and radiologic findings in these 10 patients (noted in Table 1) pertain to the recurrent tumor at the time the patients were treated at our institution. In eight additional patients, only postoperative CT or MR studies were available, because the preoperative imaging studies done in other institutions were not available when the present study was undertaken; these eight patients are noted in Table 1. Twenty-seven patients had comparable preoperative and

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TABLE 1: Radiologic and pathologic findings, treatment, and tumor recurrence in 45 patients with craniopharyngioma

Patient	Age, y/ Sex	Radiology			Pathology			Treatments and Recurrences [‡]						
		Tumor, cm ³	Cyst, cm ³	Calcification, cm ³	Adamantinomatous Epithelium, %	Keratin, %	Squamous Epithelium, %	Primary Treatment	Recurrence, mo	Second Treatment	Recurrence, mo	Third Treatment	Recurrence, mo	Observation Time, mo
1*	2/M	13.5	11.5	0.7	90	10	0	STR	24	P32	1	Drain	...	25
2	3/F	17.0	17.0	0.0	20	80	0	STR	8	P32	32
3†	4/M	...	P	P	40	60	Cyst lining	STR	26	RT	62
4	5/F	15.8	15.0	0.5	50	50	Cyst lining	STR + RT	§	31
5	5/F	56.5	53.7	2.3	45	10	45	STR	2	RT	96
6	6/F	18.0	9.0	4.5	66	33	0	STR	1	Drain	95
7*	6/F	31.2	17.2	4.7	0	0	0	STR	264	STR	5	269
8*	6/M	5.3	4.2	0.3	30	70	0	STR	44	STR + RT	72	STR	...	120
9	7/F	99.0	64.4	1.0	75	25	0	STR	3	P32 + RT	26
10	7/F	21.8	15.2	4.4	10	90	0	Biopsy + RT	20
11	8/F	10.9	6.6	2.7	85	15	0	STR + RT	1	Drain	66
12	10/F	23.6	11.8	4.7	66	33	0	STR	3	P32	3	Drain	...	11
13*	11/M	13.5	2.7	3.4	95	5	0	STR	180	Drain	93	STR + RT	...	295
14*	12/M	7.2	4.7	1.8	40	60	0	STR	60	STR + RT	6	P32	...	124
15†	12/F	...	P	A	10	90	0	STR	1
16	12/F	34.6	3.5	8.6	90	10	0	STR + RT	90
17	14/F	1.7	1.7	0.0	0	0	0	STR	54
18	14/M	14.7	10.2	4.3	0	0	0	STR	19
19*	15/M	45.0	31.5	6.8	40	60	0	STR	207	Drain	5	STR + RT	...	234
20	16/M	7.8	0.4	0.8	100	0	0	STR + RT	31
21†	17/M	...	P	P	10	90	0	STR + RT	§	Drain	6
22	19/M	14.0	12.6	0.0	95	5	0	STR + RT	16
23	21/F	80.4	48.2	12.1	10	90	0	P32	6	STR + RT	50
24*	21/F	2.4	1.9	0.0	60	40	0	STR	24	STR	12	STR	12	156
25†	23/M	...	P	P	30	70	Cyst lining	STR + RT	18
26	25/F	15.6	10.9	0.0	100	0	0	STR	1	P32 + RT	37
27†	26/F	...	P	P	50	50	0	STR + RT	72
28	26/F	23.8	4.8	2.4	85	0	15	STR + RT	1
29†	29/M	...	P	P	40	60	Cyst lining	STR	2	Drain	77
30	30/M	10.2	8.7	0.8	90	10	0	STR + RT	6
31*	31/F	31.3	9.4	23.4	60	40	0	STR + RT	82	STR	9	Drain	...	128
32	33/F	13.5	13.5	0.0	85	15	0	STR + RT	§	100
33	40/M	9.5	7.6	0.9	40	60	0	STR	12	144
34	41/M	2.9	2.5	0.3	0	0	0	STR + RT	79
35	42/F	3.4	0.5	0.0	80	0	20	STR + RT	§	9
36*	42/M	12.6	10.1	0.6	0	0	0	STR	9	STR	16	P32 + RT	...	84
37	44/F	19.4	6.8	0.1	50	0	50	Biopsy + RT	4
38	47/M	38.3	11.5	5.7	15	85	0	STR + RT	0
39*	47/F	4.0	3.8	0.0	95	0	5	STR + RT	7	P32	67
40†	50/F	...	P	A	45	55	0	STR + RT	7
41	51/F	9.5	3.8	1.0	80	20	0	STR + RT	18
42†	52/F	...	A	A	70	15	15	STR + RT	47
43	57/M	14.8	14.1	0.0	70	25	5	Drain	4	Drain	11	STR + RT	...	20
44	62/M	3.8	2.4	0.9	40	60	0	STR + RT	5
45	64/F	6.3	4.1	0.3	75	25	0	STR	13	98

Note.—P indicates present; A, absent; STR, subtotal resection; RT, radiation therapy; and P32, radioactive phosphorous.

* Patient presented from another institution with a recurrent tumor.

† No preoperative films available for measurements.

‡ Recurrence time given in months after the end of treatment; observation time given in months from the primary treatment.

§ Recurrent tumor cyst occurring before or during radiation therapy.

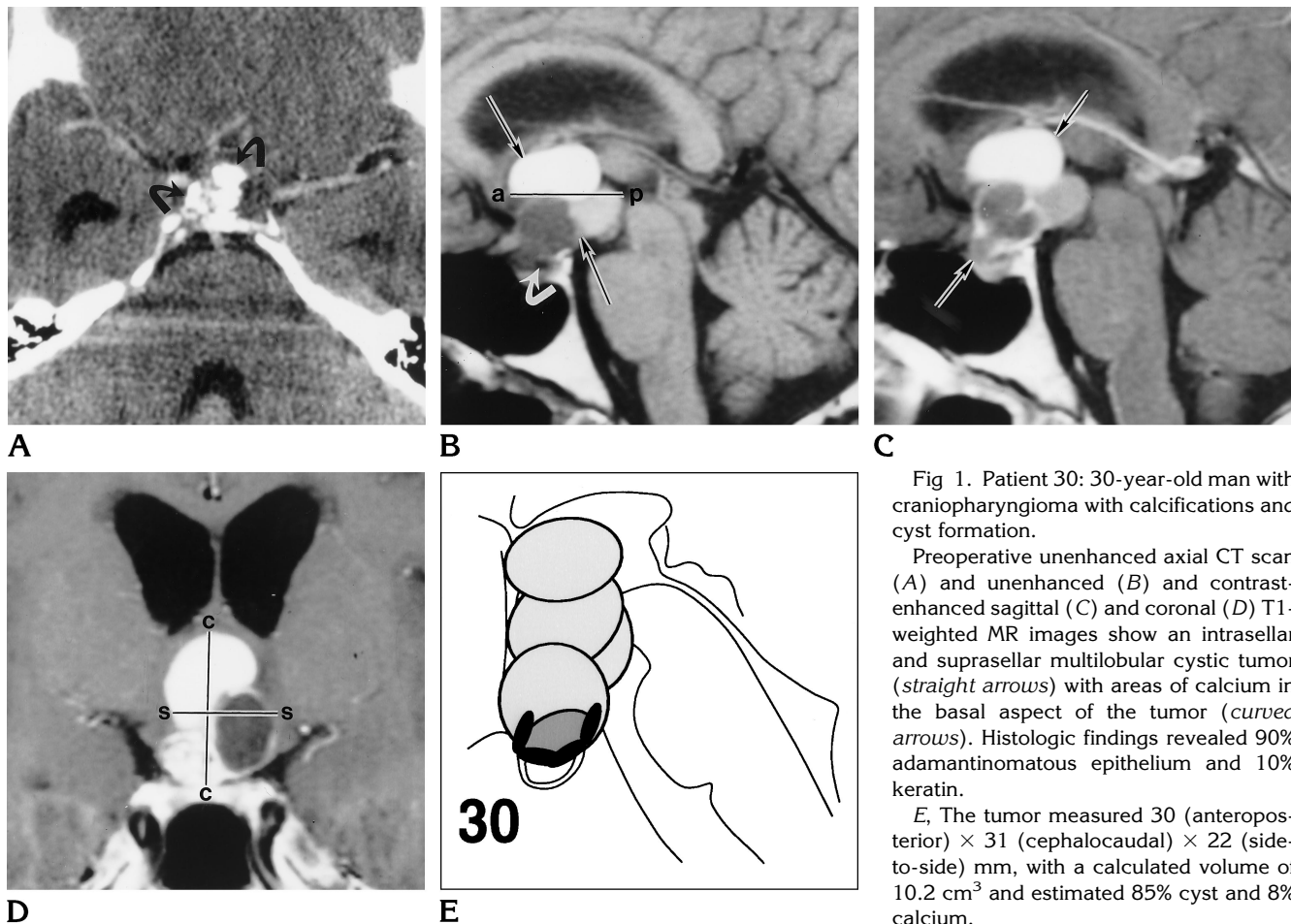


Fig 1. Patient 30: 30-year-old man with craniopharyngioma with calcifications and cyst formation.

Preoperative unenhanced axial CT scan (A) and unenhanced (B) and contrast-enhanced sagittal (C) and coronal (D) T1-weighted MR images show an intrasellar and suprasellar multilobular cystic tumor (straight arrows) with areas of calcium in the basal aspect of the tumor (curved arrows). Histologic findings revealed 90% adamantinomatous epithelium and 10% keratin.

E, The tumor measured 30 (anteroposterior) × 31 (cephalocaudal) × 22 (side-to-side) mm, with a calculated volume of 10.2 cm³ and estimated 85% cyst and 8% calcium.

postoperative MR or CT studies available for review. All clinical charts were reviewed. Note was made of the patient's age at the time of initial diagnosis, different treatments used to cure or control the craniopharyngioma, time and type of tumor recurrence, and length of observation period.

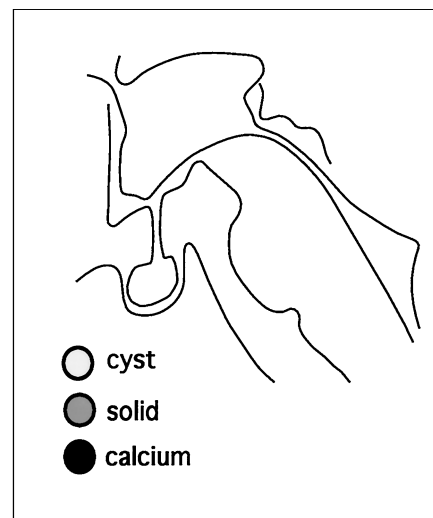
All imaging examinations were reviewed by three neuroradiologists who were blinded to the histologic findings, clinical course, and treatment. Tumor location, size, and imaging characteristics on MR and CT studies were recorded by consensus among the readers. Tumor size was measured as the largest anteroposterior, cephalocaudal, and side-to-side diameters on the hard copies of the MR images or CT scans, and the tumor volume was calculated by means of the following formula: volume = 0.5 × anteroposterior × cephalocaudal × side-to-side dimensions (7). A preliminary survey indicated that consistent, reliable measurements of tumor size and especially tumor components often could not be made, and only rough estimates of the relative size of some tumor components like multiple small cysts or scattered calcification could be obtained. The percentage of the tumor volume that represented soft tissue, calcium, or cyst was estimated (not measured) on the hard copies of the imaging studies (Fig 1). This percentage was then multiplied by the calculated

tumor volume to arrive at approximate volumes of the cystic and calcified portions of the tumors (Table 1). The solid portion of the tumor was considered to be the enhancing soft tissue. Cystic portions of the tumor were identified as homogeneous, nonenhancing, sharply delineated areas on CT and MR images (8, 9). Tumor calcifications were identified as areas of high attenuation on CT scans or as low signal (usually) on MR images (10). The presence or absence of calcium was determined by preoperative CT in 27 patients, by early postoperative CT in 13 other patients, and by preoperative MR imaging in five additional patients.

To obtain a visual impression of the size, location, and gross composition of the craniopharyngiomas, we made a line drawing of each tumor, attempting to depict different parts of the tumor (even paramedian compartments) on a template of a midsagittal image of the sella turcica region, with the use of a computer drawing program (Figs 1 and 2).

The surgical specimens were fixed in 10% formalin and embedded in paraffin, and the sections were stained with hematoxylin-eosin. The slides were reviewed, and the presence and proportion of adamantinomatous epithelium, "wet" keratin, and squamous epithelium were noted

Fig 2. Twenty-seven craniopharyngiomas in patients younger and older than 20 years. A, Template used for the line drawings shows a midsagittal image of the pituitary fossa, pituitary stalk, third ventricle with the optic chiasm, interventricular foramen, and the brain stem. The cystic, solid soft tissue and calcified portions of the tumor are shown in different shades of gray, as indicated. Facing page: Craniopharyngiomas in 13 patients aged 3 to 19 years (B), and in 14 patients aged 21 to 64 years (C), starting with the youngest patient in the upper left corner. (Patients' numbers correspond to those in Table 1.)



A

and estimated. Presence of calcium in the surgical specimens was recorded.

The Student's *t* test and Fisher's Exact Test were used for the statistical analysis.

Results

Pertinent data, including radiologic and pathologic findings, treatment, and tumor recurrence, for the 45 patients are summarized in Table 1. The 10 patients treated initially at other institutions between 1966 and 1986 are not included in the drawings of the radiologic appearances of the tumors as depicted in Figure 2. Eight additional patients had only postoperative CT or MR studies available; these are noted in Table 1. Because no actual measurements of preoperative tumor volume or estimates of preoperative tumor composition volumes could be made in these eight patients, line drawings of these tumors are not included in Figure 2. However, the presence or absence of calcium and cyst was noted in Table 1 from information available in the charts and postoperative images.

Histologic Findings

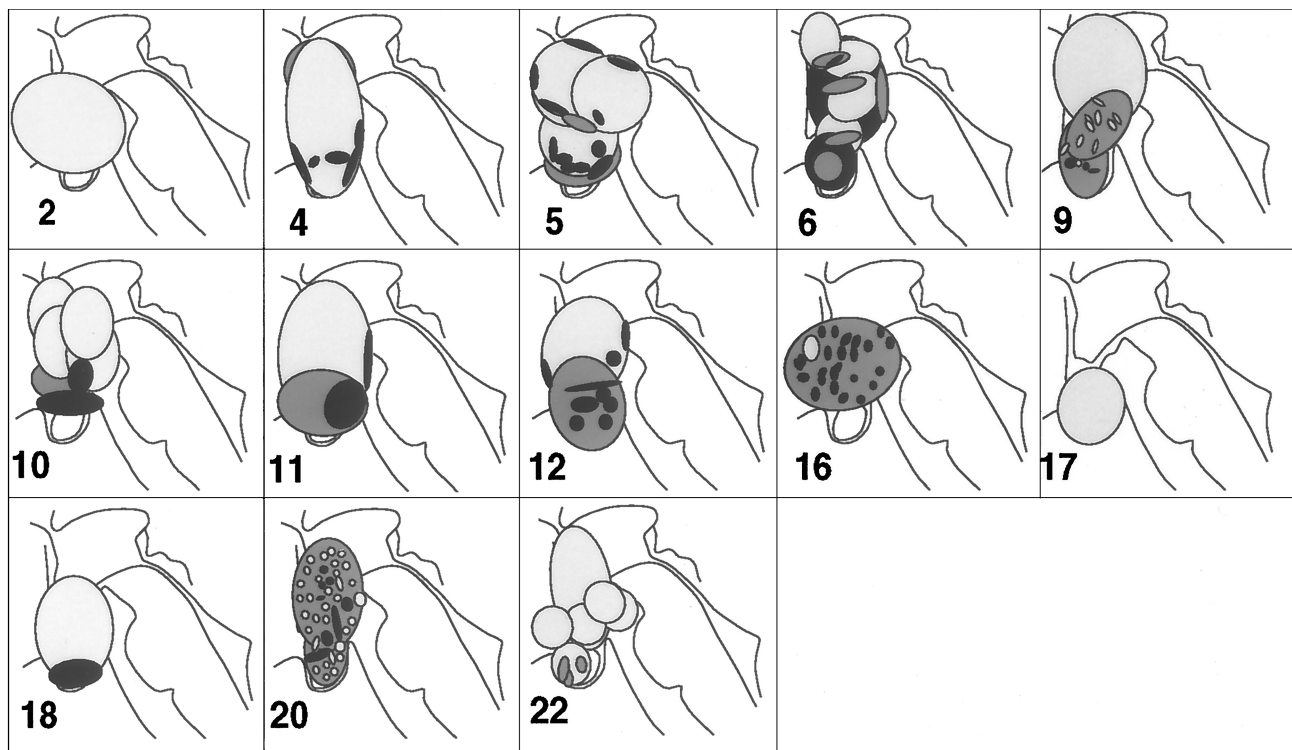
There was no statistically significant difference in the histologic pattern (percentage of adamantinomatous cells, squamous cells, or keratin) in the surgical specimens of patients younger versus older than 20 years of age (Table 2). Typical adamantinomatous epithelium with peripheral palisading of a single cell layer

bordering clusters of loose stellate cells was present in the majority of the patients (Fig 3C). It was associated with various amounts of "wet" keratin and keratohyaline granules. Squamous epithelium was found in 11 patients, and it either replaced portions of the adamantinomatous epithelium or lined a segment or the entire cyst wall. It was formed by stratified squamous cells joined by intercellular bridges, with occasional focal papillae and lack of palisading (Fig 3D). No "pure" squamous papillary pattern was found. Mixed or transitional forms where squamous epithelium was present in continuation with adamantinomatous epithelium were identified in all 11 patients with squamous epithelium (Figs 3C and D and 4D). Other histologic components, such as cysts, cholesterol clefts, inflammation, giant cell reaction, and calcifications, were present in various quantities.

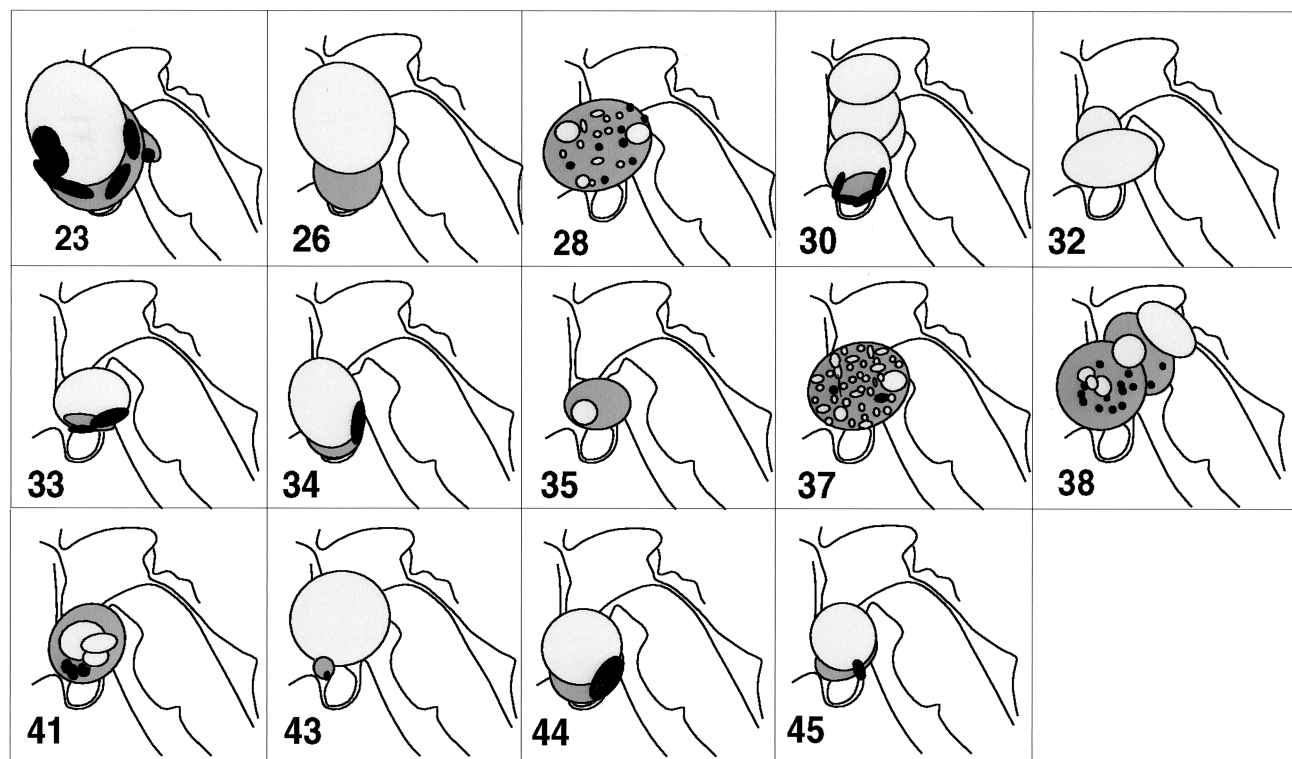
Radiologic Findings

The objective of making the computer line drawings shown in Figure 2 was not to depict accurately the complexity of the architecture of the tumors but to obtain a simplified two-dimensional visual portrayal of the tumors for the purpose of comparing tumor size, location, and composition. Such a direct visual comparison between tumors otherwise was difficult to achieve owing to the different techniques, parameters, and planes used to acquire the imaging studies.

The relation between tumor composition and histology in patients younger versus older than



B



C

TABLE 2: Tumor composition related to patients' age in 27 patients with craniopharyngiomas

	All Patients	Patients Less than 20 Years Old	Patients 20 Years Old or Older	<i>P</i>
No. of patients	27	13	14	...
Age, y, median	21	10	42	...
Female patients	18	10	8	...
Male patients	9	3	6	...
Tumor size, cm ³	21.7	25.8	17.9	.38
Cyst size, cm ³	13.3	17	9.9	.26
Calcification size, cm ³	2.2	2.6	1.7	.47
Adamantinomatous cell content, %	56	54	59	.73
Keratin content, %	27	27	28	.94
Squamous cell content, %	5	4	6	.62

Note.—Volumes and percentages are given as averages.

20 years of age is given in Table 2. Patients under 20 years of age had, on average, larger tumors (25.8 cm³) than older patients (17.9 cm³), but the difference in tumor volumes was not statistically significant ($P = .38$). The volumes of the cystic tumor components and the tumor calcifications showed the same tendency: slightly larger cysts and more calcification in the younger age group, but without statistical significance in this study population. An example of a calcified and cystic tumor in an adult appears in Figure 1, and an example of a predominantly solid tumor with little calcification in a child is shown in Figure 5. The percentages of adamantinomatous epithelium and keratin in the surgical specimens were slightly larger in patients older than 20 years of age, but the differences were not statistically significant.

Tumor appearance as shown in the line drawings (Fig 2B and C) is not reliably different in younger versus older patients. There is a tendency for patients under the age of 20 to have larger and more calcified tumors, but the presence of calcium or cyst does not distinguish younger from older patients. In grouping the patients by histologic findings (more or less than 50% adamantinomatous epithelium) or by tendency for tumors to recur (patients with no tumor recurrence versus patients with tumor recurrence), we could not see any significant difference in tumor appearance between the groups by comparing the line drawings.

The presence or absence of calcium in the craniopharyngiomas was evaluated on CT scans in 35 patients who underwent primary

treatment in our institution. Calcium was present (on preoperative CT scans) in 24 patients and not present in 11 patients. Patients with calcium deposits tended to be younger than patients with uncalcified craniopharyngiomas (average, 24 years versus 32 years; $P = .09$), and tumors with calcification, as a group, were larger (25.6 cm³ versus 12.3 cm³; $P = .01$). There was no statistically significant difference in the histologic patterns between tumors with and without calcification.

The mere presence or absence of cyst in the craniopharyngiomas could not be used as a distinguishing characteristic between groups of patients because all patients except one (patient 42) had at least one cystic component.

Tumor location relative to the sella turcica and the ventricular system was evaluated in the 27 patients for whom preoperative imaging studies were available. Only one patient (patient 12) had a definite infrasellar tumor component. This was a large tumor (23.6 cm³) with calcifications and cyst formation in a 10-year-old girl. No patient had a purely intrasellar tumor. Seventeen patients had an intrasellar component of tumor, most of them with enlargement of the pituitary fossa or erosion of the dorsum sellae. The 17 patients with an intrasellar tumor component as a group were younger (average, 21 years) than the 10 patients with no intrasellar tumor (average, 36 years; $P = .006$). All 27 patients had tumor in the suprasellar cistern. In 22 of the 27 patients the craniopharyngioma produced a deformity of the ventricular system, most often an elevation of the floor of the third ventricle with elevation and deformation of the optic chiasm (Figs 1 and 3–6). It was not always possible to separate frank tumor infiltration into brain parenchyma from remodeling of the brain around the tumor. Invasion into brain was seen in surgical specimens of seven of 45 patients, all with evidence of deformity of the third ventricle or compression of the optic chiasm on preoperative imaging studies. The 22 patients with craniopharyngiomas indenting or infiltrating the third ventricle as a group were younger (average, 23 years versus 40 years; $P = .003$), had a higher percentage of adamantinomatous epithelium in the surgical specimens (average, 64% versus 33%; $P = .005$), and had larger tumors (average, 25.7 cm³ versus 4.0 cm³; $P = .035$) than the five patients without ventricular deformity.

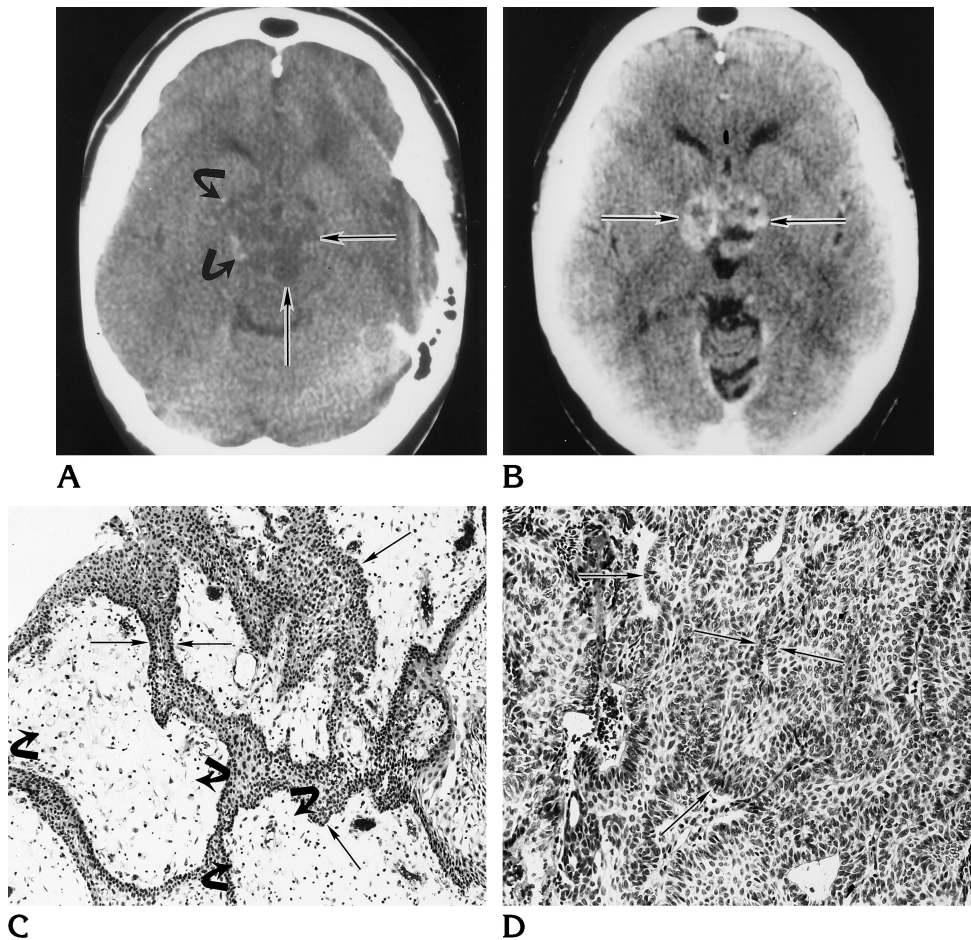


Fig 3. Patient 37: 44-year-old woman with craniopharyngioma.

Axial unenhanced (A) and contrast-enhanced (B) CT scans show an inhomogeneous, enhancing soft-tissue mass (*straight arrows*) in the suprasellar cistern extending into the third ventricle. Specks of calcium (*curved arrows*) and small cysts are seen. A mixture of adamantinomatous epithelium and squamous epithelium was present in the surgical specimen.

C, Histologic specimen of adamantinomatous portion of the tumor shows strands of adamantinomatous epithelium (*straight arrows*) outlining loose "reticulate" hypocellular regions (*curved arrows*) (hematoxylin-eosin; original magnification $\times 117.5$).

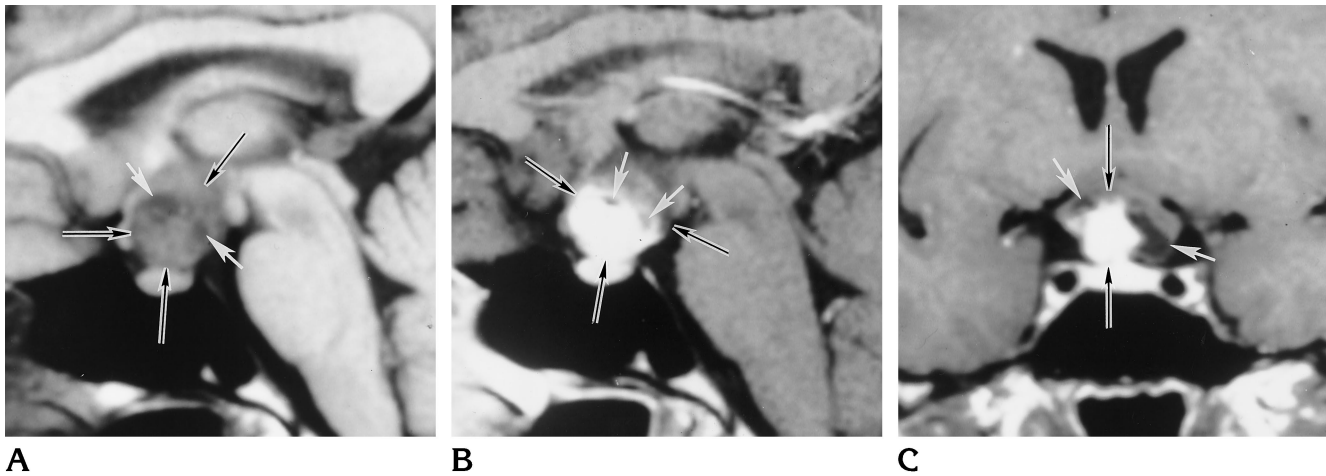
D, Histologic specimen of squamous portion of the tumor shows papillary arrangement of squamous epithelium (*arrows*) (hematoxylin-eosin; original magnification $\times 188$).

Tumor Recurrence

Tumor recurrences after different treatments are listed in Table 3. Five patients were lost to follow-up less than 6 months after the initial treatment; none had evidence of recurrence during the time they were seen (Table 1). These five patients are not included in Table 3 or in the discussion dealing with tumor recurrences. Four patients (cases 4, 21, 32, and 35) had recurrence of tumor cysts either before or during radiation therapy (Fig 6). These recurrent cysts disappeared during the subsequent few months (one cyst in case 21 was drained stereotactically). These four patients with transient recurrent cysts are included in Table 3 but were not

considered to have recurrent tumor. Three patients (cases 10, 23, and 43) did not undergo subtotal resection of the tumor. Instead they had stereotactic biopsy or cyst drainage with or without instillation of radioactive phosphorous 32 or external radiation therapy.

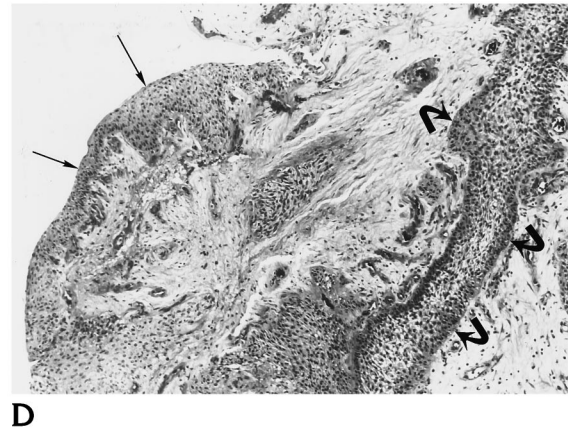
The following factors were considered for possible association with tumor recurrence: age, sex, radiologic findings (ie, tumor size, location, presence of cyst, presence of calcification, deformity of the ventricular system), tumor histology, and treatment. The recurrence rate was compared in males versus females, younger patients (<20 years) versus older patients, patients with calcified tumors versus pa-



A **B** **C**

Fig 4. Patient 35: 42-year-old woman with craniopharyngioma with "transitional"-type epithelium. Sagittal unenhanced (A) and contrast-enhanced (B) and coronal contrast-enhanced (C) T1-weighted images show a suprasellar inhomogeneous, enhancing mass (*two-toned arrows*) extending into the third ventricle and down into the superior aspect of the pituitary fossa. The homogeneous, nonenhancing portions of the tumor (*white arrows*) were considered cystic tumor elements.

D, The histologic specimen shows a transitional-type cyst lining, with the squamous epithelium on the left (*straight arrows*) and the adamantinomatous epithelium to the right (*curved arrows*) (hematoxylin-eosin; original magnification $\times 117.5$).



tients with no calcium, patients with dominant adamantinomatous pattern ($\geq 50\%$) versus patients with tumors in which keratin or squamous cells were dominant, and patients treated with subtotal resection as the only treatment versus patients treated with subtotal resection followed by external radiation therapy (55 Gy over 6 weeks beginning 6 to 9 weeks after surgery). No statistically significant differences could be found with regard to tumor recurrence rate correlated to sex, age, radiologic findings, or dominant histologic pattern.

Of the 40 patients who were followed up for a period of at least 6 months, 23 had recurrence of their craniopharyngioma after the primary treatment, including all types of primary treatment. Ten patients had recurrent tumor after the second treatment (regardless of treatment type), and one patient had recurrence after the third treatment. In total, 71 treatments were given to primary and recurrent tumors. In addition, two patients with recurrent tumor after

subtotal resection were observed but were not given specific treatment because the tumor recurrences were small, slowly growing, and without definite symptoms. An observation time of at least 6 months was recorded for 65 of the 71 treatments, and the recurrence rate in these 65 treatments was used for statistical evaluation (Table 3). There were 26 recurrences after 30 treatments not involving any form of irradiation; these recurrences ensued 1 to 264 months after treatment (median, 12 months). There were eight recurrences among the 35 treatments involving external or internal (phosphorous 32) irradiation; these occurred 1 to 82 months (median, 6 months) after the end of treatment. Statistically, there was a highly significant difference ($P < .0001$) between the two treatment groups, with fewer recurrences after some form of radiation treatment. In several instances we observed shrinkage or disappearance not only of cysts and solid tumor but even of calcified elements after irradiation.

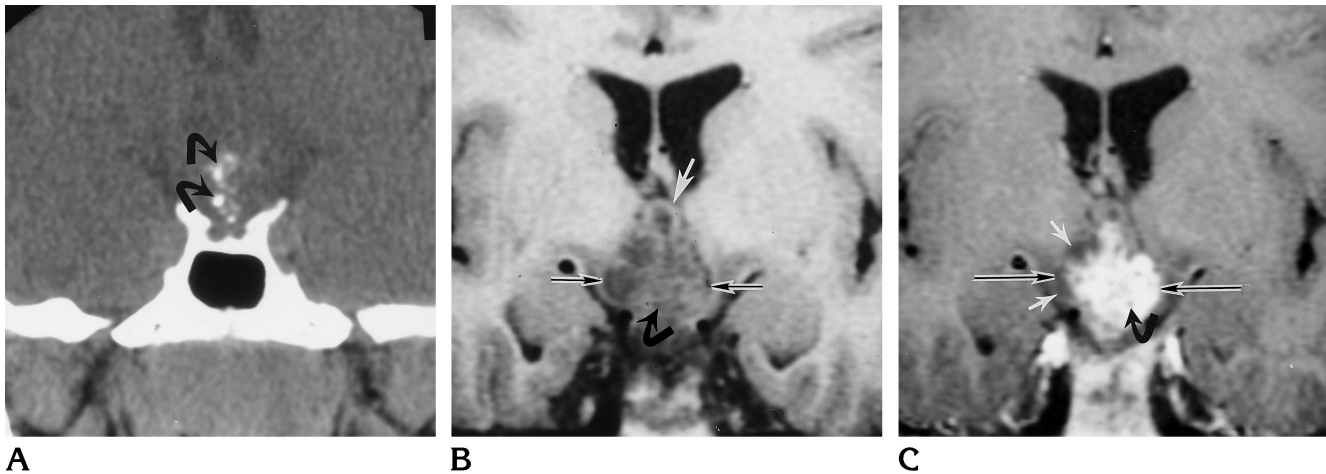


Fig 5. Patient 20: 16-year-old boy with predominantly solid craniopharyngioma. Preoperative nonenhanced coronal CT (A) and nonenhanced (B) and contrast-enhanced (C) coronal T1-weighted MR images show intrasellar and suprasellar enhancing soft-tissue tumor extending up into the third ventricle (*two-toned arrows*) with multiple small calcifications (*curved arrows*) and small cysts (*white arrows*). The surgical specimen demonstrated adamantinomatous epithelium (not shown).

Discussion

The classic description of craniopharyngioma usually refers to a nonmalignant, often cystic or calcified tumor in the suprasellar region with a spectrum of presenting signs and symptoms, including visual changes, endocrine abnormalities, motor deficits, mental changes, and increased intracranial pressure. Craniopharyngiomas are the most common nonglial brain tumors in children and account for half of all suprasellar masses in this age group (11). More than half of craniopharyngiomas occur in children and young adults (1). Several previous investigators have stated that the microscopic patterns delineate two distinct, clinicopathologic variants of craniopharyngioma, differing not only in microscopic appearance but also in radiologic appearance and clinical behavior (2, 4, 12).

Depending on the authors' experience, craniopharyngiomas have been viewed as a single tumor type with a multitude of histologic features or as two distinct histopathologic subtypes, as described by Kahn et al (2). One type was characterized by squamous epithelium, no keratinization, no calcification, and a good prognosis. This type was found only in adults, except for one such case in a 15-year-old boy. The other type, called the childhood type, was characterized by an adamantinomatous pattern with keratinization, calcification, and a poor prognosis. This second type was found in all children (except one), and in 25% of adult patients. Giangaspero et al (3) described six adult

patients with suprasellar tumors formed of papillary, well-differentiated squamous epithelium without calcifications, palisaded cells, or keratoid nodules. This constellation of histologic features was named *papillary craniopharyngioma*, and corresponded to Kahn's adult type. Adamson et al (4) referred to the squamous papillary type in 15 of their 93 patients with craniopharyngiomas and concluded that the squamous papillary craniopharyngioma did not occur in children but was found in one third of adult patients, and was associated with a good functional postoperative outcome and no recurrences. Half of these tumors were cystic and none was calcified. All 46 children in the group studied by Adamson et al (4) had classic adamantinomatous histology of childhood type; more than 90% of them were cystic and calcified. Of the 73 patients with an adamantinomatous pattern, eight recurrences were seen (observation time not stated).

Because of the frequent association of adamantinomatous tumors with large squamous epithelium-lined cysts, many investigators have suggested that craniopharyngiomas represent a single group of tumors, with a range of characteristics from purely adamantinomatous type through a mixed variety to the squamous papillary type (1, 6). Russel and Rubinstein (1) stated that highly papillary architecture in the epithelial formations of craniopharyngiomas was an unusual feature seldom seen in their experience and, when seen, was associated with aggressive brain invasion. Petito et al (6)

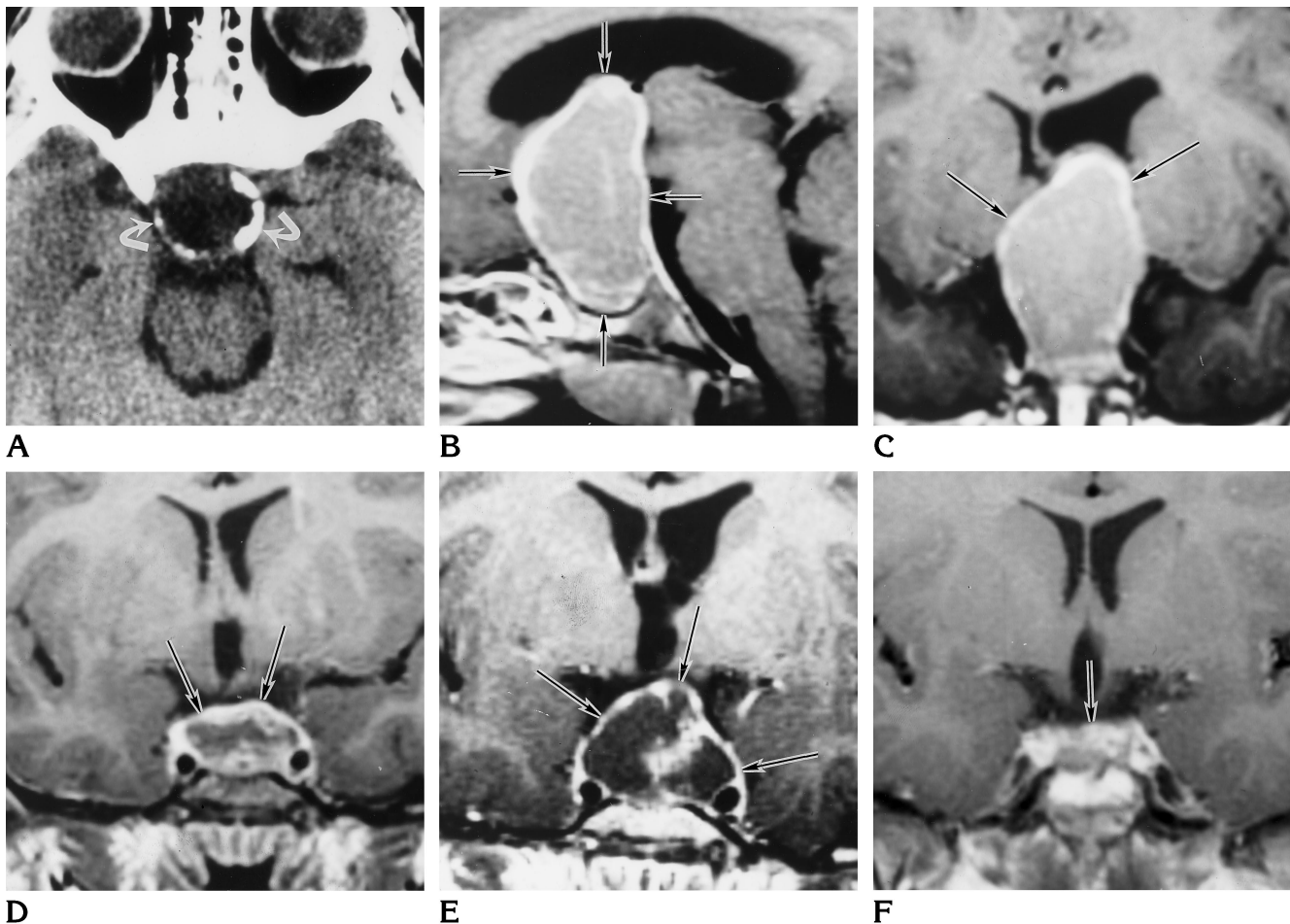


Fig 6. Patient 4: 5-year-old girl with craniopharyngioma. The cystic portion of the tumor recurred temporarily after surgery, during radiation therapy, and shrank thereafter without additional treatment.

Preoperative axial unenhanced CT scan (A) and sagittal (B) and coronal (C) contrast-enhanced T1-weighted MR images show intrasellar and suprasellar tumor with enhancing cyst walls extending into the third and left lateral ventricles (*straight arrows*). Calcium can be seen in cyst wall (*curved arrows*).

Coronal contrast-enhanced T1-weighted MR images obtained 2 weeks (D), 18 weeks (E), and 20 months (F) after surgery. External radiation therapy (55 Gy) was administered over a 6-week period from week 9 to week 15 after surgery. The tumor size was reduced after surgery (*arrows in D*), increased thereafter (*arrows in E*), and shrank during the following months (*arrow in F*).

reviewed a large historical collection of 245 cases from several centers and found that the majority of tumors were cystic and that, microscopically, cysts were formed by squamous epithelial maturation and degeneration, by degeneration of stellate cells at the centers of adamantinomatous nests, or by degeneration of stroma. Transitional forms were seen between adamantinomatous and squamous epithelium. Our findings were mostly in agreement with the latter statement, since in 11 patients from our series we could identify adamantinomatous epithelium within the cyst wall alternating with stretches of squamous epithelium.

We could not find any association between the dominant histologic pattern of the cranio-

pharyngiomas and the recurrence rate; however, among our cases there was no papillary squamous type in pure form. Similar results were reported by Weiner et al (12), who did have cases of papillary squamous type and did not find any significant difference in recurrence rate between patients with squamous papillary and adamantinomatous craniopharyngiomas.

Tumor appearances on plain films and CT scans, such as tumor size and presence of calcification, have been claimed to be associated with patients' age at the time of diagnosis of the craniopharyngioma as well as with recurrence rate or outcome (2, 4, 13, 14). Petitto et al (6) found that those patients with tumors lacking calcification on skull radiographs had a signifi-

TABLE 3: Treatments and recurrences in 40 patients with craniopharyngiomas

Treatment	No. of Treatments	Recurrence	Median Time to Recurrence, mo	Median Observation Time in Patients Without Recurrence, mo
Treatment not involving irradiation				
Subtotal resection	24	22	12	37
Stereotactic cyst drainage	6	4	8	51
Treatment involving irradiation				
Irradiation alone	2	0	...	65
Subtotal resection + irradiation	21	5	7	22
Stereotactic cyst drainage + irradiation	2	0	...	85
Stereotactic biopsy + irradiation	1	0	...	20
Phosphorous 32 instilled into tumor cyst	6	3	3	58
Phosphorous 32 therapy + irradiation	3	0	...	36

Note.—All patients had at least 6 months follow up after each treatment listed. Included are treatments of both the primary and recurrent tumors, for a total of 65 treatments. There was a highly significant difference in recurrence rates between patients who received radiation treatment and those who did not ($P < .0001$). *Irradiation* indicates external radiation therapy with 55 Gy given over 6 weeks.

cantly better 5-year survival rate than patients whose tumors showed calcification. Other reports have stated that the absence of tumor calcification is associated with a better survival rate and is characteristic of craniopharyngiomas in adults (2, 13). It has been suggested that the biological behavior of craniopharyngiomas in children differs from that in adults (15). In the present study, we found that, on average, the tumors were somewhat larger and more calcified in children; however, large calcified tumors were seen in adults, and small tumors without calcifications were found in children. We could not establish any clear and significant difference in CT or MR imaging characteristics related to children versus adults. The discrepancy between this study and prior studies may be due in part to the higher sensitivity of CT over plain radiography for the detection of calcium and in part to the fact that we estimated the volume of calcification that was present instead of merely noting its presence or absence. If we assume that at least 0.5 cm^3 of calcium is necessary for its detection on plain skull films, 12 of 16 children and nine of 19 adults would have had positive plain film findings for calcium in our series, which is comparable to earlier reports of 80% calcified craniopharyngiomas in children and 40% in adults (13). Calcification deposits are difficult to assess reliably by MR imaging alone, since the signal on T1-weighted and T2-weighted images is variable (9, 10).

Even though the concept of two distinct histologic tumor types could not be confirmed in the present study, there could still be radiologic imaging differences between tumors of different

histologic composition. However, when we compared tumors with dominant (more than 50%) adamantinomatous epithelium to tumors that consisted predominantly of keratin or squamous cells, we could not find any correlation between the dominant histologic pattern and imaging characteristics, such as tumor size, cyst size, MR signal/CT density, degree of calcification, or tumor location relative to the pituitary fossa, pituitary stalk, or third ventricle.

Although recurrences of craniopharyngioma have been reported as late as 30 years after surgery (2), in most series half the recurrences developed within 2 to 5 years (12, 13, 16–18). In our series the median time to recurrence was less than 12 months in patients treated with surgery alone, and only 7 months in patients treated with adjuvant irradiation. This might be explained by our close follow-up routines, which included repeat CT or MR studies at 3- to 6-month intervals during the first year and every 12 months thereafter, or more frequently if clinically indicated.

We could not identify any imaging characteristics of tumors that corresponded to a high or low rate of recurrence. The younger age group (<20 years) was more often chosen to undergo surgery without irradiation than was the older age group ($P = .01$), but there was no significant difference in tumor size, calcification, or cyst size between treatment groups, or between patients with or without recurrence.

There was a significantly longer observation time ($P = .004$) for patients who had surgery alone as the primary treatment (median, 90 months) than for patients treated with surgery

plus adjuvant irradiation (median, 39 months). This longer observation period may in part be explained by the 10 patients who were referred to our institution with recurrent tumor: eight of these 10 patients had surgery as the primary treatment, with a median observation time of 140 months. The shorter observation time in patients undergoing primary treatment with a combination of surgery and irradiation is in part due to an increasing tendency in our institution to use adjuvant radiation therapy during the study period of 11 years, so that the patient population treated in the last half of the period was more likely to receive radiation therapy (64% versus 35%). Looking at patients with primary treatment in our institution, there was no statistical difference ($P = .14$) in observation time between patients undergoing surgery as the primary treatment (median, 54 months) and patients undergoing surgery followed by irradiation (median, 27 months). All patients who had a recurrence after surgery as the primary treatment had their recurrence within 26 months (median, 3 months). Of the two patients with recurrence after irradiation as the primary treatment, one had a recurrence 1 month after completed radiation therapy and one patient had a recurrence 6 months after instillation of radioactive phosphorous 32. It is, however, possible that some of the 21 patients who received radiation therapy in our institution eventually may turn out to have a higher than indicated recurrence rate, owing to recurrences developing at a later time.

Gross total tumor resection was not a primary objective in the treatment of these patients. The neurosurgical aim was to obtain a biopsy, drain cysts, and remove as much of the tumor as could be done safely without overly aggressive tumor resection that could damage the brain, optic chiasm, or pituitary gland.

We found the same overall recurrence rate (17%) after conservative tumor resection followed by irradiation as that reported by Weiner et al (12) in patients after radical gross total tumor resection without radiation therapy. However, there was no surgical mortality among our patients and no tumor-related deaths over a mean observation time of 65 months, whereas Weiner et al reported 5.4% postoperative mortality and 12.5% mortality from tumor, for a total mortality of 17.9% over a mean observation time of 49 months (12). As we were unable to collect reliable data for patient outcome other

than deaths, a clinical comparison with other reports in this respect cannot be made. However, when comparisons have been made of different treatment approaches within a single study, the morbidity and mortality rates tend to be greater in patients undergoing gross tumor resection (19, 20).

The recurrence rate in our patients who had subtotal tumor resection without irradiation is high (87%), with a median recurrence time of less than 1 year after surgery. This probably reflects the conservative surgical approach in our institution. The selection criteria for radiation therapy or phosphorous 32 instillation differed between neurosurgeons and over time during the study period. Most recurrent tumors were treated with radiation therapy, and eventually 29 of the 45 patients underwent external irradiation. Six additional patients received both external and internal irradiation (phosphorous 32), and three further patients received only internal irradiation. Overall, surgery without any type of irradiation was performed on only seven of the 45 patients.

In our series, patients with an intrasellar tumor component as a group were younger than those without any intrasellar component, and there was a similar strong trend with respect to presence versus absence of brain deformity or infiltration, with a higher percentage of adamantinomatous epithelium in the tumors with brain deformity or infiltration. These findings arguably could be used to support some of the previously reported differences between craniopharyngiomas in children versus adults, including differences in recurrence or prognosis, especially in patients treated with surgery alone and no radiation therapy. However, when we started our analysis by treating children and adults as separate groups, as opposed to analyzing the subgroups indicated above, these findings did not appear to be useful distinguishing characteristics and, importantly, did not appear to correlate well with either imaging versus histologic findings or tumor recurrence. Nevertheless, it is interesting to speculate whether some of these different trends might have assumed greater significance with respect to tumor recurrence if radiation therapy had not been used with such apparent benefit in so many of our patients. Furthermore, this at least in part may account for some differences between our findings and some of those reported previously.

In conclusion, craniopharyngiomas in our series could not be divided into two distinct histologic types, but they showed a spectrum of histologic features ranging from adamantinomatous to squamous epithelium, including transitional and mixed forms. No differentiating histologic or radiologic characteristics could be established for craniopharyngiomas in children versus adults. No histologic or radiologic characteristics could be used to predict tumor recurrence. Radiation treatment after conservative subtotal tumor resection was strongly associated with tumor regression or lack of recurrence.

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