

# Ectopic Recurrence of Craniopharyngioma after an Interhemispheric Transcallosal Approach: Case Report

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**OBJECTIVE AND IMPORTANCE:** Ectopic recurrence of a craniopharyngioma is a rare postoperative complication. We present a case of a craniopharyngioma that ectopically recurred along the tract of a previous surgical route.

**CLINICAL PRESENTATION:** A 73-year-old female patient presented 8 years earlier with a suprasellar craniopharyngioma. She underwent a right frontal craniotomy, with an interhemispheric transcallosal approach, for total microsurgical resection of the tumor. No postoperative radiotherapy was administered. Four years after surgery, magnetic resonance imaging studies revealed a well-circumscribed, heterogeneously enhancing, parasagittal mass with significant vasogenic edema in the right frontal lobe. Enlargement of the lesion was noted in subsequent radiological evaluations until 8 years after surgery, when the patient experienced a significant decline in neurocognitive status and the mass was surgically resected.

**INTERVENTION:** Gross total resection of a histologically confirmed craniopharyngioma was achieved.

**CONCLUSION:** To our knowledge, only eight previous case reports described the ectopic recurrence of a craniopharyngioma. Transplantation of tumor cells along the tract of a previous surgical route in six cases and dissemination in cerebrospinal fluid in two cases are presumed to be the primary mechanisms by which these ectopic recurrences occurred. The results of our literature review led us to conclude that total surgical resection, combined with careful inspection and irrigation of the surgical field, is the optimal treatment for preventing ectopic recurrences. Furthermore, it is recommended that, after primary craniopharyngioma resection, patients undergo long-term clinical and radiological follow-up monitoring for the rare development of an ectopically recurring tumor. (Neurosurgery 50:639–645, 2002)

**Key words:** Craniopharyngioma, Ectopic tumor, Intracranial tumor seeding, Recurrent tumor

Craniopharyngiomas are neoplasms that account for 2 to 3% of all intracranial tumors (4). These histologically benign tumors arise from the epithelial nests of Rathke's pouch, which is an embryological structure that develops into the anterior pituitary gland and surrounds the hypothalamic stalk. Microscopically, craniopharyngiomas consist of stratified epithelium that gradually enlarges into partially calcified, solid and cystic masses in the suprasellar region (13).

Although craniopharyngiomas exhibit a benign histopathological character, these tumors have a tendency to recur (19). Conventional treatment modalities for craniopharyngiomas include total surgical resection (15, 17, 19), subtotal removal (1, 9), and subtotal removal followed by radiotherapy (1, 15, 17). With all of these forms of treatment, recurrence is a disturbing complication (18).

It is highly unusual for a craniopharyngioma to recur in a site distinct from the region of the original tumor or its contiguous areas (12). The first report of remote tumor recurrence was presented by Sumi and Alvord (7, 13), who observed, during an autopsy, a suprasellar craniopharyngioma with associated bilateral cerebellopontine angle craniopharyngiomas. These findings suggest that cerebrospinal fluid (CSF) dissemination is one mechanism by which a primary craniopharyngioma can metastasize to different anatomic areas of the brain. Two additional cases involved dissemination of tumor through CSF, resulting in tumor recurrence in anatomic areas unrelated to the surgical route (5, 7). Six case reports described the ectopic recurrence of craniopharyngiomas after inadvertent seeding along the tract of a previous surgical route (2, 6, 8, 10, 12, 16). One of those cases occurred in the epidural space (10), another after repeated, stereotactically guided, needle aspiration (2), and four after intracranial seeding (6, 8, 12, 16).

We present a unique case of a craniopharyngioma that recurred in the frontal lobe 3 years after tumor resection via

a right frontal craniotomy involving an interhemispheric transcallosal approach. In addition, we review the literature on ectopic recurrent craniopharyngiomas and discuss the controversies surrounding the ideal management of these types of tumors.

## CASE REPORT

A 73-year-old Korean woman initially presented 8 years earlier with progressive headaches, dizziness, and loss of short-term memory. Magnetic resonance imaging (MRI) demonstrated significant hydrocephalus and a tumor in the anterior third ventricle. The patient underwent a right frontal craniotomy, with an interhemispheric transcallosal approach, for total resection of the tumor. A histopathological examination confirmed the diagnosis of a craniopharyngioma. Postoperatively, the patient developed many complications, including central hypothyroidism, diabetes mellitus, and diabetes insipidus. In addition, she developed deep venous thrombosis, requiring anticoagulation therapy, and subsequently developed massive lower gastrointestinal

bleeding, requiring multiple transfusions. No postoperative radiotherapy was administered.

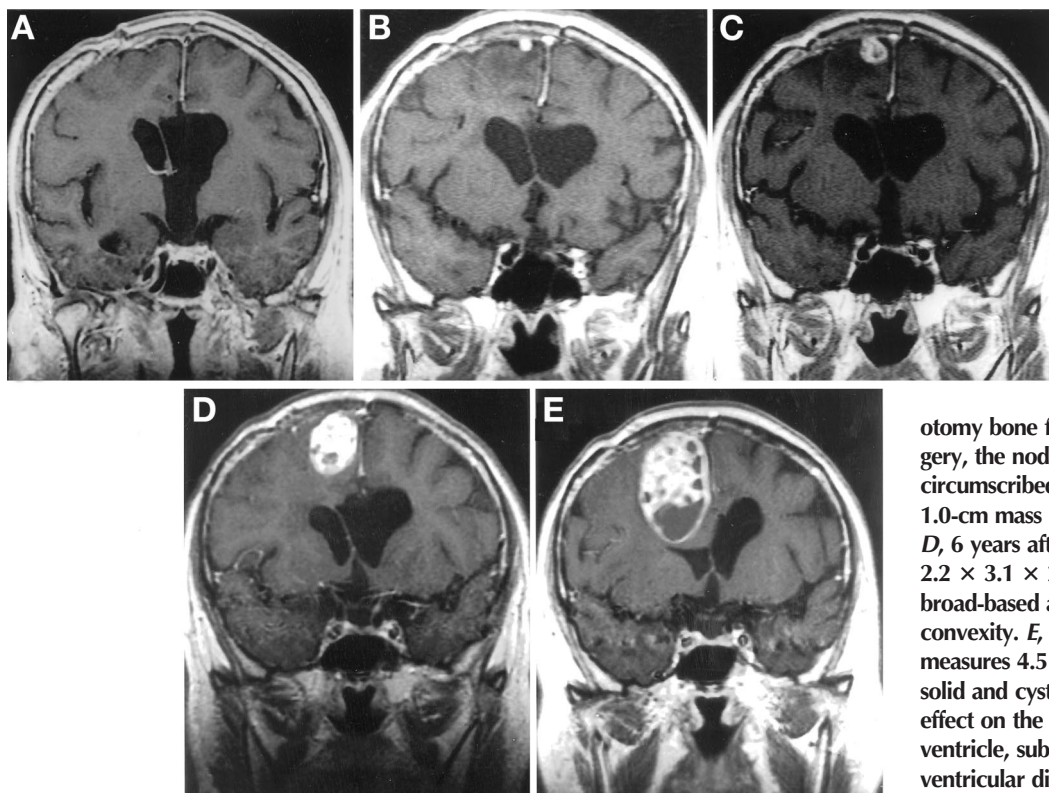
MRI scans obtained 1 year after surgery demonstrated no evidence of a recurrent suprasellar craniopharyngioma (Fig. 1A). Routine follow-up MRI scans obtained 3 years after surgery indicated no evidence of recurrence. During reevaluation 4 years after surgery, contrast-enhanced MRI scans revealed a well-circumscribed, heterogeneously enhancing, 1-cm nodule associated with moderate edema in the right frontal area, under the craniotomy bone flap (Fig. 1C). A review of previous radiological studies revealed that a smaller lesion (3 mm in diameter) was present at the same site on MRI scans obtained the previous year (Fig. 1B). It was decided that the patient would be monitored conservatively, with annual clinical and radiological evaluations.

Subsequent MRI scans demonstrated progressive growth of the patient's lesion in the right frontal lobe. Six years after surgery, the heterogeneously enhancing mass measured  $2.2 \times 3.1 \times 2.3$  cm and appeared to have a broad-based at-

tachment along the falx and convexity (Fig. 1D). Surgery was recommended at that time, but the patient and her family refused because of the complicated postoperative course after her original resection.

Eight years after surgery, the patient exhibited a decline in functional status, characterized by significant weakness, dizziness, and generalized fatigue. The patient also complained of intermittent headaches, which had begun occurring 4 months earlier. MRI scans were obtained (Fig. 1E) and demonstrated that the size of the convexity parasagittal mass in the right frontal region had doubled in size, to  $4.5 \times 3.0 \times 6.2$  cm, in the preceding 2 years. The lesion was noted to have both solid and cystic components. Vasogenic edema in the right frontal lobe was extensive, extending to the corpus callosum. There was also evidence of significant mass effect on the frontal horn of the right lateral ventricle, with subfalcine herniation and moderately dilated ventricles.

During surgery, the previous right frontal craniotomy was reopened, and an additional craniotomy flap was cre-



**FIGURE 1.** Coronal, T1-weighted, gadolinium-enhanced MRI scans obtained at various times throughout the postoperative course. *A*, 1 year after surgery, there is no evidence of a recurrent suprasellar craniopharyngioma. *B*, 3 years after surgery, a 3.0-mm, well-enhancing nodule is detected in the right frontal lobe, under the crani-

otomy bone flap. *C*, by 4 years after surgery, the nodule has grown into a well-circumscribed, heterogeneously enhancing, 1.0-cm mass in the right parasagittal region. *D*, 6 years after surgery, the mass measures  $2.2 \times 3.1 \times 2.3$  cm and appears to have a broad-based attachment along the falx and convexity. *E*, 8 years after surgery, the mass measures  $4.5 \times 3.0 \times 6.2$  cm, with both solid and cystic components. There is mass effect on the frontal horn of the right lateral ventricle, subfalcine herniation, and marked ventricular dilation.



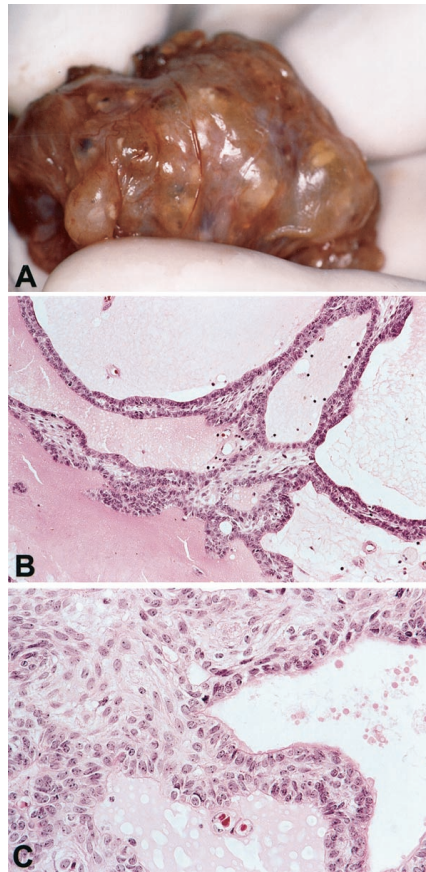
ated anterior to the previous flap. A well-circumscribed lesion was exposed below the dura. There was a well-delineated plane between the dura and the underlying tumor, as well as between the arachnoid membrane and the tumor. With microsurgical techniques, a plane was developed around the tumor and the arachnoid membrane. The tumor, including its cysts, was removed as a single mass (Fig. 2A). The cysts contained fluid that resembled crankcase oil. Histopathological analyses confirmed that the tumor was a craniopharyngioma (Fig. 2, B and C).

The patient experienced postoperative weakness in her left lower extremity, which steadily improved. MRI scans obtained 2 days after surgery confirmed complete removal of the mass. The patient was discharged from the hospital on the 12th postoperative day and continues to be monitored clinically and radiologically.

## DISCUSSION

The case we present has unique aspects that call attention to the interesting entity of ectopically recurring craniopharyngiomas. First, initial resection of the suprasellar craniopharyngioma was achieved via an interhemispheric transcallosal approach, for total microsurgical resection. Second, the recurrent tumor was parasagittal and well circumscribed, with heterogeneous enhancing characteristics. In addition, there was significant vasogenic edema in the right frontal lobe. Third, the differential diagnosis for a mass with these particular characteristics would most likely include a high-grade astrocytoma or an atypical meningioma, but the histopathological diagnosis revealed a recurrent ectopic craniopharyngioma.

To our knowledge, the ectopic recurrence of a craniopharyngioma is a rare postoperative complication that has been cited in only eight previously published case reports. Six reports in the literature described ectopic recurrence after transplantation of residual tumor cells along the tract of a previous surgical route (2, 6, 8, 10, 12, 16). One of those cases occurred in the epidural space (10), another after repeated, stereotactically guided, needle aspiration (2), and



**FIGURE 2.** Gross and microscopic histological analyses of the tumor. **A**, intact tumor mass resected from the parasagittal right frontal lobe. The tumor contained both solid and multiloculated cystic components. The cystic compartments were filled with brown-black fluid. Numerous calcifications were present. **B**, adamantinomatous craniopharyngioma with multiple cysts and a loose matrix (stellate reticulum) surrounded by a peripheral palisade of cells (original magnification,  $\times 40$ ). **C**, squamous tumor cells with peripheral palisading and cysts (original magnification,  $\times 64$ ).

four after intracranial seeding (6, 8, 12, 16), as demonstrated in our case. Two additional reports cited ectopic craniopharyngiomas after CSF dissemination, which resulted in recurrent tumors that were anatomically separate from both the primary site and the previous surgical tract (5, 7). Tables 1 and 2 contain a summary of these case reports of ectopic recurrent craniopharyngiomas.

In a review of the literature on ectopic recurrent craniopharyngiomas, other unique aspects of the case presented here can be appreciated. The age at presentation for the patients ranged from 5 to 73 years, with three pediatric patients (2, 6, 10), five adult patients (5, 7, 8, 12), and one patient of unknown age (16). At 66 years of age, our patient was the second oldest. For every case reported, the primary craniopharyngioma was located in the suprasellar region. Seven of nine patients, including our patient, underwent total surgical resection of the tumor (5–8, 12, 16). Of the two patients who did not undergo total surgical resection, one was treated with partial resection and drainage of the cystic tumor (10). The other was treated with subtotal resection and repeated puncture of the cystic tumor through right frontal craniotomy burr holes (2). Both of those patients received adjuvant radiotherapy (2, 10). The surgical approach for treatment of the initial craniopharyngiomas was a right frontal craniotomy for three patients, including our patient (5, 10), a right pterional craniotomy for one patient (8), a right subfrontal craniotomy for three patients (7, 10, 16), a right frontotemporal craniotomy for one patient (12), and repeated cyst punctures through right frontal lobe craniotomy burr holes for one patient (2). Three patients (2, 8, 10), including the two who were treated with subtotal resection and radiotherapy (2, 10), experienced recurrence of craniopharyngiomas in the suprasellar region before ectopic tumor recurrence.

The time between the initial presentation of the craniopharyngioma and evidence of ectopic recurrence ranged from 1 to 21 years. For our patient, radiological evidence of an ectopic recurrent craniopharyngioma in the right frontal lobe was noted 3 years after surgery. For six of nine patients, the period between presentations was 1 to 4 years (2, 6–8, 12). One patient, who had been treated with three resections, cyst drainage, and radiotherapy, developed an ectopic recurrent craniopharyngioma 21 years after his initial operation (10).

Determination of the relationship between the surgical approach to a primary craniopharyngioma and the ectopic site of recurrence is important for

**TABLE 1. Characteristics of the Primary Craniopharyngioma in Case Reports of Ectopic Recurrent Craniopharyngiomas**

Series (Ref. No.)	Age at Initial Presentation (yr)/Sex	Location of Primary Craniopharyngioma	Surgical Treatment of Primary Craniopharyngioma	Surgical Approach for Primary Craniopharyngioma	Radiotherapy for Primary Craniopharyngioma
Liu et al., 2002 (present study)	66/F	Suprasellar, anterior third ventricle	Total resection	Right frontal craniotomy with a transcallosal approach	None
Ito et al., 2001 (7)	62/M	Suprasellar	Total resection	Subfrontal craniotomy	None
Gupta et al., 1999 (5)	73/M	Suprasellar	Total resection	Right frontal craniotomy	None
Lee et al., 1999 (8)	31/M	Suprasellar	Total resection	Right pterional approach	None
Israel and Pomeranz, 1995 (6)	10/M	Suprasellar	Total resection	Right subfrontal craniotomy	None
Tomita and McLone, 1993 (16)	Unknown/Unknown	Suprasellar	Total resection	Right subfrontal craniotomy	None
Malik et al., 1992 (10)	6/M	Suprasellar	Partial resection and drainage of the cystic tumor	Right frontal craniotomy	Multiple radiation treatments, 2800 rad from a cobalt-60 source for 8 mo
Ragoowansi and Piepgras, 1991 (12)	47/M	Suprasellar, extending into the hypothalamus	Total resection	Right frontotemporal craniotomy with approach through the sylvian fissure and lateral terminalis	None
Barloon et al., 1988 (2)	5/M	Suprasellar	Subtotal resection and repeated punctures of the cystic tumor through craniotomy burr holes	Repeated cyst punctures through right frontal lobe craniotomy burr holes	Multiple radiation treatments of unspecified type and dose

understanding the mechanisms of spread after surgical manipulation. Ectopic craniopharyngiomas are thought to develop from the transplantation of tumor cells along the tracts of previous surgical routes, as well as through the seeding of tumor cells in the CSF, where remote sites of tumor recurrence are anatomically separate from the areas of the initial operations. Three of nine patients, including our patient, experienced ectopic craniopharyngioma recurrence in the frontal lobe (2, 6). One of nine patients experienced recurrence in the right temporal lobe along the surgical tract (8), one in the epidural space in the right frontal lobe (10), one in the right frontal subdural space (16), and one in the right frontal and temporal lobes (12). These seven of nine patients experi-

enced tumor recurrence along the tracts of previous surgical approaches.

Two patients developed tumor recurrence in areas with no anatomic relationship to the previous surgical tract (5, 7). The spread of tumor cells through CSF seeding is thought to be the mechanism underlying this phenomenon. In one of the cases, the ectopic craniopharyngioma occurred in the right temporal lobe, which was a region distinct from the area of the previous surgical approach, as confirmed by intraoperative observation (7). In the second case, the ectopic craniopharyngioma occurred in the left frontal and parieto-occipital lobes, contralateral to the initial right frontal craniotomy (5).

We agree with other authors (6–8, 10) that protecting the surgical area from

inoculation with tumor cells, inspecting the operative site for tumor fragments, and irrigating the surgical field can be effective strategies to prevent the recurrence of craniopharyngiomas in ectopic sites. However, it has not yet been determined which of the current treatment modalities for craniopharyngiomas, i.e., total surgical resection (15, 17, 19), subtotal removal (1, 9), or subtotal removal followed by radiotherapy (1, 15, 17), can prevent the ectopic recurrence of these tumors.

The results of our literature review led us to conclude that total surgical resection is the preferred treatment for preventing the rare complication of ectopically recurring craniopharyngioma. Seven of the nine patients in the reviewed reports, including our patient,

TABLE 2. Characteristics of the Recurrent Ectopic Craniopharyngioma in Case Reports of Ectopic Recurrent Craniopharyngiomas<sup>a</sup>

Series (Ref. No.)	Episodes Involving Recurrent Tumor in the Initial Location	Period between Initial Presentation and Evidence of Ectopic Recurrence (yr)	Radiological Findings of Recurrent Tumor	Location of Ectopic Recurrent Tumor	Treatment of Ectopic Recurrent Tumor	Presumed Cause of Ectopic Recurrent Craniopharyngioma
Liu et al., 2002 (present study)	None	3	MRI: enhancing convexity, 4.2 × 3.0 × 6.2-cm, parasagittal mass in the right frontal region, with solid and cystic components	Convexity parasagittal aspect of the right frontal lobe	Right frontal craniotomy	Seeding along the tract of the surgical route
Ito et al., 2001 (7)	None	3	MRI: enhancing cystic and solid mass in the right temporal cortex	Right temporal lobe	Right temporal craniotomy	Cerebrospinal fluid seeding
Gupta et al., 1999 (5)	None	7	MRI: two dura-based, lobulated, enhancing lesions in the left frontal and parieto-occipital lobes	Left frontal and parieto-occipital lobes	Left craniotomy	Meningeal seeding through cerebrospinal fluid
Lee et al., 1999 (8)	1 yr postoperatively, tumor recurred in the suprasellar region; second operation via a right pterional approach	3	MRI: five well-enhanced nodules (5.0–10.0-mm diameter) along the right sylvian cistern, in the anteromedial aspect of the right temporal lobe	Anteromedial aspect of the right temporal lobe	Right pterional craniotomy; gamma knife surgery for remaining nodules	Seeding along the tract of the surgical route
Israel and Pomeranz, 1995 (6)	None	2	CT: 4-cm, ring-enhancing lesion in the right frontal and subfrontal regions, with significant surrounding edema	Right frontal lobe	Right subfrontal craniotomy	Seeding along the tract of the surgical route
Tomita and McLone, 1993 (16)	None	Unknown	MRI: enhancing lesion in the right frontal subdural space	Right frontal subdural space	Right frontal craniotomy	Seeding along the tract of the surgical route
Malik et al., 1992 (10)	Within 1 yr postoperatively, the patient underwent a second partial resection of the tumor; 2 yr postoperatively, the patient developed visual changes and underwent a third operation, which involved total resection of the tumor and hypophysectomy	21	CT: partially calcified, 3.5-cm, cystic, epidural lesion in the right frontal area; MRI: extra-axial right frontal mass with high signal intensity	Epidural right frontal region	Right frontal craniotomy	Seeding into the epidural space during surgical manipulation
Ragoowansi and Piegras, 1991 (12)	None	1	MRI: 2.5 × 1.5-cm, enhancing nodule in the anterior aspect of the right sylvian fissure	Right frontal and temporal lobes	Right frontotemporal craniotomy	Seeding along the tract of the surgical route
Barloon et al., 1988 (2)	Subtotally resected suprasellar tumor enlarged	4	CT: well-defined, high-density mass in the right frontal lobe, with minimal edema and calcification, and low-density, suprasellar craniopharyngioma with calcification; MRI: linear needle tract extending inferiorly from the mass in the frontal lobe toward the suprasellar craniopharyngioma	Right frontal lobe	Needle biopsies	Seeding from the suprasellar craniopharyngioma from multiple needle aspirations

<sup>a</sup> CT, computed tomography; MRI, magnetic resonance imaging.



were treated with total surgical excision of their original suprasellar tumors (5–8, 12, 16). The use of adjuvant radiotherapy for the remaining two patients (2, 10) was not effective in preventing ectopic tumor recurrence. These patients also developed recurrent tumors in the suprasellar region and in an ectopic site. Although radiotherapy may inhibit tumor growth, it is associated with serious side effects, such as radiation necrosis, vasculopathy, endocrine deficiency, optic neuritis, dementia (19), and the development of secondary tumors, including malignancies (3, 11).

## CONCLUSION

To our knowledge, we present the ninth case of an ectopically recurring craniopharyngioma along the tract of a previous surgical route. Tumor recurrence, whether at a local or ectopic site, is attributed to the replication of residual epithelial cells (4). It has been suggested that neoplastic cells that are inadvertently spilled during a surgical procedure have the ability to undergo mitosis at the operative site and develop into an isolated ectopic recurrence (6). Protecting the surgical area from tumor cell inoculation is critical (6–8, 10), because a residual tumor mass or fragment deposited in the surgical field may be sufficient for development of a recurrent craniopharyngioma. It is important to recognize that this complication can be prevented with careful inspection and irrigation of the operative site (10). Furthermore, it is recommended that, after the resection of a primary craniopharyngioma, patients undergo long-term clinical and radiological follow-up monitoring for the rare but possible development of an ectopically recurring tumor.

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## COMMENTS

The value of this case report is that it reminds us of the possibility of ectopic recurrence of craniopharyngiomas after the use of a transcallosal surgical approach for tumor removal. Therefore, when an intra-

cranial tumor is discovered along the surgical route for a previously resected craniopharyngioma, the possibility of an ectopic recurrent craniopharyngioma should be considered in the differential diagnosis.

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In this report, Liu et al. present a case of a recurrence of craniopharyngioma along the surgical trajectory after an interhemispheric transcallosal approach. In the experience of the senior commentator with the treatment of 162 craniopharyngiomas, one case of tumor recurrence on the falx along the interhemispheric transcallosal surgical route was recognized. These reports demonstrate that craniopharyngiomas are resilient lesions with a predilection for recurrence at the initial site or, in rare cases, at the surgical trajectory site, as illustrated here. Because of this type of tumor behavior, we advocate aggressive resection during the initial operation, when safely possible. In cases in which the tumor extends to the foramen of Monro, with unilateral or bilateral hydrocephalus, and adhesions are suspected in this region, we use a combined pterional-transcallosal approach to achieve maximal tumor resection during the initial operation. The pterional approach alone may limit access to the superior and posterior portions of the tumor within the third ventricle, even after the lamina terminalis has been opened. The pure transcallosal-transforaminal approach, however, may limit access to the anterosuperior portion of the tumor under the optic chiasm and limits the ability to release tumor adhesions to branches of the anterior communicating artery (1). The authors conducted long-term follow-up monitoring of their patients, and their report calls attention to this rare but clinically significant form of recurrence in craniopharyngioma management.

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- Yaşargil MG: *Microneurosurgery: Microneurosurgery of CNS Tumors*. Stuttgart, George Thieme, 1996, vol IVB, pp 205–223.

The authors describe a unique case of ectopic recurrence after transcallosal removal of a third ventricular craniopharyngioma. The old age of the patient (73 yr) and the very slow progression of the tumor deserve to be mentioned.

A more accurate explanation of metastatic tumor in this case involves implantation of craniopharyngioma cells along the surgical route. This type of craniopharyngioma recurrence is probably not so rare, but it is impossible to distinguish such recurrence from original tumor progression if tumor cell implantation occurs not far from the primary tumor nest.


The biological activity of the tumor may play an important role in craniopharyngioma recurrence. Our investigation of proliferative activity via mea-

surement of the labeling index for topoisomerase II (or Ki-67) deoxyribonucleic acid demonstrated that elevation of the topoisomerase II deoxyribonucleic acid labeling index above 1.0 was strongly correlated with tumor recurrence.

Our observations included two cases of distant metastatic recurrence of craniopharyngioma. In the first case, a 29-year-old female patient underwent a right frontotemporal craniotomy. A suprasellar craniopharyngioma was totally removed. At 6 months, two metastatic lesions in the right parietal and frontal lobes were detected. Both tumors, which were determined in microscopic investigations to be adamantinomatous craniopharyngiomas, were successfully removed.

In the second case, involving a 32-year-old male patient, a secondary tumor (1 cm in diameter) in the fourth ventricular cavity was revealed by routine magnetic resonance imaging 2 years after resection of a papillary third ventricular craniopharyngioma. In that case, ultrasonographic aspiration was used for tumor removal. This method of tumor ablation probably results in tumor cell dispersion, facilitating cell spread along the subarachnoid space. It is noteworthy that, in both cases, immunohistochemical studies revealed high scores for both Ki-67 and topoisomerase II deoxyribonucleic acid.

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