RETREATMENT OF RECURRENT CYSTIC CRANIOPHARYNGIOMA WITH CHROMIC PHOSPHORUS P 32

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A cystic craniopharyngioma in a two-year-old boy recurred six months after surgery and postoperative external-beam radiotherapy. Successful retreatment was accomplished with radioisotope injection of 0.5 mCi of chromic phosphorus P 32 into the intracranial cyst, which delivered approximately 300.00 Gy to the cyst wall. The patient's symptoms were relieved, and he is without evidence of disease or cystic fluid accumulation four years after intracavitary ^{32}P irradiation.

Craniopharyngioma is a histologically benign, slow-growing childhood suprasellar tumor, which arises from the embryonic remains of the craniopharyngeal (cranio-buccal) duct[1] and frequently exhibits a locally malignant clinical behavior[2] by attaching to, or pressing on, adjacent hypothalamic structures, pituitary, temporal lobes of the brain, internal carotid artery, optic chiasm, and cavernous sinus. Approximately 60 percent of these tumors occur in the form of a single large cyst.[3] Permanent neurological complications, such as visual field loss and cranial nerve deficits, result from pressure effects of the adjacent cyst on the optic chiasm and cavernous sinus. An acute rupture of a cyst can result in rapid neurological deterioration. Evacuation of the cyst is a temporary measure used to relieve cystic pressure; however, early refilling of the cyst usually occurs.[4-8] Intermittent aspiration of the cystic contents by stereotaxic puncture[9] or drainage via Ommaya systems[10,11] frequently fails to control cystic fluid secretion.[12] Intracystic chemotherapy[13] has been tried without success.

Unfortunately, craniopharyngiomas are frequently considered inoperable[14] due to extensive local attachment of the cyst wall to adjacent vital structures. In a series of children treated by radical excision of craniopharyngiomas, Katz[15] noted that children whose tumors had a large cystic component generally did less well than those with noncystic tumors. This was attributed to the fact that it was easy for the surgeon to lose contact with the extremely thin sinus cyst wall, which later resulted in tumor recurrence.

Today there are strong advocates and many reports of good local control for both radical surgical extirpation[1,15,16] and limited surgery followed by postoperative radiotherapy.[16-18] Although there have been no controlled comparative studies, the latter approach offers the maximum chance of local control with minimal morbidity, and has become the preferred treatment method in the United States.

Cases of large cystic craniopharyngiomas are more difficult to manage because there is a reduced chance for complete total surgical excision and an increased chance for local recurrence following surgical excision.[15] The mortality and morbidity following reoperation for these recurrent cases, even in the absence of previous external-beam radiotherapy, is exceedingly high.[15] Because of these problems, a successful alternative mode of therapy for recurrent cystic craniopha-

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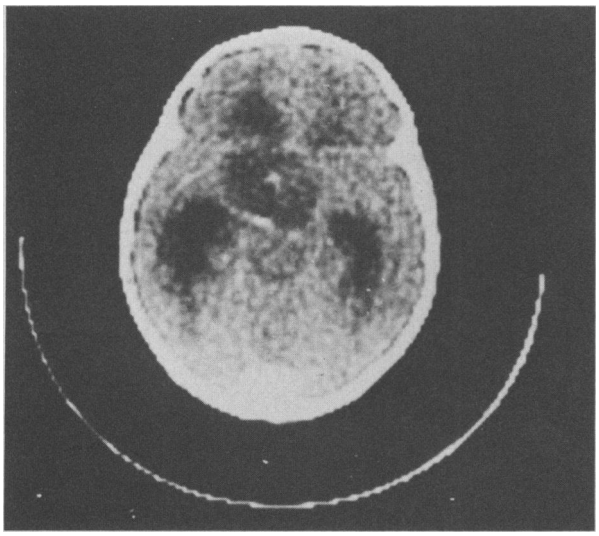

Figure 1. A large suprasellar cystic craniopharyngioma with central and cyst wall calcification can be seen on computed tomography scan

ryngiomas has been gradually developed, first in Europe and later in Japan—treatment by stereotaxic instillation of radioisotopes into the craniopharyngioma cyst. Leksell and Liden[19,20] first introduced (1951) the technique of stereotaxic injection of phosphorus P 32 into the craniopharyngioma cyst in order to destroy the secreting epithelium. Klar[21] (1953) treated two patients in this way with satisfactory results. Later, many other European and Japanese authors also reported good results following stereotaxic intracranial injection of various radioisotopes including gold Au 198, yittrium Y 90 and phosphorus P 32.

Unfortunately, this successful modality has been used only infrequently in the United States. In 1963 Overton and Sheffel[22] at the University of Texas reported a 26+ month remission after instillation of 1 mCi of ^{32}P into a cystic craniopharyngioma in an 18-year-old man. In 1969, Trippi et al,[14] in California, reported successful treatment of cystic craniopharyngioma in two patients with an Ommaya system after repeated instillation of 1 mCi of ^{32}P into the balloon catheter within the cyst. In 1980, Gunby[23] reported improvement in a 6-year-old girl following intracavitary injection of 0.5 mCi ^{32}P. The authors' recent experience with successful retreatment of a recurrent craniopharyngioma via intracystic injection of chromic ^{32}P in a 2-year-old boy is described in the following case report.

CASE REPORT

In December of 1980, a 2-year-old, black, male child was admitted to hospital for dehydration with a one-week history of vomiting. On examination the child was lethargic. The head circumference was 49 cm, which is at the 50th percentile. Height was at the 10th percentile and weight was at the 5th percentile. Neurological examination revealed slight nuchal rigidity. Fundoscopic examination was normal. All cranial nerves were normal except the eighth on the right. There was slight facial asymmetry on the right side when he smiled. Deep tendon reflexes were slightly increased symmetrically in the lower extremities compared with the upper extremities. The patient's gait was abnormal in that he had posturing, and he was clumsy on the right side when he ran. A spinal tap revealed increased intracranial pressure. An x-ray film of the skull revealed suprasellar calcification and the sutures were at the upper limits of normal width. A computed tomography (CT) scan of the head showed a midline suprasellar cystic lesion with asymmetric ventricular dilatation, the left ventricle was larger than the right (Figure 1).

A clinical diagnosis of craniopharyngioma was made, and a left frontal craniotomy was performed; the cyst was drained; and the cyst wall was resected. The pathological examination of the tissue confirmed the diagnosis of craniopharyngioma.

A postoperative CT scan of the head showed complete resolution of the cyst. No postoperative irradiation was given at this time. The patient returned to the hospital in June 1981, with asymmetry of the right side of the face. A repeat CT scan of the head revealed a recurrent suprasellar cyst with ventricular dilatation. Under fluoroscopy, 11 mL of yellowish fluid was aspirated from the cyst, and a left ventriculo-peritoneal shunt with a left temporal Richam reservoir was put in place to decompress the ventricles. The patient received 40.00 Gy in five weeks to the suprasellar area through a 5×5 cm port using 10 meV photons. The patient was well until September of the same year, when a follow-up CT of the head showed a reaccumulation of fluid in the suprasellar cyst. Under fluoroscopy the cyst was aspirated and 3 mL of metrizamide was injected into the cyst to determine that the needle was in the cyst and the cyst was not communicating with the ventricu-

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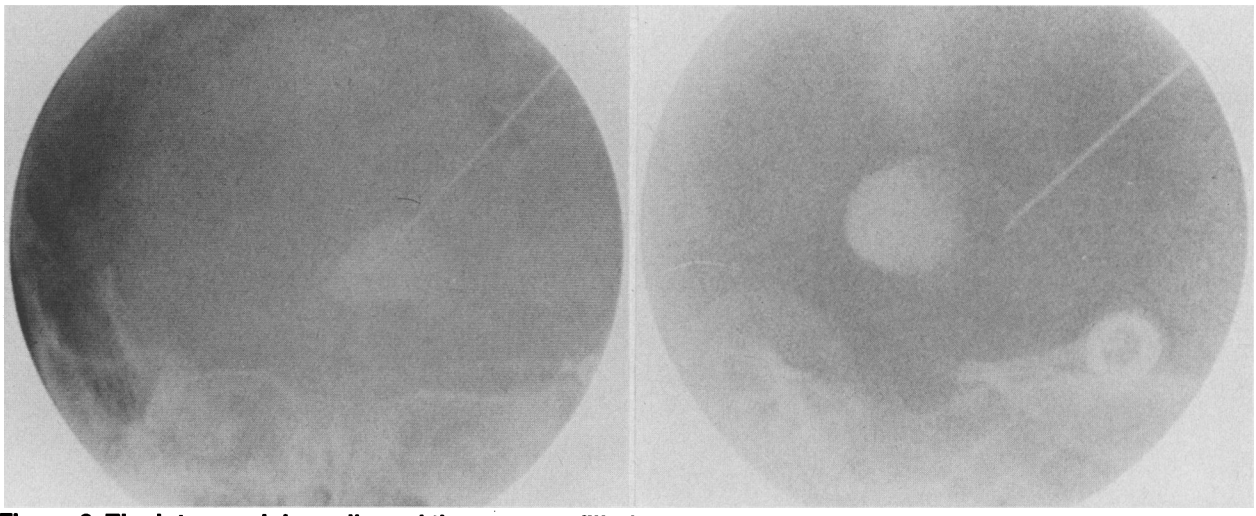

Figure 2. The intracranial needle and the contrast-filled cyst just prior to final aspiration and ^{32}P injection are seen on intraoperative anterior-posterior (left) and lateral (right) skull x-ray films

lar system (Figure 2). The remainder of the cystic fluid was then aspirated, and 5 mL of ^{32}P with an activity of 0.5 mCi was instilled into the cyst, and the needle was removed. There were no postoperative complications from the procedure, and the patient was discharged the next day on tapering doses of prednisone. The patient was followed with repeat CT scans of the head. A CT scan of the head in November 1982 showed complete resolution of the suprasellar cyst with an area of calcification (Figure 3).

DISCUSSION

Intracavitary irradiation with instillation of radioactive chromic phosphorus P 32 in the treatment of recurrent cystic craniopharyngioma has the advantages of high probability of long-term local control combined with low operative morbidity and mortality.[3,4,9,12] Essentially no radiation reaches vital structures beyond the cyst wall. For most patients with recurrent cystic craniopharyngiomas who have received prior external-beam radiotherapy, the surrounding brain, hypothalamus, and optic chiasm will have received tolerance doses of radiation, and further external-beam radiotherapy cannot be safely delivered without great risk of brain necrosis, temporal bone necrosis, or permanent optic nerve damage and blindness. On the other hand, reoperation of recurrent cystic craniopharyngiomas has been associated with an unacceptably high postoperative morbidity and mortality rate.[15]

Because ^{32}P is a pure beta-emitting isotope with an ideal mean energy of 0.69 meV,[24] the secretory cells within the cyst wall can be theoretically ablated effectively without unnecessarily irradiating adjacent structures. These physical characteristics allow re-irradiation of the cyst wall with chromic ^{32}P in the retreatment of recurrent cystic craniopharyngiomas in patients who have undergone surgery and received postoperative external-beam radiotherapy. The maximum range of the beta particle (with a maximum kinetic energy of 1.71 meV[24]) in soft tissue is 7.9 mm, and less than 50 percent of the given dose penetrates beyond 0.8 mm.[12] Even with these ideal physical characteristics of the ^{32}P source, in order to prevent accidental overdosage, during the treatment-planning stage, it must be kept in mind that critical and radiosensitive structures, such as optic chiasm and cavernous sinus with its contents, can be directly attached to the thin cyst wall and may be separated by a distance of less than 1 mm.

Yittrium 90 is another ideal radioisotope for intracystic irradiation because it is also a pure beta emitter, but it has a half-life of 64 hours, a slightly higher mean energy of 0.93 meV,[12] and a higher maximum energy of 2.27 meV.[24] Gold 198 has also been used for intracystic irradiation, but in addition to two different beta particles, there are three separate gamma emissions,[24] which could give a significant dose to tissues at some distance from the source. Although the proportion of gamma emission is a small percentage of the total

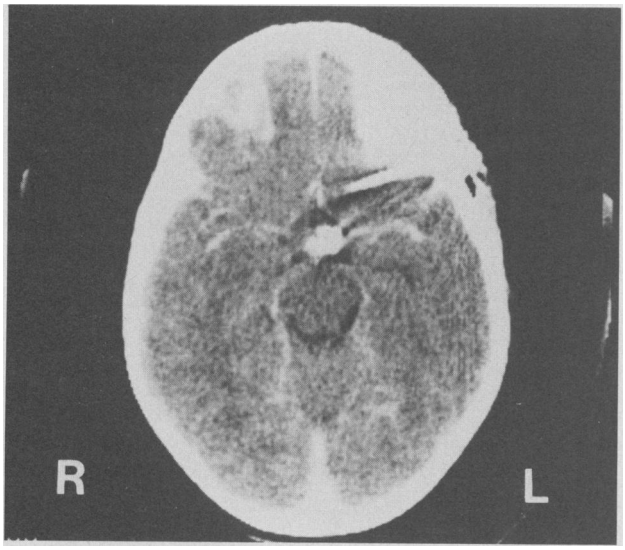

Figure 3. One year after intracavitary instillation of 5 mL of ^{32}P with a total activity of 0.5 mCi, the cyst with residual suprasellar calcification is seen completely collapsed on computed tomography scan of the head

beta emission, this gamma emission makes ^{198}Au a less than ideal radioisotope for the retreatment of previously irradiated patients.

There is a theoretical, radiobiological advantage[25,26] to the use of intracystic ^{32}P over ^{90}Y in treating the secretory cellular layer of these cystic craniopharyngiomas because ^{32}P with a 14.3 day half-life[24] provides a source of continuous low dose-rate irradiation that is theoretically superior to the higher dose rate produced by ^{90}Y with a much shorter (64 hour) half-life. For example, with activities that deliver 200.00 Gy to the cyst wall, in the first 10 hours ^{90}Y produces a dose rate of 206 rad/h compared with 40 rad/h for ^{32}P.

Dosimetry

Using the methods of Kobayashi et al[12] and Loevinger and colleagues[27] for beta-particle emission, the radiation dose at the cyst wall and at a chosen distance from the wall can be calculated beforehand as a function of the estimated volume of the cyst and the desired amount of ^{32}P activity. Although the optimum dose for treatment of cystic craniopharyngioma remains to be determined, Kobayashi et al[12] recommend that the optimum safe dose to the cyst wall is between 90.00 to 300.00 Gy. Kobayashi and associates[12] reported the development of damage to the third cranial nerve attached to a thin cyst wall, which received a dose of 1000.00 Gy. In the case reported here, 5 mL of 0.5 mCi of ^{32}P was administered, which delivered approximately 300.00 Gy to the cyst wall.

Complications

It has been presumed that most of the ^{32}P activity remains in the cyst cavity following injection,[14] and it appears to have a great affinity for the walls of the cyst upon which it becomes plated.[28,29] Inhomogenieties during this plating period may possibly result from the effects of gravity on the mixture, as in Riechert and Mundinger's case[30] where the extra accumulation of ^{32}P on the inferior portion of the cyst resulted in a complication. In 1956, Riechert and Mundinger[30] reported the development of an inflammatory intracystic radiation reaction due to a high collection of radioactive chromic phosphate in the inferior part of the cyst, which led to a complete cavernous sinus syndrome nine days after stereotactic instillation of 2.5 mCi of chromic ^{32}P. For this reason, intraoperative and postoperative prophylactic use of a systemic steroid may be indicated to prevent complications related to acute inflammation.

There are various methods used to introduce the isotope into the cyst. In the case described here, a direct intracranial puncture through a burr hole with an injection of metrizamide contrast was used, followed by fluid aspiration, then injection of chromic ^{32}P under C-arm fluoroscopic guidance, combined with preoperative treatment planning, computed head tomography, and angiography. One possible complication of this method of application is leakage of ^{32}P into the ventricular system through the needle track, although this has not been reported to date. Also, after the needle is removed, there is no vent for increased cystic pressure. Excessive intracranial vasospasm may infrequently result from intracranial needle puncture of a vessel. Backlund[9] reported one such complication in a series of 14 consecutive patients with cystic craniopharyngiomas treated with intracavitary ^{90}Y. Removal of 25 mL of cystic fluid was followed by visual improvement, but deterioration of mental status and coma followed. Immediate carotid angiography showed complete occlusion of the anterior cerebral artery on the side of the puncture with an excessive vasospasm, resulting in death. Use of the Ommaya drainage system is initially more invasive, but may avoid these types of problems.

CONCLUSION

Use of radioisotope therapy with chromic ^{32}P is an effective and safe treatment method for management of recurrent cystic craniopharyngiomas. Recently, Strauss et al[3] in Germany reported that 8 of 11 patients with cystic craniopharyngioma had significant volume decrease in the cyst following delivery of 200.00 Gy to the cyst wall after a ^{90}Y injection. Kobayashi and associates in Japan reported elimination of fluid or collapse in all cysts in 8 of 8 patients followed for 13 to 156 months after injection of either ^{32}P or ^{198}Au through an Ommaya drainage system.[12] Backlund in Sweden reported on 12 patients with cystic craniopharyngiomas treated with intracavitary injections of ^{90}Y delivering a dose to the cyst wall of approximately 200.00 Gy. X-ray films showed a gradual decrease of the size of the cysts, and all cases with symptoms and signs due to increased intracranial pressure obtained relief. The treatment also rescued threatened optic pathways.[9]

The case described here represents one of the few cases in which this method of therapy was used in the United States. The patient with recurrent cystic craniopharyngioma was successfully treated via an intracystic injection of chromic ^{32}P. Complete elimination of the cyst was obtained without radiation-related complications, even though the patient had been treated previously with surgery and full doses of external-beam megavoltage radiotherapy. The patient is doing well, now six years of age, four years after retreatment with intracavitary chromic ^{32}P.

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