Internal irradiation for cystic craniopharyngioma

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The authors report the results of internal irradiation with labeled chromic phosphate ($^{32}$P) and gold-198 ($^{198}$Au) colloid in eight cases of cystic craniopharyngiomas. They used a newly developed dosimetric formula, by which the radiation dose at the cyst wall and at any point far from the radioactive source can be calculated. Ten courses of irradiation in eight patients were carried out by injection of either $^{32}$P or $^{198}$Au colloid into the cyst through an Ommaya drainage system that had been placed at craniotomy. Follow-up studies ranging from 13 to 156 months revealed that all cysts were effectively treated, with elimination of fluid or collapse of the cyst. This was confirmed by Conray cystography and/or computerized tomography.

Not only the dose delivered to the wall but also the thickness of the cyst wall and the location of the cyst are important factors in planning internal irradiation. A safe and adequate dose to the cyst wall could range between 9000 to 30,000 rads for craniopharyngioma. This treatment is suitable for large cysts that are thought to be difficult to remove radically, recurrent cysts resistant to previous treatment, or multiple cysts. Internal irradiation may also be applicable in other cystic intracranial tumors if dosimetry is calculated accurately.

KEY WORDS • cystic craniopharyngioma • internal irradiation • dosimetry • radioisotope • gold • phosphate

It is well known that the majority of patients with craniopharyngiomas have a single large cyst or multiple cysts, and such cystic tumors are often resistant to radical operation.

Sudden onset and rapid progression of neurological signs and symptoms are attributed to increased volume or rupture of the cyst in such patients. Various treatment modalities have been advocated to alleviate or decrease the secretion of cyst fluid. They are 1) intermittent aspiration of the cyst by stereotaxic puncture or by placement of an Ommaya drainage system; 2) intracystic corrosion of the cyst wall by a fixative solution or chemotherapeutic agents; and 3) internal irradiation with radioisotopes.

The former two methods have often been unsuccessful in controlling fluid secretion. However, internal irradiation has the theoretical potential of eradicating the tumor and alleviating fluid secretion with proper dosimetry.

Summary of Cases

Technique

Before internal irradiation, the patients are subjected to craniotomy for identification of the cyst and placement of the Ommaya drainage system into the subgaleal space. Pathological diagnosis of the tumor is established, and the location, thickness, and shape of the cyst can be measured directly. Two weeks later, when the system becomes “fixed,” the reservoir is tapped to check if the cyst-drainage system is an enclosed cavity. This is confirmed by the introduction of a small amount of air or positive contrast material into the cyst. The volume of the cyst is determined by cystography or, recently, by computerized tomography (CT).

The irradiation schedule is agreed between the neurosurgeon and radiotherapist based on the above data. The simple beta-particle formula for dosimetry developed by Loevinger, et al., was used previously; however, in most of the present cases, doses were determined using our formula (Appendix). This calculation has allowed the protection of the surrounding vital tissues from radiation injury. Volume-dose relationship and distant dose can be tabulated by a computer from the formula.

Based on the dosimetric formula, a certain amount of radioisotope, which mainly emits beta particles, is introduced into the cyst via the Ommaya reservoir,
TABLE 1

Results of internal irradiation for cystic craniopharyngiomas

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs), Sex</th>
<th>Radioisotope, Dose (mCi)</th>
<th>Cyst Volume (cc)</th>
<th>Cyst Wall Width (mm)</th>
<th>Cyst Wall Dose (rads)</th>
<th>Effectiveness*</th>
<th>Follow-Up Period (mos)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5, M</td>
<td>^198^Au, 20.0</td>
<td>120.0</td>
<td>0.5</td>
<td>6000</td>
<td>±</td>
<td>6</td>
</tr>
<tr>
<td>2</td>
<td>4, M</td>
<td>^198^Au, 20.0</td>
<td>90.0</td>
<td>0.5</td>
<td>9000</td>
<td>+</td>
<td>50</td>
</tr>
<tr>
<td>3</td>
<td>15, M</td>
<td>^198^Au, 10.0</td>
<td>40.0</td>
<td>1.0</td>
<td>8000</td>
<td>++</td>
<td>57</td>
</tr>
<tr>
<td>4</td>
<td>21, F</td>
<td>^32^P, 2.5</td>
<td>20.0</td>
<td>-</td>
<td>16,000</td>
<td>+++</td>
<td>69</td>
</tr>
<tr>
<td>5</td>
<td>62, M</td>
<td>^198^Au, 10.0</td>
<td>16.0</td>
<td>0.5</td>
<td>20,000</td>
<td>+++</td>
<td>39</td>
</tr>
<tr>
<td>6</td>
<td>16, F</td>
<td>^32^P, 3.7</td>
<td>60.0</td>
<td>2.0-7.0</td>
<td>29,000</td>
<td>+</td>
<td>69</td>
</tr>
<tr>
<td>7</td>
<td>26, M</td>
<td>^198^Au, 10.0</td>
<td>10.0</td>
<td>&lt; 0.5</td>
<td>30,000</td>
<td>+++</td>
<td>38</td>
</tr>
<tr>
<td>8</td>
<td>39, M</td>
<td>^32^P, 5.0</td>
<td>5.0</td>
<td>&lt; 0.5</td>
<td>&gt; 100,000</td>
<td>+++++</td>
<td>69</td>
</tr>
</tbody>
</table>

* Effectiveness ranged from ± (equivocal) to +++ (excellent).
† Death due to tumor regrowth.
‡ This patient developed third nerve palsy.

and scheduled irradiation is started. The changes in the cyst size are checked periodically during and after the irradiation by cystography or CT.

Results

We performed 10 courses of internal irradiation in eight cases of cystic craniopharyngioma, using chromic phosphate (^32^P) or gold-198 (^198^Au) colloid (Table 1). The cysts were all (except one in Case 8) more than 10 ml in volume. Three cysts were huge, more than 60 ml in volume (Cases 1, 3, and 6), and radical removal was considered too difficult. Three patients had multiple cysts (Cases 1, 2, and 3). Another three patients (Cases 4, 5, and 8) had unmanageable cysts, and repeated taps were necessary to combat the accumulation of the cyst fluid. In the two remaining patients (Cases 6 and 7), tumors with cysts recurred after previous surgery and external irradiation. Eight courses of irradiation were performed under our scheduled dosimetry. Two cases (Cases 4 and 8) had initially been treated empirically.

The effects of internal irradiation determined over a follow-up period of 13 to 156 months were excellent in all cysts, with reduction of cyst fluid retention and/or collapse of the cyst. One patient (Case 4) died 13 years after the initial treatment from regrowth of the tumor, although the irradiated cyst had collapsed. The other patient with poor outcome developed permanent unilateral oculomotor palsy after the treatment, but the cyst had collapsed and no reaccumulation of the cyst fluid or tumor recurrence was found in more than 5 years.

Illustrative Cases

Case 1

This 5-year-old boy had loss of vision in his right eye and facial palsy 6 months prior to admission. He was brought to our department on January 19, 1976, with severe headaches and vomiting. Craniopharyngioma was suspected because of radiographic evidence of suprasellar calcification and an enlarged sella. A ventriculoperitoneal shunt was placed for hydrocephalus, and a left frontotemporal craniotomy with partial removal of solid tumor from the suprasellar region was carried out on February 10, 1976. Extracranial drainage of the associated cyst was performed.

Two months following the operation, the patient had the onset of right hemiparesis, headaches, high fever, and episodes of unconsciousness. Neuroradiological examinations revealed a huge mass in the left frontoparietal region, associated with subfrontal and suprasellar masses. At a second craniotomy on May 17, three isolated cysts were found in the left frontal lobe, the left subfrontal region, and the suprasellar region respectively. Each cyst was connected to the solid calcified tumor. A different drainage system was set up for each cyst. A schedule of internal irradiation was made for the largest cyst: the volume of the cyst was measured as 120 ml by cystography (Fig. 1A), and 20 mCi of ^198^Au colloid was injected on December 18, 1976. The dose at the cyst wall was determined as 6000 rads.

Fluid formation in the cyst continued for 3 months after irradiation, and repeated aspiration of 30 to 40 ml of fluid per week was necessary. Conray cystography at 4 months after irradiation showed a slight decrease in the size of the cyst, but its volume was still 90 ml (Fig. 1B). A second course of irradiation of the same cyst was scheduled and another 20 mCi of ^198^Au colloid was injected into the cyst on October 10, 1976 (Fig. 1C). The size of the cyst was evaluated by repeat CT. Fluid accumulation decreased at 2 months and stopped at 5 months after the second treatment. At 5 months, CT showed a huge collapsed cyst (Fig. 1D). At present, 4 years after the initial treatment, the
FIG. 1. Case 1. Conray cystograms (upper) and comput-
erized tomography scans of a huge cyst (lower). A: A huge
cyst, one of multiple cysts, with a 120-ml volume, is seen in
the left frontal lobe. B: Four months after irradiation with
20 mCi of radioactive gold, the volume of the cyst was
measured as 90 ml. C: Another 20 mCi of radioactive gold
was injected into the same cyst. D: The cyst is collapsed
5 months after the injection.

patient is doing well and attending elementary school.
The other two cysts are still untreated.

Case 2

This 4-year-old boy's symptoms began with head-
aches and vomiting in December, 1974. Plain skull
films revealed suprasellar calcification and sellar en-
largement. Carotid angiography and pneumoventriculography showed a suprasellar mass with marked
hydrocephalus, suggesting craniopharyngioma. A
ventriculoperitoneal shunt was placed, and a right
frontotemporal craniotomy on January 7, 1975, re-
vealed a large suprasellar cystic craniopharyngioma.
Biopsy of the cyst wall and evacuation of the cyst
fluid were carried out. The cyst was drained into the
subgaleal space using an Ommaya drainage system.
The patient recovered well after these procedures;
however, frequent taps of the Ommaya reservoir were
necessary to control the fluid retention. On March 9,
cystograms using Conray instilled into the Ommaya
reservoir revealed a large, irregular-shaped cyst in the
suprasellar region (Fig. 2A). The calculated volume
was 15 ml, and no leakage of the dye into the sub-
arachnoid space or ventricular system was found.
Internal irradiation was initiated by injection of 2.3
mCi of radioactive chromic phosphate into the cyst.
The dose to the wall was calculated according to our
formula to be about 17,000 rads. Following initial
periods of hypersecretion, the fluid retention de-
creased by 2 months postoperatively, and the cyst was
almost collapsed at 6 months (Fig. 2B).

The patient was doing well until November 12,
1975, when he developed sudden left hemiparesis. A
new mass lesion was found in the interpeduncular
fossa. A right frontotemporal craniotomy on Decem-
ber 5 revealed the collapsed suprasellar cyst at the
prechiasmatic cistern and a new thin-walled cyst oc-
cupying the interpeduncular fossa. The irradiated su-
prasellar cyst was removed easily without damage to
the surrounding vital structures. Histological study of
the cyst wall revealed complete necrosis of tumor cells
(Fig. 3). The new cyst had a thin wall measuring less
than 0.5 mm and was drained into the subcutaneous

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FIG. 2. Case 2. Conray cystograms of multiple cysts. The suprasellar cyst with a 15-ml volume (A) collapsed 6 months after the injection of 2.3 mCi of radioactive phosphate (B). The large interpeduncular cyst with a 40-ml volume (C) showed a gradual decrease in size at 3 (D), 6 (E), and 9 months (F) after the injection of 10 mCi of radioactive gold.

The patient’s hemiparesis improved soon after the operation, but periodic taps of the reservoir were necessary to control fluid secretion.

Conray cystography on March 9, 1976, showed a large round cyst at the interpeduncular fossa, with a volume calculated as 40 ml (Fig. 2C). Internal irradiation was started using 10 mCi of 198Au colloid with an estimated dose to the cyst wall of 8000 rads. Repeat Conray cystography demonstrated a gradual decrease in the size of the cyst (Fig. 2D and E), and at 9 months it had almost totally collapsed (Fig. 2F). The patient had two other episodes of progressive tumor growth into the right temporal and posterior fossa in the following 3 years. However, they were controlled by surgical removal and cyst drainage by the Ommaya system, respectively.

Case 3

This 15-year-old boy had had a speech disturbance and poor balance since the age of 2 years. He became blind at the age of 3 years and was found to have optic atrophy. He also suffered from diabetes insipidus and dwarfism for a long time.

The diagnosis of craniopharyngioma was first made in August, 1979, when CT scans (Fig. 4A) were taken for evaluation of worsening headaches, dizziness, mental retardation, and loss of recent memory. At craniotomy on October 8, 1979, a huge suprasellar cyst was evacuated: 60 ml of motor oil-like fluid was obtained, and an Ommaya drainage system was set up. The cyst wall was calcified and thick, measuring 3.0 to 5.0 mm. After the procedure, signs of intracranial hypertension disappeared, but hypersecretion of the fluid followed. Conray cystography on October

FIG. 3. Case 2. Photomicrograph of the collapsed cyst wall. The tumor cells had been rendered completely necrotic by the irradiation and stained homogeneously. Calcification and hyalinization remained. H & E, x 200.
TABLE 2

Radioisotopes used for internal irradiation

<table>
<thead>
<tr>
<th>Feature</th>
<th>$^{198}$Au</th>
<th>$^{32}$P</th>
<th>$^{90}$Y</th>
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</thead>
<tbody>
<tr>
<td>physical half-life (days)</td>
<td>2.69</td>
<td>14.2</td>
<td>2.67</td>
</tr>
<tr>
<td>maximum beta energy (MeV)</td>
<td>0.96</td>
<td>1.71</td>
<td>2.27</td>
</tr>
<tr>
<td>mean beta energy (MeV)</td>
<td>0.32</td>
<td>0.69</td>
<td>0.93</td>
</tr>
<tr>
<td>maximum range in soft tissue (mm)</td>
<td>3.8</td>
<td>7.9</td>
<td>11.0</td>
</tr>
<tr>
<td>half-value depth in soft tissue (mm)</td>
<td>0.4</td>
<td>0.8</td>
<td>1.1</td>
</tr>
<tr>
<td>major gamma energy (MeV)</td>
<td>0.41</td>
<td>--</td>
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</tr>
</tbody>
</table>

19, 1979, revealed a huge calcified suprasellar cyst with a daughter cyst in the intraventricular region (Fig. 4B). The total volume was measured as 113 ml and on November 19 the cyst was treated by intracystic administration of 20 mCi of $^{198}$Au colloid. The dose at the cyst wall was estimated as 12,600 rads. The size of the cyst was unchanged 1 year after the treatment; however, no further signs of intracranial hypertension or hypersecretion of the cyst have been found so far.

Case 5

This 62-year-old man’s symptoms began in August, 1975, with thirst and polyuria. By March, 1977, the symptoms progressed to headaches, nausea, vomiting, and visual disturbance. Suprasellar cystic craniopharyngioma was confirmed at craniotomy on April 21, and cyst drainage was performed using the Ommaya system. The symptoms and signs disappeared soon after the operation; however, frequent aspirations of the cyst fluid were necessary. Conray cystograms and CT scans showed an irregular, multiloculated cyst in the suprasellar region (Fig. 5A). Volumetry of the cyst was determined using Conray and CT scanning. The volume was calculated to be 16 ml, and internal irradiation was carried out on September 10, 1977, with a total of 10 mCi of $^{198}$Au colloid. The dose at the cyst wall was estimated as 20,000 rads. Secretion of the fluid decreased gradually, and stopped 4 months after the irradiation. The effectiveness of treatment was confirmed by Conray cystography at 3 months (Fig. 5B). Three years and 3 months after irradiation, the patient is able to have a full-time job.

Discussion

Internal irradiation for cystic craniopharyngioma was first performed by Leksell and Lidén\textsuperscript{12} in 1952 using stereotaxic injection of $^{32}$P chromic phosphates into cysts. Considerable improvement in the method has been made since that time, and $^{198}$Au and yttrium-90 ($^{90}$Y) have been used recently as the nuclear source.\textsuperscript{1,2} Ideal isotopes for internal irradiation must have a short half-life, easy applicability, and pure beta emitter. The strength of the beta energy must be adequate.\textsuperscript{1} Phosphorus-32 has moderate beta energy but the half-life is too long; $^{198}$Au has both beta and smaller amount of gamma emission with a short half-life. The most suitable radiation source so far reported\textsuperscript{1} is $^{90}$Y (Table 2).

Fig. 4. Case 3. A huge suprasellar cyst with a thick calcified wall was demonstrated by computerized tomography (A), and a daughter cyst was found in the intraventricular region by Conray cystography (B). After irradiation with 20 mCi of radioactive gold, the size of the cyst was unchanged but the secretion of fluid was diminished.
There are various means of introduction of the isotopes into a cyst. Leksell and his associates\textsuperscript{11,12} used the stereotaxic method. This is simple and less invasive to the patients, but there can be a problem concerning leakage of the isotope into the brain or subarachnoid space through the needle track. It is also difficult to control hypersecretion of the cyst fluid during and after irradiation. Furthermore, it is impossible to obtain information regarding the condition of the cyst and the relationship of the adjacent vital structures. Many other authors\textsuperscript{3,4,9,16} have used surgical insertion of the Ommaya drainage system, whereby the isotope is safely introduced about 2 weeks after operation.\textsuperscript{2} Removal of cyst fluid or reinjection is easily performed by puncture of the reservoir. This method also permits rapid Conray cystography, with easy evaluation of treatment.\textsuperscript{9} However, more than one craniotomy for newly growing cysts is inevitably required with this method. A second craniotomy was necessary in two patients (Cases 1 and 2) in the present series. Leakage of the radioisotope by oversecretion of cyst fluid is a possibility. We had no such experience, but this possibility is monitored by external detection with a Geiger counter or gamma camera if $^{198}$Au is used. With $^{32}$P, beta activity in the cerebrospinal fluid (CSF) can be measured directly.

The most important factor in internal irradiation should be the determination of the minimum effective radiation dose to the wall of the cyst. The thickness and evenness of a cyst wall is variable: a paper-thin wall of a cyst often attaches to or invades the optic nerve, hypothalamus, or internal carotid artery. The dosimetry had been empirical\textsuperscript{13,17,18} until the single dosimetric formula was proposed by Loevinger for beta particle radiation in 1956.\textsuperscript{14} It has been possible to calculate the radiation dose to the inner surface of the cyst as a function of cyst volume and radioisotope activity administered. Using our formula\textsuperscript{16} (Appendix), we can calculate radiation dose not only at the cyst wall but also at a point far from the source, thus preventing radiation damage to adjacent structures. For example, if a beta energy were high enough to penetrate beyond the width of the cyst wall, the adjacent vital tissue would be damaged by radiation.

Deleterious side-effects occurred in only one patient (Case 8). This patient complained of nausea, headache, and blurred vision of the left eye 6 hours after injection of 5 mCi of $^{32}$P. The reservoir became tense, and frequent removal of the cyst fluid was necessary to relieve the complaints after 1 week. No leakage of the radioisotope into the subarachnoid space was detected by CSF examination. The patient showed progression of a left oculomotor palsy in the following weeks, in spite of intrathecal injection of steroids and hyperbaric oxygen therapy. From our retrospective calculation, it was concluded that the higher dose to the cyst wall (more than 100 Krads) gave rise to a high dose (10 Krads) to the oculomotor nerve which was attached to a thin wall of the cyst (less than 0.5 mm).\textsuperscript{2}

The optimum dose to alleviate fluid retention or to cause collapse of a cyst is still to be determined. Bond, et al.,\textsuperscript{3} concluded that the effective dose of $^{198}$Au

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**FIG. 5.** Case 5. A: Conray cystograms of a multilobulated suprasellar cyst with a volume of 16 ml. B: Conray cystogram 3 months after administration of 10 mCi of radioactive gold shows the cyst had decreased in size.
colloid would be 10 to 15 mCi for a cyst. Leksell, et al., determined that the dose to the cyst surface must be more than 100 Krads to collapse a cyst. From our present results, the optimum and safe dose to the cyst wall is between 9000 and 30,000 rads, and this in agreement with the results of Wycis, et al., and Backlund, et al. However, the differences of the optimum doses delivered by internal and external irradiation have yet to be clarified.

The effectiveness of this treatment has been evaluated by clinical improvement or by the decreased size of the cyst using Conray cystogram. However, recent progress with CT scanning has made evaluation easier. In Case 2, the effectiveness of the treatment was also confirmed histologically when the collapsed cyst was removed during the second craniotomy.

The indication for internal irradiation of cystic craniopharyngioma includes many factors, such as the size, location, and multiplicity of the cyst; the feasibility of radical operation; whether the cyst is recurrent or primary; whether the cyst is recurrent or primary; resistance to other treatments; and/or the age of the patients. The best candidates are patients with a huge cyst with a volume of more than 60 ml (Cases 1, 3, and 6), or with an uncontrollable cyst invading vital areas (Cases 4, 5, and 8), or with multiple (Cases 1, 2, and 3) or recurrent cysts (Cases 6 and 7). The treatment is contraindicated in cases with predominantly solid tumors, mixed tumors with small cysts, or mainly intrasellar tumors.

APPENDIX

The Dosimetric Formula for Internal Irradiation

\[ R_p = \frac{A n k E}{4 \pi \rho \times 90 V} \int_0^V \frac{F(\xi)}{r^2} dV \]

\[ \text{R}: \text{radius of the source} \]
\[ \text{P}: \text{point where absorbed dose is calculated} \]
\[ \text{V}: \text{volume of the source} \]
\[ \text{Z}: \text{distance from the nearest point on the surface of the source to point P} \]
\[ \text{r}: \text{distance between point P and any point in the source} \]
\[ \text{dr}: \text{element of distance r} \]
\[ \text{R_p}: \text{radiation dose at point P (rad/s)} \]
\[ \text{X}_{90}: \text{90 percentile distance (cm)} \]
\[ \text{A}: \text{source activity (d.p.s.)} \]
\[ n: \text{number of beta particles emitted per disintegration} \]
\[ k: \text{1.602} \times 10^{-8} \text{ (g-rad/Mev)} \]
\[ E: \text{average energy of beta particle (MeV)} \]
\[ \rho: \text{density (gm/cm}^3\text{)} \]
\[ \xi: \text{distance ratio of X to X}_{90} (X/X_{90}) \]
\[ F(\xi): \text{scaled absorbed dose distribution} \]

Using this formula, the radiation dose (R_p) at the wall of a cyst (Z = 0) and at the point P, of which the distance is Z from the inner surface of the cyst, can be calculated separately.

References


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Internal irradiation of cystic craniopharyngioma


Manuscript received February 16, 1981.
Accepted in final form July 2, 1981.
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