Jamshid Ahmadi, MD • Sylvie Destian, MD • Michael L. J. Apuzzo, MD
Hervey D. Segall, MD • Chi-Shing Zee, MD

Cystic Fluid in Craniopharyngiomas: MR Imaging and Quantitative Analysis[1]

A prospective study of cystic fluid in craniopharyngiomas in 10 patients was performed to correlate signal intensity on T1-weighted magnetic resonance (MR) images and biochemical analysis. Within 2 days before surgery, each patient underwent MR imaging before and after administration of gadopentetate dimeglumine. Five patients had cystic fluid lower in signal intensity than white matter, with protein levels less than 9,000 mg/dL (90.00 g/L) and no free methemoglobin. One of the five patients had the highest triglyceride concentration (84 mg/dL [0.95 mmol/L]) of all 10 patients; another of these five had the highest cholesterol concentration of all (270 mg/dL [6.98 mmol/L]). It is concluded that the increased signal intensity of cystic fluid in craniopharyngiomas on T1-weighted MR images can be caused by a protein concentration greater than or equal to 9,000 mg/dL (90.00 g/L), the presence of free methemoglobin, or both. In the ranges of concentrations measured in this study, cholesterol and triglyceride did not increase signal intensity.

Index terms: Brain neoplasms, MR, 13.1214 • Cholesterol • Craniopharyngioma, 13.3611 • Magnetic resonance (MR), tissue characterization • Proteins • Triglycerides

Radiology 1992; 182:783–785

THE high signal intensity of the cystic fluid of craniopharyngiomas on T1-weighted spin-echo (SE) magnetic resonance (MR) images has been attributed to protein, hemorrhage, and cholesterol, other fatty materials, or a combination of these (1–6). In most of the in vivo studies reported in the literature, however, the relationship between the various substances within the cystic fluid and signal intensity has not been substantiated by a quantitative biochemical analysis of the cystic contents. In addition, in vitro studies in which experimental models are used measure a single substance in solution and thus do not adequately represent the more complex nature of in vivo cystic fluid and the effect on signal intensity (7–9).

In this article we present a prospective study that correlates the signal intensity characteristics of the cystic fluid from craniopharyngiomas with quantitative biochemical analyses of the cystic contents.

PATIENTS AND METHODS

Cystic craniopharyngiomas in 12 consecutive patients were evaluated prospectively. Two patients were excluded from the study because the cystic fluid was contaminated with blood or saline during surgery. The 10 other patients were five male and five female subjects aged 16–57 years. The diagnosis of craniopharyngioma was confirmed by means of histologic examination of the surgical specimens, which revealed the presence of (ameloblastic) squamous epithelial lining, typical for craniopharyngioma. No evidence of columnar epithelium (Rathke cleft cyst) or flattened squamous epithelium with laminated keratin (epidermoid) was found.

The cysts were aspirated at surgery prior to resection of the tumor, and the cystic fluid was immediately sent for quantitative analysis of protein, cholesterol, triglyceride, and methemoglobin. The volume of aspirated cystic fluid was 1.5–5.0 mL. Total protein and cholesterol levels were quantitated with an automated analyzer (Cobas B10; Roche Diagnostic Systems, Montclair, NJ). Hemoglobin levels were measured with a blood oximeter (OSM3 Hemoximeter; Radiometer, Copenhagen). Total hemoglobin was measured in whole fluid, and free methemoglobin was measured in supernatant components, obtained by centrifugation at 3,000 rpm for 10 minutes.

Within 2 days before surgery, each patient underwent MR imaging before and after administration of gadopentetate dimeglumine. The MR examinations were performed with a 1.5-T superconducting magnet (515 HP; Philips Medical Systems North America, Shelton, Conn) with a head coil. T1-weighted images were obtained with the following parameters: repetition time (TR) msec/echo time (TE) = 550/18, two to four signal averages, and a 180 × 256 matrix. Multiecho images were obtained with a TR of 2,000 msec, TEs of 18 and 80 msec, one signal average, and a 204 × 256 matrix.

RESULTS

The cystic portion of all 10 craniopharyngiomas was complex, containing several substances (ie, protein, cholesterol, and triglycerides), as well as blood by-products in the hemorrhagic craniopharyngiomas. Signal intensity on non-contrast material–enhanced T1-weighted images and fluid composition are correlated in the Table.

The cystic fluid from five of the seven nonhemorrhagic craniopharyngiomas (Table, patients 1–5) had lower signal intensity than white matter on T1-weighted images (Fig 1). Quantitative analysis of the cystic fluid in these five patients revealed the following ranges in content: protein, 4,100 mg/dL (41.00 g/L) to 6,500 mg/dL (65.00 g/L); cholesterol, 135 mg/dL (3.49 mmol/L) to 270 mg/dL (6.98 mmol/L); and triglyceride, 42

[1] From the Departments of Radiology (J.A., S.D., H.D.S., C.S.Z.) and Neurosurgery (M.L.J.A.), University of Southern California School of Medicine, 1200 N State St, Rm 5139, Los Angeles, CA 90033. Received April 29, 1991; revision requested May 28; revision received September 25; accepted October 3. **Address reprint requests to** J.A.

Abbreviations: SE = spin echo, TE = echo time, TR = repetition time.

Comparison of Cystic Fluid Composition and Signal Intensity in 10 Patients with Craniopharyngiomas

Patient No.	Cystic Fluid Composition (mg/dL)			Total Hemoglobin (g/dL)/Methemoglobin (%)	T1 Signals Relative to White Matter
	Protein	Cholesterol	Triglyceride		
1	4,100 (41.00)	135 (3.49)	42 (0.47)	0	Hypointense
2	4,300 (43.00)	228 (5.90)	84 (0.95)	0	Hypointense
3	4,900 (49.00)	185 (4.78)	62 (0.70)	0	Hypointense
4	5,400 (54.00)	149 (3.85)	50 (0.56)	0	Hypointense
5	6,500 (65.00)	270 (6.98)	63 (0.71)	0	Hypointense
6	9,000 (90.00)	90 (2.33)	22 (0.25)	0	Isointense
7	12,400 (124.00)	187 (4.84)	64 (0.72)	0	Hyperintense
8	8,300 (83.00)	176 (4.55)	66 (0.74)	3(30)/15	Hyperintense
9	8,600 (86.00)	168 (4.34)	54 (0.61)	3(30)/14	Hyperintense
10	10,400 (104.00)	144 (3.72)	8 (0.09)	4(40)/18	Hyperintense

Note.—Numbers in parentheses are SI units: column 2 (protein), grams per liter; columns 3 (cholesterol) and 4 (triglyceride), millimolar; column 5 (total hemoglobin), grams per liter.

mg/dL (0.47 mmol/L) to 84 mg/dL (0.95 mmol/L).

The cystic fluid was isointense to white matter on T1-weighted MR images in patient 6 (Table). This patient had the lowest levels of cholesterol and triglycerides in the nonhemorrhagic group but had a protein concentration of 9,000 mg/dL (90.00 g/L) (Fig 2).

The cystic fluid in patients 7–10 (Table) was hyperintense to white matter on the T1-weighted images. Biochemical analysis of the cystic fluid from patient 7 revealed a protein concentration of 12,400 mg/dL (124.00 g/L), a cholesterol concentration of 187 mg/dL (4.84 mmol/L), and a triglyceride concentration of 64 mg/dL (0.72 mmol/L) (Fig 3).

Biochemical analysis of the cystic fluid in the three other patients (patients 8–10) revealed evidence of hemorrhage in addition to protein, cholesterol, and triglyceride (Table). The free methemoglobin ranged from 14%–18% of the total hemoglobin concentration of the cystic fluid (Fig 4). Protein concentration ranged from 8,300 mg/dL (83.00 g/L) to 10,400 mg/dL (104.00 g/L); cholesterol, 144 mg/dL (3.72 mmol/L) to 176 mg/dL (4.55 mmol/L); and triglycerides, 8 mg/dL (0.09 mmol/L) to 66 mg/dL (0.74 mmol/L).

DISCUSSION

In our study, the cystic fluid in all seven patients with nonhemorrhagic craniopharyngiomas contained cholesterol and triglyceride. It has been suggested that cholesterol and triglyceride in a liquid suspension cause hyperintensity of cystic fluid on T1-weighted images (1–2,5), but in five of the seven patients (Table, patients 1–5), the cystic fluid was hypointense to white matter on T1-weighted SE MR images despite a wide range of protein (4,100 mg/dL [41.00 g/L]) to 6,500 mg/dL) [65.00 g/L]), cholesterol (135 mg/dL [3.49 g/L] to 270 mg/dL [6.98 mmol/L]), and triglyceride (42 mg/dL [0.47 mmol/L] to 84 mg/dL [0.95 mmol/L]). Even in patient 2, who had the next to highest level of cholesterol and the highest level of triglyceride, the cystic fluid was hypointense relative to white matter. This would indicate that neither a cholesterol concentration lower than or equal to 270 mg/dL (6.98 mmol/L) nor a triglyceride concentration lower than or equal to 84 mg/dL (0.95 mmol/L) are responsible for the hyperintensity of the cystic fluid on T1-weighted SE MR images. In 1981, Lipper et al described a craniopharyngioma with a hyperdense CT appearance (10). Biochemical analysis of the cystic fluid revealed the highest protein level (17,300 mg/dL [173 g/L]) and cholesterol concentrations (413 mg/dL) [10.68 mmol/L] ever recorded; at that time MR images were not available for clinical use.

Isointense signal was noted only in patient 6, who had the lowest concentration of cholesterol, the next to lowest concentration of triglyceride, and a protein level of 9,000 mg/dL (90.00 g/L). Therefore, it would appear that such an increase in the protein level increases the signal intensity of cystic fluid on T1-weighted MR images. In an experimental model, Hackney et al (7) detected very small differences in signal intensity in protein concentrations that ranged from 0 mg/dL (0 g/L) to 6,100 mg/dL (61.00 g/L). Such small changes are easily obscured by noise and the wide windows normally used in clinical imaging (7,11). In an in vitro imaging and spectroscopic study, Vock et al (12) showed no reliable T1 changes with an albumin concentration of 8,000 mg/dL (80.00 g/L) on a 1.5-T imager. In our study, only one of the nonhemorrhagic craniopharyngiomas (in patient 7) showed hyperintense cystic fluid on T1-weighted MR images. Of the substances measured, only the high protein level of 12,400 mg/dL (124.00 g/L) would account for this hyperintensity. Therefore, it appears that protein in high concentration (>9,000 mg/dL) [90.00 g/L]) increases the signal intensity of the cystic fluid relative to white matter, but that, at the concentrations we measured, cholesterol and triglyceride do not. Som et al (13) analyzed chronically obstructed sinonasal secretions and found a similar increase in T1 signal

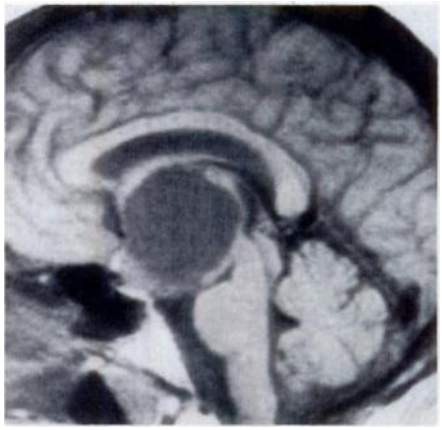

Figure 1. Patient 5. Sagittal SE 550/18 MR image of craniopharyngioma. The cystic tumor shows a lower signal intensity than white matter on this T1-weighted image. Biochemical analysis revealed that the turbid yellow cystic fluid contained 6,500 mg/dL (65.00 g/L) of protein, 270 mg/dL (6.98 mmol/L) cholesterol, and 63 mg/dL (0.71 mmol/L) triglyceride. Note that neither the high cholesterol nor the high triglyceride content increased signal intensity on the T1-weighted image.

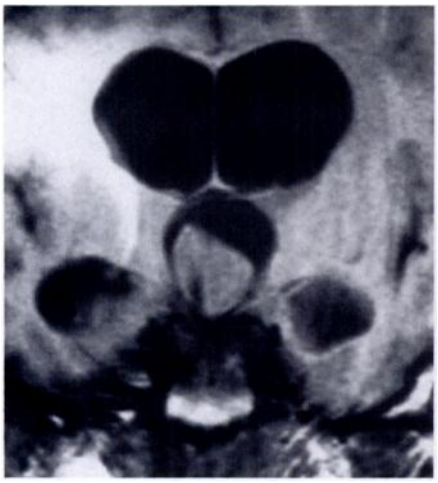

Figure 2. Patient 6. Coronal SE 550/18 MR image of craniopharyngioma. The cystic portion of the tumor is isointense relative to white matter on this T1-weighted image. Yellowish fluid obtained from the cystic drainage catheter contained 9,000 mg/dL (90.00 g/L) of protein, 90 mg/dL (2.33 mmol/L) cholesterol, and 22 mg/dL (0.25 mmol/L) triglyceride. Artifact in the right side was caused by the metallic susceptibility effect of a shunt reservoir.

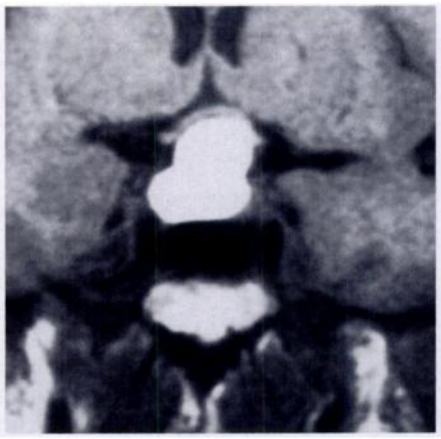

Figure 3. Patient 7. Coronal SE 550/18 MR image of nonhemorrhagic craniopharyngioma. High signal intensity of the cystic fluid is seen on this T1-weighted image. Viscous cystic fluid contained 12,400 mg/dL (124.00 g/L) of protein, 187 mg/dL (4.84 mmol/L) cholesterol, 64 mg/dL (0.72 mmol/L) triglyceride, and 0 mg of methemoglobin.

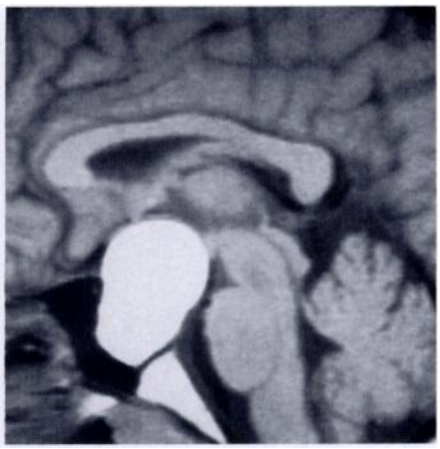

Figure 4. Patient 8. Sagittal SE 550/18 MR image of hemorrhagic craniopharyngioma. High signal intensity of the cystic fluid is seen on this T1-weighted SE MR image. The cystic fluid contained 8,300 mg/dL (83.00 g/L) of protein, 176 mg/dL (4.55 mmol/L) cholesterol, 66 mg/dL (0.74 mmol/L) triglyceride, and 3 mg/dL (30 g/L) of hemoglobin. Fifteen percent of the total hemoglobin was in the form of methemoglobin (0.465 mg/dL).

intensity with very high protein concentration. However, they also showed that at ultrahigh protein concentration (equal to or higher than 28,000 mg/dL [280.00 g/L]), signal intensity on T1-weighted MR images can decrease. In their study, the sinonasal fluid was also graded in terms of viscosity as one of the possible factors influencing signal intensity.

In the three patients with hemorrhagic craniopharyngiomas (patients 8–10), the cystic fluid was markedly hyperintense on the T1-weighted SE MR images because of the presence of free methemoglobin, an elevated protein level, or both. In two of the three patients (patients 8 and 9) the protein level was less than 9,000 mg/dL [90.00 g/L]). In the third patient (patient 10), the protein level was 10,400 mg/dL (104.00 g/L). In this patient, protein could also have a great influence on the hyperintense signal. Ebisu et al (14) studied nonacute subdural hematomas and found that, among the types of hemoglobins in whole fluid, only methemoglobin was related to the shortening effect during relaxation time (14).

In experimental models it is possible to measure the signal intensity of a single substance in water (eg, purified protein in solution [7]), but intracranial cystic masses contain a complex mixture of substances. Therefore, the experimental models do not adequately represent the more complex nature of in vivo cysts and the effect that the contents of such cysts have on signal intensity (7–9). On the other hand, because of the complexity of in vivo cystic fluid, the relationship between signal intensity and fluid content is harder to define, but some conclusions may be drawn. Our data show that a protein level greater than or equal to 9,000 mg/dL [90.00 g/L]), the presence of free methemoglobin, or both can increase the signal intensity of the cystic fluid of craniopharyngiomas on T1-weighted MR images. At the concentrations we measured, however, cholesterol and triglyceride do not increase the signal intensity of the cystic fluid. ■

References

1. Daniels DL, Haughton VM, Czervionke LF. Skull base. In: Stark DD, Bradley WG Jr, eds. Magnetic resonance imaging. St Louis: Mosby, 1988; 524–569.
2. Elster AD. The skull base in cranial magnetic resonance imaging. New York: Churchill Livingstone, 1988; 281–336.
3. Gentry LR, Jacoby CG, Turski PA, Houston LW, Strother CM, Sackett JF. Cerebellopontine angle—petromastoid mass lesions: comparative study of diagnosis with MR imaging and CT. Radiology 1987; 162:513–520.
4. Greenberg JJ, Ott RF, Wismer GL, et al. Cholesterogranuloma of the petrous apex: MR and CT evaluation. AJNR 1988; 9:1205–1214.
5. Lee BCP, Deck MDF. Sellar and juxtasellar lesion detection with MR. Radiology 1985; 157:143–147.
6. Kjos BO, Brant-Zawadzki M, Kucharczyk W, Kelly WM, Norman D, Newton TH. Cystic intracranial lesions: magnetic resonance imaging. Radiology 1985; 155:363–369.
7. Hackney DB, Grossman RI, Zimmerman RA, et al. Low sensitivity of clinical MR imaging to small changes in the concentration of nonparamagnetic protein. AJNR 1987; 8:1003–1008.
8. Barnhart JL, Berk RN. Influence of paramagnetic ions and pH on proton NMR relaxation of biologic fluids. Invest Radiol 1986; 21:132–136.
9. Kang YS, Gore JC, Armitage IM. Studies of factors affecting the design of NMR contrast agents: manganese in blood as a model system. Magn Reson Med 1984; 1:396–409.
10. Lipper MH, Kishore PRS, Ward JD. Craniopharyngioma: unusual computed tomographic presentation. Neurosurgery 1981; 9:76–78.
11. Abrahams JJ, Lidon M, Artiles C. MR imaging of intracranial fluid levels. AJNR 1989; 153:597–604.
12. Vock P, Hedlund LW, Herfkens RJ, Effmann EL, Brown MA, Putman CE. Work in progress: in vitro analysis of pleural fluid analogs by proton magnetic resonance—preliminary studies at 1.5T. Invest Radiol 1987; 22:382–387.
13. Som PM, Dillon WP, Fullerton GD, Zimmerman RA, Rajagopalan B, Marom Z. Chronically obstructed sinonasal secretions: observation on T1 and T2 shortening. Radiology 1989; 172:515–520.
14. Ebisu T, Naruse S, Horikawa Y, Tanaka C, Higuchi T. Nonacute subdural hematoma: fundamental interpretation of MR images based on biochemical and in vitro MR analysis. Radiology 1989; 171:449–453.