CSF imaging in benign intracranial hypertension

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SYNOPSIS The cisternographic images in 10 patients with benign intracranial hypertension were reviewed. Nine were normal. Transfer of labelled tracer from the subarachnoid space was measured in five patients and was found to be abnormal in only two. The relation of these findings to the proposed pathophysiological alterations is discussed.

Benign intracranial hypertension (pseudotumor cerebri) is a transient entity of unknown aetiology usually manifest by clinical symptoms of headache, visual blurring, ophthalmological dis-

orders of choked discs, retinal haemorrhages, and sixth nerve palsies. Except for raised pressure, other parameters of the cerebrospinal fluid (CSF) are normal (Hagberg and Sillanpää, 1964). This association of abnormalities is of limited duration (average in 100 patients, 10 weeks) (Guidetti *et al.*, 1968) and may be managed by 'conservative means' (diet, fluid restriction, serial drainage of CSF by lumbar punctures) or by surgical subtemporal decom-

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FIG. 1. (a) Right lateral view of cisternogram six hours after lumbar subarachnoid injection (1 mCi ¹⁶⁹Yb DTPA). Normal distribution over cerebral cortex is present. (b) Anterior view at six hours. The radiopharmaceutical is present in the basal cisterns, laterally over the cerebral convexities, and between the cerebral hemispheres. No ventricular radioactivity is seen. (c) Left lateral view at 24 hours. Generalized distribution of radiopharmaceutical over the cerebral convexities is present with concentration in the parasagittal area superiorly and anteriorly.

TABLE
CLINICAL DETAILS OF 10 PATIENTS

Name	Age (yr)	Sex	Duration* (mth)	LP (OP) (mm H ₂ O)	Radiopharmaceutical	CSF image				Abnormal parasagittal concentration	Ventricular entry	Therapy
						2 hr	6 hr	24 hr	48 hr			
F.F.	60	F	12	500-600	¹⁰⁰ μ ¹³¹ I HSA	Basal	Convex	Clearing	—	—	—	Cons.
G.M.	19	F	48	500-600	1mCi ¹⁶⁹ Yb DTPA	Basal ±	—	Convex	Para	+	—	Cons.
D.C.	30	F	36	400	1mCi ¹⁶⁹ Yb DTPA	Basal	Sylvian	Sylvian	—	—	—	—
G.R.	33	F	4	280	100 μCi ¹³¹ I HSA	Basal	Sylvian	Convex	—	—	—	Cons.
J.C.	39	F	1½	210	100 μCi ¹³¹ I HSA	Basal	Sylvian	Convex	—	—	—	—
J.W.	31	F	7	200	100 μCi ¹³¹ I HSA	Basal	Sylvian	Convex	—	—	—	Surg. decomp.
C.W.	20	F	48	500	100 μCi ¹³¹ I HSA	Basal	Convex	Para	—	—	—	—
A.S.	22	F	84	650	100 μCi ¹³¹ I HSA	Basal	Convex	Para	—	—	—	—
G.L.	44	M	6	350	450 μCi ¹¹¹ In DTPA	Basal	Convex	Para	Para	—	—	Surg. decomp.
S.E.	6	M	12	250	2mCi ^{99m} Tc HSA	Basal	Convex	Convex	—	—	—	Surg. decomp.

CSF image: cisternogram. Para: parasagittal region. Convex: cerebral convexity. Cons.: conservative therapy. Surg. decomp.: surgical decompression. * Total duration; recurrent episodes lasted two to six weeks.

FIG. 2. (a) Anterior view of a cisternogram two hours after lumbar injection (100 μCi ¹³¹I HSA). Rapid movement over the cerebral convexities is present. No ventricular entry is detected. (b) Anterior view at 24 hours demonstrates normal concentration of radioactivity in the parasagittal region.

pression and CSF diversionary shunting (Jacobson and Shapiro, 1964).

Skull radiographs, cerebral angiograms, and pneumoencephalograms have been employed in the diagnostic examination of these patients and the findings described. Radiological evaluation of these patients is important as it allows exclusion of more serious causes of similar symptomatology (posterior fossa neoplasms, hydrocephalus). Recently cisternography has been used to evaluate patterns of CSF movement and absorption in patients with pseudotumor cerebri (Schlesinger *et al.*, 1965; Bercaw and Greer, 1970). The 'characteristic' image patterns described were at variance with those noted in our patients, thus stimulating this report.

METHODS

The cisternograms, clinical summaries, and other pertinent data on 10 patients with benign intracranial hypertension from four institutions were reviewed. Special emphasis was placed upon correlation at the time of study with the status of the patients' symptoms and whether or not treatment had been instituted. If cerebral angiograms and pneumoencephalograms had been obtained, these were compared with the isotope cisternograms (CSF images).

Since two of the radiopharmaceuticals employed, ^{169}Yb and ^{111}In in diethylenetriaminepentaacetic acid (DTPA) differ in molecular size from ^{131}I human serum albumin (HSA) (600 *vs.* 67,000 M.W.), we correlated the CSF images with the radiopharmaceutical employed in the individual patient to deter-

FIG. 3. (a) Anterior view cisternogram six hours after lumbar intrathecal injection of $450\mu\text{Ci } ^{111}\text{In DTPA}$. Abnormal collections of radioactivity are present in the area of the surgical subtemporal decompression. (b) The posteroanterior skull radiograph shows surgical defects, metallic clips, and burr holes.

mine if there were differences that could be explained by this property alone.

Particular attention was directed to the temporal sequence of radioactivity movement from the basal cisterns to the parasagittal area and the presence or absence of ventricular entry. Since increased concentration of radiopharmaceutical in the area of the arachnoid villi in the parasagittal region has been reported, we specifically noted the presence or absence of this particular sign.

RESULTS

In this series of 10 patients, none showed ventricular entry of the radiopharmaceutical (Table). Seven patients had their cisternograms performed with labelled human serum albumin and in three chelates were used. Nine of 10 patients had basal radioactivity on the two hour study. By six hours, radioactivity was present over the cerebral convexities in five patients but had only reached the Sylvian area in four. By 24 hours there was activity over the cerebral hemispheres, either diffuse or concentrated in the parasagittal region in nine of the 10 patients (Fig. 1). In one patient increased radioactivity was present over the cerebral convexities by two hours. Concentration in the parasagittal area was present on the 24 hour study (Fig. 2). The three patients with bitemporal surgical decompression revealed concentration of radioactivity in the site of bone removal throughout the study (Fig. 3).

A single patient, with CSF opening pressure measurement of 500–600 mm H₂O, had delayed flow of the radiopharmaceutical from the lumbar site of injection to the basal region. The cisternogram performed with ¹⁶⁹Yb DTPA showed abnormal parasagittal concentration of radioactivity after 24 hours.

DISCUSSION

Pseudotumor cerebri was first described by Quincke in 1893 under the appellation of 'serous meningitis'. In 1914 Nonne introduced the term 'pseudotumor cerebri'. Pneumoencephalographic reports by Davidoff and Dyke, some 20 years later, documented that this syndrome occurs in the presence of an anatomically normal ventricular system, although a certain percentage of these patients will have 'small' ventricles (Jacobson and Shapiro, 1964).

Bercaw and Greer (1970) and Schlesinger *et al* (1965) have described a CSF image pattern of delayed movement of ¹³¹I human serum albumin with persistent concentration of radiopharmaceutical in the parasagittal area on delayed views (24 hours). No ventricular entry of radiopharmaceutical (characteristic of communicating hydrocephalus) was present in their patients.

In this series of 10 patients, delayed flow of radiopharmaceutical was encountered in only four (40%) and prolonged parasagittal concentration occurred in only one (10%). From a combined experience of the four authors of approximately 1,000 cisternograms, delayed flow and prolonged parasagittal activity occur in approximately 20% of normal subjects. Systematic review of 436 cisternograms (performed with ¹³¹I and ^{99m}Tc HSA or ¹⁶⁹Yb and ¹¹¹In DTPA) revealed that approximately one-fifth of normal subjects will require 48 hours to show parasagittal accumulation of radioactivity. Conversely, in two patients in this series (C.W., A.S.) unusually rapid movement of the radiopharmaceutical from the lumbar to the parasagittal region was encountered.

In these 10 patients, six cisternograms were performed utilizing ¹³¹In HSA (RISA) with molecular weight of 67,000. The other four patients had cisternograms employing radioactive chelates (molecular weight 600). From comparative studies, it appears that the smaller molecule of the chelate is more rapidly transported into the blood than is albumin. However, in the one patient with persistence of the radiopharmaceutical in the parasagittal region, ¹⁶⁹Yb DTPA was the radiopharmaceutical injected. On the two hour study in this patient only minimal radioactivity was seen in the basal cisterns suggesting slow ascension in the spinal canal.

Four patients had not received treatment before the cisternogram, three had conservative therapy consisting of diuretics and diet, and three had surgical subtemporal decompression. Except for persistence of radiopharmaceutical at the surgical sites bitemporally, treatment of any type did not appear to alter the cisternographic pattern.

Correlation of cisternograms and pneumoencephalograms as well as animal data suggest that images alone are not as sensitive as a combination of CSF images and measurements

transfer of labelled molecules from the CSF space into the blood. Abbott and Alksne (1968) measured the transport of intrathecal ^{125}I RISA to circulating plasma in 10 normal and four dogs with hydrocephalus which was produced by the kaolin technique. In the normal dogs the mean percentage of injected radioactivity found in the circulatory plasma at 24 hours was 46%, whereas in the hydrocephalic animals only 16% was present. These findings correspond to those published by Van Wart *et al.* (1960) and in animals with communicating hydrocephalus by Strecker *et al.* (1973). In seven normal patients and six patients with communicating hydrocephalus the values were 48 and 24%. It was concluded the 'RISA transport test' provided a sensitive means of detecting patients with communicating hydrocephalus. Bercaw and Greer (1970) employed the same test in three patients with benign intracranial hypertension and found that 'a decreased rate of plasma uptake' was present in two. In one patient the transfer test and cisternogram were repeated when the patient was asymptomatic and both studies were normal.

Three patients in this series had quantification of the disappearance of radiopharmaceutical from the CSF spaces utilizing a method previously described by Curl *et al.* (1972). A corrected count of intracranial activity for each imaging period up to 48 hours is obtained and normalized to represent percent of peak activity. In non-hydrocephalic patients, peak intracranial activity is maximal at six to 12 hours, falls to 40–80% of peak by 24, and 25–40% by 48 hours. The three patients with pseudotumor cerebri demonstrated completely normal radionuclide clearances (Abbott and Alksne, 1968) and were very different from the patient with communicating hydrocephalus in which the peak activity is not reached until 24 to 30 hours after injection and clearance is delayed. One patient had the CSF blood transfer determined by the method described by Bercaw and Greer (1970). There was delayed transfer. In a single patient in our series, transfer of the radiopharmaceutical (chelate) from the subarachnoid space into the urine was measured to be $1\frac{1}{2}$ times normal.

The basic pathophysiological abnormality present in pseudotumor cerebri is unknown. Only limited pathological specimens have been obtained. Sahs and Joynt (1956) examined

cortical biopsies in 10 patients with pseudotumor cerebri and found both intracellular and extracellular cerebral oedema in all. Yet in three patients with this syndrome who had post-mortem examinations, no evidence of cerebral oedema was found (Foley, 1955). Albumin transfer studies of Schlesinger and Greer would tend to support the concept that a primary mechanism in the development of benign intracranial hypertension is an abnormality in CSF absorption.

Hakim (1973) has stressed the relation between intracranial venous pressure and the CSF pressure. Elevation of the venous pressure could result in both increased CSF pressure and an absorption defect (James *et al.*, 1973). Why these patients have transient, remittant symptoms, normal sized ventricles, and do not appear subsequently to develop communicating hydrocephalus is unexplained.

In conclusion, from this limited series, we would question the value of a 'transfer test' in the differential diagnosis of pseudotumor cerebri and expect the cisternographic image pattern to be in the normal range in these patients.

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REFERENCES

- Abbott, M., and Alksne, J. F. (1968). Transport of intrathecal I^{125} RISA to circulating plasma. *Neurology (Minneapolis)*, **18**, 870–874.
- Bercaw, B. L., and Greer, M. (1970). Transport of intrathecal ^{131}I RISA in benign intracranial hypertension. *Neurology (Minneapolis)*, **20**, 787–790.
- Curl, F. D., Harbert, J. C., and McCullough, D. C. (1972). Quantitative cisternography: an aid to diagnosis. *Cisternography and Hydrocephalus*, pp. 441–451. Edited by J. C. Harbert. Thomas: Springfield, Ill.
- Foley, J. (1955). Benign forms of intracranial hypertension—'toxic' and 'otitic' hydrocephalus. *Brain*, **78**, 1–41.
- Guidetti, B., Giuffrè, R., and Gambacorta, D. (1968). Follow-up study of 100 cases of pseudotumor cerebri. *Acta Neurochirurgica*, **18**, 259–267.
- Hagberg, B., and Sillanpää, M. (1970). Benign intracranial hypertension (pseudotumor cerebri). *Acta Paediatrica Scandinavica*, **59**, 328–339.
- Hakim, S. (1972). Biomechanics of hydrocephalus. In *Cisternography and Hydrocephalus*, pp. 25–55. Edited by J. C. Harbert. Thomas: Springfield, Ill.

- Jacobson, H. G., and Shapiro, J. H. (1964). Pseudotumor cerebri. *Radiology*, **82**, 202–210.
- James, A. E., Jr, Strecker, E.-P., Novak, G., and Burns, B. (1973). Correlation of serial cisternograms and cerebrospinal fluid pressure measurements in experimental communicating hydrocephalus. *Neurology (Minneap.)*, **23**, 1226–1233.
- Saahs, A. L., and Joynt, R. J. (1956). Brain swelling of unknown cause. *Neurology (Minneap.)*, **6**, 791–803.
- Schlesinger, E. B., Bailey, S., and Groover, R. (1965). Patterns of central nervous system pathology as depicted by isotope encephalography. *Transactions of the American Neurological Association*, **90**, 292–294.
- Strecker, E.-P., Scheffel, U., Kelley, J. E. T., and James, A. E., Jr (1973). Cerebral fluid absorption in communicating hydrocephalus. Evaluation of transfer of radioactive albumin from subarachnoid space to plasma. *Neurology (Minneap.)*, **23**, 854–864.
- Van Wart, C. A., Dupont, J. R., and Krintz, L. (1960). Transfer of radioiodinated human serum albumin (RISA) from cerebrospinal fluid to blood plasma. *Proceedings of the Society of Experimental Biology*, **103**, 708–710.