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CEREBROSPINAL FLUID DYNAMICS IN THE FIELD OF NEUROSURGERY

BY

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ABSTRACT

Alteration in the cerebrospinal fluid (CSF) circulation was studied in 62 patients with neurosurgical diseases by CT cisternography using a water-soluble contrast medium, metrizamide, and also with radionuclide (^{169}Yb- or ^{111}In-DTPA) cisternography. As a rule, the patterns of both methods were in good agreement. The findings were classified into 3 types and 5 subdivisions.

CT cisternography is useful for sequential observation of the CSF circulation with detailed morphological definition, and radionuclide cisternography is useful for observing the general flow of CSF. Some patients with hydrocephalus showed hypodensity around the ventricle, where migration of metrizamide was observed on CT images after its ventricular reflux. This suggests an increased transependymal resorption of CSF. The mathematical analysis of attenuation coefficients on CT cisternography provided more objective and quantitative data for study of CSF dynamics.

INTRODUCTION

The cerebrospinal fluid (CSF), a constituent of the extracellular fluid, together with other brain tissue fluids is in a constant flow into one direction so that the brain environment is protected and its homeostasis is maintained. Disturbances of the CSF circulation are due to various pathologically abnormal conditions, particularly neurosurgical lesions such as normal pressure hydrocephalus (NPH, idiopathic), subarachnoid hemorrhage (SAH), subdural hematoma (effusion), brain tumor, meningitis, etc. Since Di Chiro's report,[1] the CSF dynamics under various abnormal conditions have been studied by radionuclide cisternography (RNC). We reported during the last several years on changes of CSF dynamics mainly in patients with hydrocephalus after SAH.[2,3] On the other hand, the computed tomography (CT) reported by Hounsfield in 1972[4] is now accepted widely as a remarkable diagnostic apparatus for intracranial lesions. Moreover, the use of metrizamide, a water-soluble medium reported by Greitz and Hindmarsh in 1974 in CT cisternography (CTC) has brought a great improvement in CT scanning and enabled a far advanced study of CSF dynamics.[6,7] This new method enables CSF enhancement by the new contrast medium so that all the details of venticles, cisterns, and other subarachnoid spaces become clearly observable with passage of time.[8]

We have studied CSF dynamics in 348 cases with RNC in the past 10 years, and with CTC in 177 cases in the last 3 years, out of which cases, 62 were studied simul-

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taneously by the two methods. Hence, we are going to discuss the CSF dynamics of these patients with neurosurgical diseases.

Materials and Methods

The subjects were the cases in whom both CTC and RNC were carried out. Their age was widely distributed from 3 months to 69 years old, and 44 were males and 18, females. Table 1 shows that most of them were for diagnostic purposes with regard to the communicating hydrocephalus after subarachnoid hemorrhage caused by rupture of intracranial aneurysms or arteriovenous malformation and others were for diagnosis of hydrocephalus after meningitis, differentiation of subdural collection and their allied diseases, diagnoses of skull base tumors, etc.

Table 1. Clinical diagnosis

Diagnosis	No. of case	
Subarachnoid hemorrhage	24	
Aneurysm		18
A-V malformation		2
Moya-Moya		1
Unknown		3
Brain tumor	8	
Parasellar		4
CP angle		3
Other		1
Subdural hematoma and its allied diseases	20	
Arachnoid cyst	2	
Normal pressure hydrocephalus (idiopathic)	3	
Miscellaneous	5	
Total	62	

For CTC scanning, the nonionic, water-soluble contrast medium, metrizamide, was intrathecally injected through a lumbar puncture, and the scanning was made after 1, 3, 6, 24, and 48 hr, or sometimes after 72 hr. The volume and concentration of metrizamide used was 6–10 ml of 170 mg I/ml isotonic solution. One hour before CT scanning 10 mg of Diazepam or 100 mg of phenobarbital was injected intramuscularly, as a premedication in adults, and the same in reduced volume in children depending on their body weight. For 30 min after the lumbar puncture, the body was kept in the position either with the lumbar region raised by a pillow under the head to prevent direct flow of metrizamide into the skull or without raising the waist but keeping the body flat and level on the back. To patients, who were the direct observation subjects of this report, 0.3–1.0 mCi of ^{169}Yb-DTPA or ^{111}-In-DTPA was injected through the same needle after the metrizamide injection. The CT scanner used was EMI CT 1010, which provided visual images and simultaneously enabled specification of the region of interest (ROI), where the attenuation coefficient (expressed in Hounsfield units, H.U.) was calculated, and the time course of the values with time was analyzed. On the other hand, the RN scan was made with Pho/Gamma IV type gamma camera (Nuclear Chicago), and the image was compared against that of CTC.

Results

As a rule, RNC and CTC patterns were in good agreement. Consequently, we classified the cases into three types depending on our previous RNC results[2] (Table 2).

The cases of type I were those which had the ventricular reflux of metrizamide or RN, which persists there for 24 hr or more (ventricular stasis). This type was subdivided into a group of those having entirely no flow into the convexity subarachnoid space (completely blocked cases) and the another having locally lacking or reduced flow (incompletely blocked cases). The cases of type II accompanied ventricular reflux for the first 6 hr, but it gradually disappeared in 24 hr. Most of metrizamide

Table 2. Results of CT and RN cisternography

Type	No. of cases	
	CTC	RNC
I. Persistent ventricular reflux	20 (32%)	16 (26%)
A. No convexity flow	6	7
B. Partial convexity flow	14	9
II. Trasient ventricular reflux	17 (27%)	13 (21%)
III. No ventricular reflux	25 (41%)	33 (53%)
A. Delayed convexity flow	12	17
B. Normal convexity flow	13	16
	62 (100%)	62 (100%)

or RN injected was detected as a convexity flow, revealing a normal flow, or asymmetric flow. The cases of type III were those having no ventricular reflux (excepting in the 4th ventricle) but only the convexity flow, which was further classified into the normal convexity flow in which it almost disappeared in 24 to 48 hr and delayed convexity flow in which it retarded to disappear after 48 hr. The above classification is by terms of the convexity flow while there were other findings such as local increase on pooling of metrizamide or RN, which was seen in diseases such as arachnoid cyst, porencephaly, etc. In subdural hematoma or collection, local block or reduction of metrimazide or RN was observed. Table 2 summarizes all the above findings, and the results of CT and RN cisterngraphy.

1) Normal type and delayed type (Type III) [Fig. 1]

In only 1 hr after the metrizamide injection, the cervical subarachnoidal space and part of the intracranial subarachnoidal space were opacified by metrizamide, and in 3 to 6 hr, the basal cisterns, sylvian fissures, interhemispheric fissure, and sulci of the cerebrum and cerebellum come into the picture symmetrically. After the passage of 24 hr, the medium did not remain in the basal cistern any longer but diffused in the brain substance itself with increased attenuation coefficient, particularly in the area adjacent to the subarachnoid space, presenting a hazy appearance on the image.

Absorption also increased around the superior sagittal sinus. After passage of 48 hr, almost no medium was recognized. In cases with the normal type, usually there was no ventricular reflux but the 4th ventricle was often opacified. In cases with delayed type, metrizamide was recognized in the brain substance or subarachnoid spaces after 48 hr. As shown in Fig. 2, this was confirmed by ROI applied on the parietal lobe, where the absorption coefficient (H.U.) was significantly increased at 24 hr.

RNC showed the same patterns as the CTC's, but the detailed analysis in each of the cisterns was not possible with RNC. With RNC, RN accumulation sometimes occured at around the superior sagittal sinus, but with CTC, images were well scattered all over the convexity.

2) Ventricular reflux and stasis (Type I) [Figs. 3 and 4]

The cases of Type I were those of ventricular stasis, strongly suggesting communicating hydrocephalus, in whom hypodensity area around the ventricles was often observed. This part is called periventricular lucency (PVL) or periventricular hypodensity on CT image [Fig. 5]. The images showed that PVL gradually changed to periventricular high density rim. On the other hand, the cases of communicating hydrocephalus that already received ventriculoperitoneal shunt (V-P shunt) did not show any hypodensity area, without migration of metrizamide into the white matter, showing no stochastically significant differ-

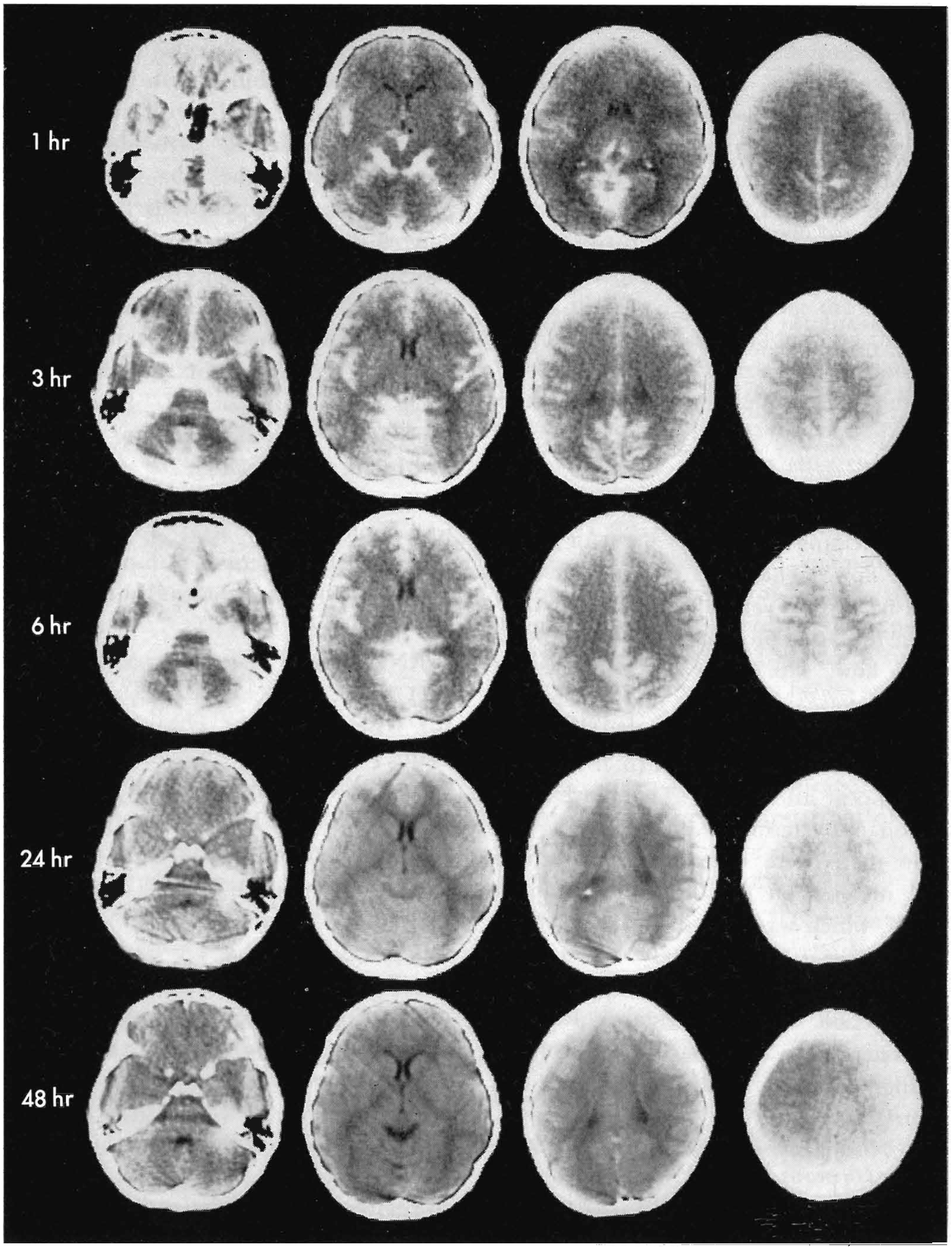

Fig. 1. CT cisternograms taken at 1, 3, 6, 24, and 48 hr after metrizamide injection. Normal pattern (III–B type)

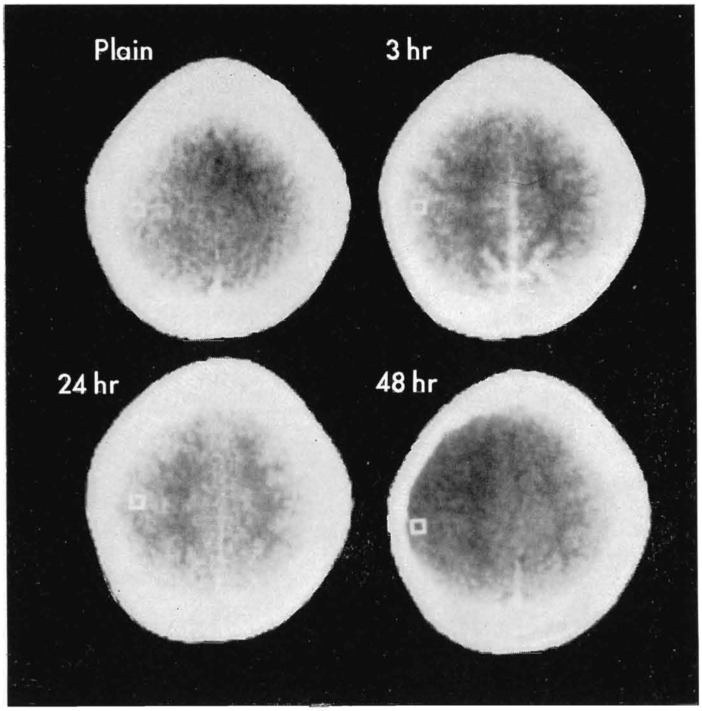

Fig. 2. Region of interest (cursor) in parietal lobe. Calculation of ROI is shown in Table 3.

Table 3. Changes in attenuation in the parietal lobe

Hours after injection	Hounsfield units[1]		Statistical significance[2]
	Mean	SD	
Plain CT	43.6666	4.6666	
3 hr	63.8888	3.4138	$p<0.005$
24 hr	66.8888	2.5579	$p<0.005$
48 hr	47.5555	2.4993	—

[1] n=9

[2] Statistical significance is calculated by comparing the Hounsfield unit at each scanning time to that of the plain CT scan.

ence in absorption values. It was almost impossible to analyse with RNC results.

3) Transient ventricular reflux (Type II) [Figs. 6 and 7]

These cases had ventricular reflux, but transient; that is, it was clearly observed in the first 6 hr, but almost undetectable after the passage of 24 hr, as most of metrizamide or RN had moved to convexity subarachnoid space. According to the absorption value by H.U., a slight amount of the medium may be recognized in ventricles after passage of 24 hr, but these cases should be specified as Type II by quantitative comparison with the convenxity flow as shown in the above. In some cases designated as Type II, RNC shows a slight amount of the medium detected in ventricles after 24 hr by CTC passage, which may reflect the difference in accuracy of the two methods. In the cases of Type II, there were no low density areas around the ventricles, and almost no penetration of metrizamide into the periventricular tissues was recognized. The blockage of the subarachnoid space was clearly seen as asymmetrical convexity flow. The convexity flow was locally indicated clearly in the region of blocked subarachnoidal space.

Fig. 8 shows a case of the aneurysm of

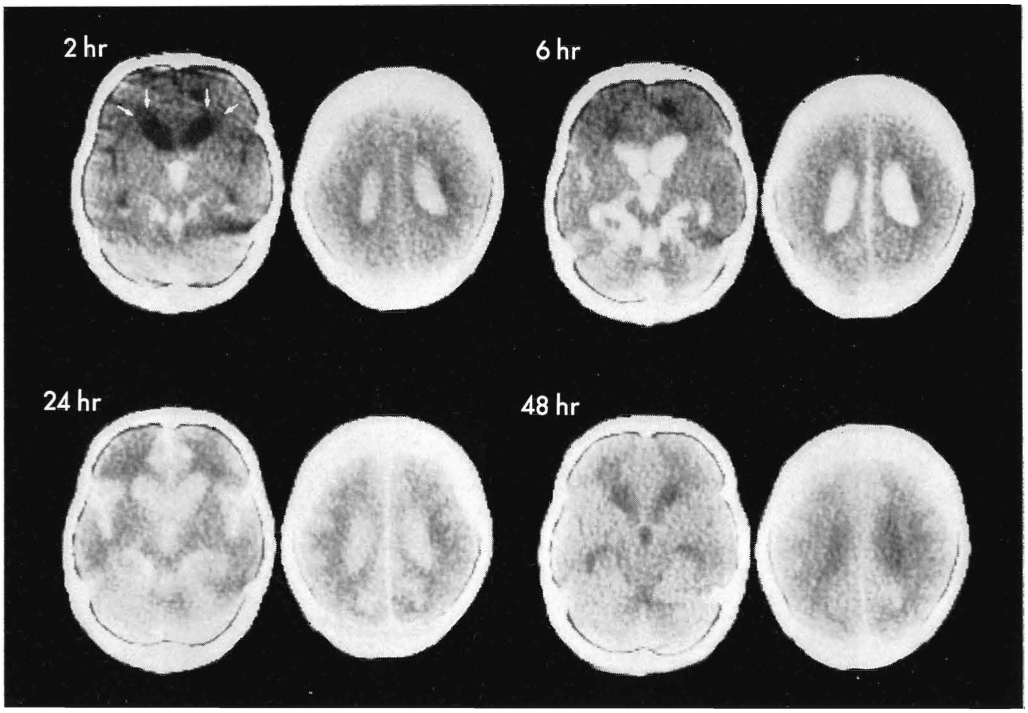

Fig. 3. Persistent ventricular reflux (I–B type). White arrows show periventricular hypodensity area.

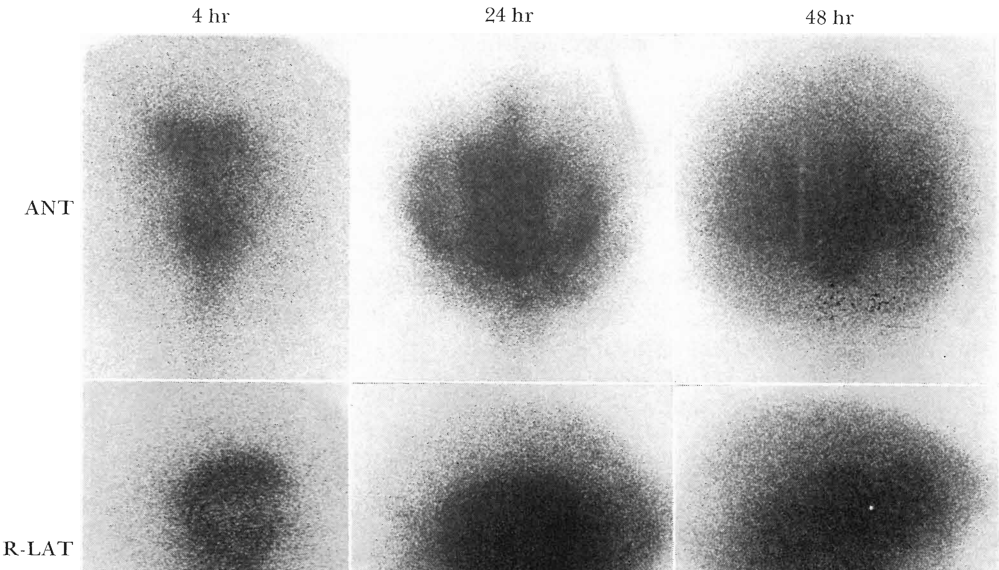

Fig. 4. Radionuclide cisternograms of the same case as Fig. 3.

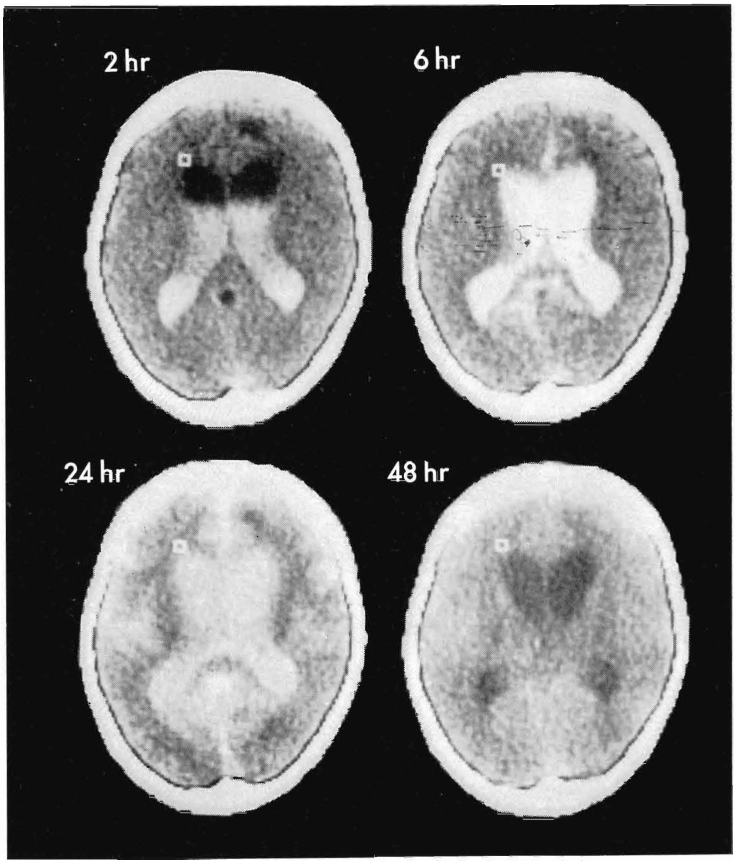

Fig. 5. Region of interest (cursor) in periventricular area after intrathecal injection of metrizamide. Calculation. of ROI is shown in Table 4.

Table 4. Changes in attenuation in the periventricular area

Hours after injection	Hounsfield units[3]		Statistical significance[4]
	Mean	SD	
2 hr	30.0000	3.2403	
6 hr	32.2500	3.4186	—
24 hr	45.7500	3.2691	$p<0.01$
24 hr	42.7500	3.0310	$P<0.01$

[3] n=4.
[4] Staistical significance is calculated by comparing the Hounsfield unit at each scanning time to that of the 2 hr CT scan.

anterior cerebral artery in the knee portion, where CTC shows most of the medium had taken the posterior route from the cisterna ambience and quadrigemina. In another case where the middle cerebral artery (MCA) aneurysm was ruptured, it was seen that metrizamide or RN had not moved into the sylvian cistern of the ruptured side. Thus the asymmetrical convexity flow is an important indication of the region of subarachnoid hemorrhage [Fig. 9].

Discussion

CSF flows constantly in one direction from the place of its creation to that of absorption, but if this route is blocked or some absorption abnormality occurs, the circulation will be disturbed and the results

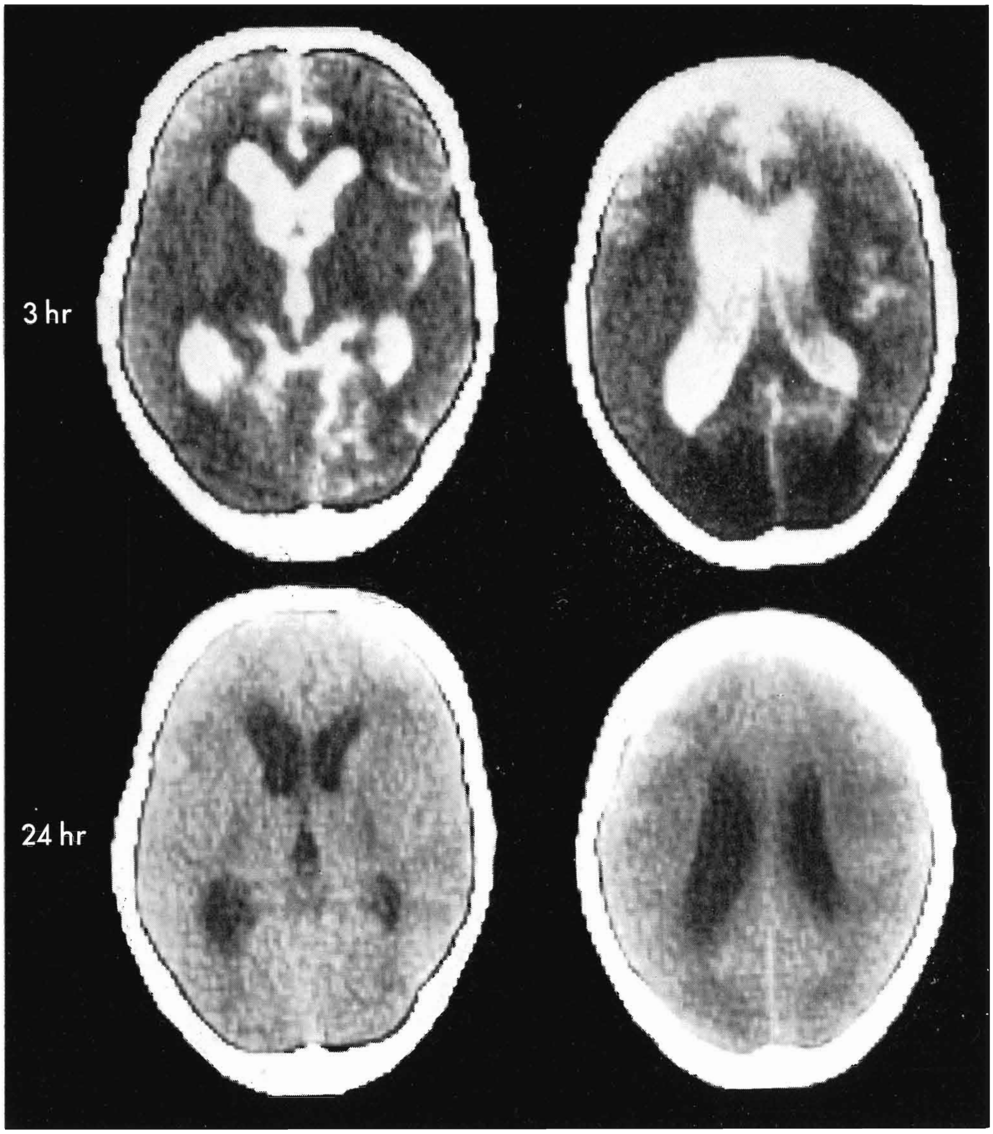

Fig. 6. Transient ventricular reflux (II type).

will be the conditions such as obstructive or communicating hydrocephalus. Examination of CSF dynamics is essential for neurosurgical treatment. Since Di Chiro's reports,[1] studies on CSF dynamics were made by RN cisternography, but CT cisternography[5,6] has now come into our attention since the introduction of CT scan to this field, which has a far better morphological definition. This method employs a nonionic, water-soluble contrast medium, metrizamide,[9] developed in Norway, which enhances CSF, so that CSF dynamics and CSF space images can be more clearly observed. Metrizamide has a molecular weight of 789.1, which is about equal to those of ^{169}Yb-DTPA and ^{111}In-DTPA, both used in RNC. The specific gravity of

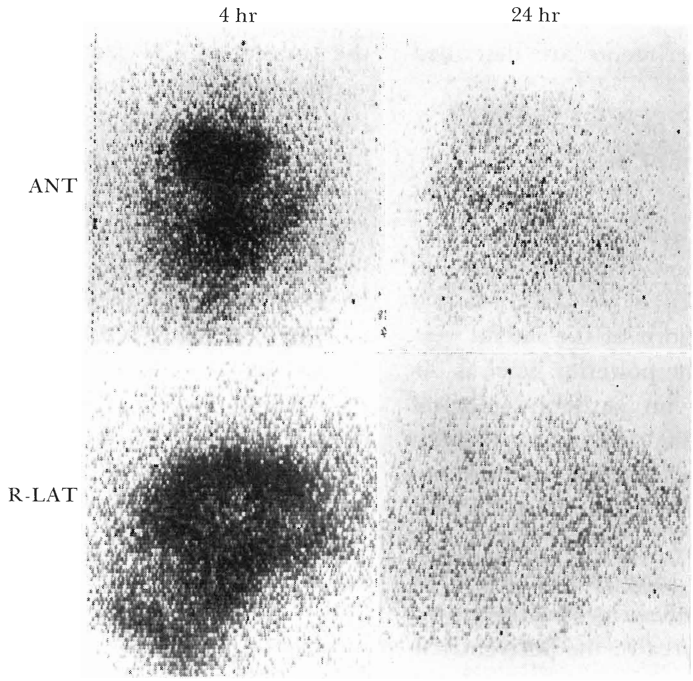

Fig. 7. Radionuclide cisternograms of the same case as Fig. 6.

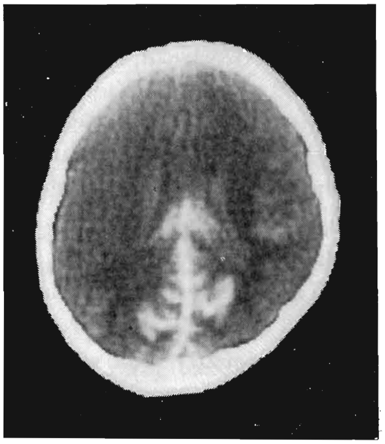

Fig. 8. Ruptured aneurysm of anterior communicating artery. Anterior interhemispheric fissure is obstructed and metrizamide is seen in posterior interhemispheric fissure.

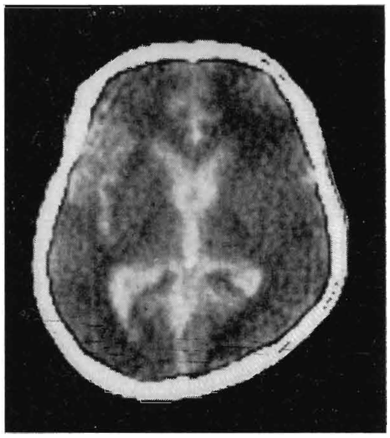

Fig. 9. Right middle cerebral aneurysm. Right sylvian fissure is obstructed.

metrizamide is $d_4=1.184$ in isotonic solution (170 mg I/ml), which is higher than that of CSF. Therefore, possible effect of postural conditions cannot be avoided to some extent. However, its representation of the CSF circulation, when it is once in the intracranial spaces, is considered to be correct. Some of the interesting findings about CSF dynamics observed with metrizamide in our experiments are described below.

1. Modification of periventricular hypodensity by migration of metrizamide

It has been pointed out that in cases of hydrocephalus, particularly in acute and hypertensive types, low density area around the ventricles, particularly at antero-lateral region of anterior horn of the lateral ventricle and around the posterior horn, is observed by CT but no pathophysiological meaning of these phenomena has yet been determined.[10,11] In the cases where metrizamide had shown reflux into ventricles, we made an observation of the migration of the medium by time passage and confirmed that the medium gradually moved to the low density area in the periventricular tissue, and also from analysis of the absorption coefficients [Fig. 5 & Table 4]. This was not seen in the patients of communicating hydrocephalus who had already received shunting operation, that is, low density area around ventricles and transfer of the medium to the surrounding tissues were not found. In the cases of transient ventricular reflux, there was almost no PVL and slight, if any, transfer of metrizamide.[12]

Milhorat *et al.*[13] demonstrated transependymal transfer of a tracer in obstructive hydrocephalus in animals, and also showed RN transfer to the surrounding area(s) of ventricle(s) as a double-density pattern by RN ventriculography in clinical cases.[14] Price *et al.*[15] recorded a transependymal bulk flow from the damaged ventricular surface of a dog with communicating hydrocephalus, which they considered to be the CSF absorption route. With CT, on the other hand, Pasquint *et al.*[11] quantitatively studied the PVL in cases of hydrocephalus before and after a shunt, and considered that the PVL showed the transfer of CSF from ventricles to the surrounding area. Hopkins *et al.*[10] stated that PVL was seen not only in obstructive hydrocephalus but in normal or hypertensive communicating hydrocephalus and concluded that PVL could most likely be explained as increased absorption of CSF by periventricular brain tissues. Our observation of the gradual transfer of metrizamide to PVL in the present study gave us reasons to believe that this indicates directly the CSF trans-ependymal absorption *in vivo* on the CT image.

There are many controversies as to the indication of surgery for NPH,[16] but if CTC shows ventricular stasis of metrizamide with penetration into PVL, shunt is considered an adequate solution.

2. CSF absorption from the brain surface

As Drayer *et al.*[7] have already pointed out, the absorption of metrizamide was found from the brain substance, particularly the part in contact with the subarachnoid space in 12 to 48 hr in CT image. In delayed cases, the absorption was seen increasing for 48 or even 72 hr at times, and this increase was found to differ significantly from the analysis of the absorption coefficients of the ROI placed on the brain surface. This suggests that metrizamide was absorbed through the Virchow-Robin space. Conventionally, CSF was recognized as it was absorbed through the arachnoid granulations near the superior sagittal sinus,[17] because RNC image (particularly with RISA) reveals increased RN-uptake in the same area after 24 hr passage. However, CTC showed that CSF was absorbed from more extensive area of the brain surface.

3. RNC and CTC

When the cases which were examined with both RNC and CTC were compared, the CSF flow patterns appeared almost identical between the two methods. RN was absorbed from the parasagittal arachnoid granulations as RN accumulates around the superior sagittal sinus on RNC.[17] However, in addition to the parasagittal blush, CTC showed a diffuse and hazy appearance in the brain substance, particularly in the part adjacent to the subarachnoid space in the passage of 12 to 24 hr, which strongly suggests that CSF absorption occurs also from the brain surface. We have already mentioned that there are evidences suggestive of trans-ependymal absorption in the cases of communicating hydrocephalus and obstructive hydrocephalus. Thus, we are of the opinion that CTC provides us means for more detailed and quantitative analysis of CSF flow. However, it is true that RNC has advantages such as the possibility of determining the degree of absorption disturbance simply by observation of the intravascular transfer curve of the blood, less side effects than CTC, and the provision of grasping the general flow pattern.

4. Side effects

The reported side effects caused by intrathecal injection of metrizamide are headaches, nausea, vomiting, convulsions,[18] etc., but compared to those caused by conventional water-soluble contrast media, they are fewer or less severe, and its safety is higher. We recognized headache, nausea, and vomiting in about one-fourth of the cases, but these were all transient and disappeared in 24 hr. No convulsions were seen, and the EEG findings were all normal except in some cases where a transient slow abnormality was observed. With RNC, there was no side effect except a headache after the spinal tap.

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