

Abnormal Cisternogram Associated with Diamox Therapy

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A cisternogram characteristic of normal-pressure hydrocephalus was obtained from a patient on Diamox who was being evaluated for rapid mental deterioration. A repeat cisternogram after Diamox was discontinued was nearly normal. We hypothesize that the initial abnormality resulted from reduced cerebrospinal fluid production caused by carbonic anhydrase inhibition; this defect (reduced flow) led to a net reflux of tracer into the ventricles. The reflux is believed to be due to the reduction of bulk cerebrospinal fluid flow from the ventricles.

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The differential diagnosis of dementia frequently focuses on the early identification of those patients with treatable disorders and their differentiation from patients with cerebral atrophy due to such degenerative processes as Alzheimer's disease or senile cortical atrophy. An important treatable condition to consider is normal-pressure hydrocephalus (1,2). Although the clinical features in the two groups of patients are frequently similar, the patient with normal-pressure hydrocephalus is classically described as exhibiting a triad of dementia, incontinence, and gait disturbance. In addition, cisternography in these patients frequently shows ventricular filling with failure of tracer to migrate over the cerebral convexities. Because these findings on radionuclide scanning often lead to treatment with ventricular shunting procedures, the following patient, in whom an abnormal cisternographic examination was obtained during Diamox therapy, is of particular interest.

CASE REPORT

A 70-year-old white man was admitted to the Peter Bent Brigham Hospital for evaluation of a rapidly deteriorating mental state over a 6-mo period. Specific symptoms and complaints included loss of memory, intellectual impairment, unsteady gait, and, latterly, urinary incontinence.

The EEG showed generalized slowing with excessive theta activity. A CT scan demonstrated mild ventricular enlargement and some prominence of the cerebral sulci, consistent with cerebral cortical atrophy. CSF chemistry was unremarkable.

Because of the possible diagnosis of normal-pressure hydrocephalus, the patient was placed on Diamox before his admission. However, he failed to take it regularly. He was continued on Diamox for the first 4 days of hospitalization (250 mg orally, three times a day). A radionuclide cisternogram was performed on the second hospital day. Under fluoroscopic control, 400 μ Ci of In-111 DTPA were injected into the subarachnoid space of the lumbar spine. Images taken at 4 hr postinjection showed radioactivity only along the spinal canal. At 20 hr there was also activity in the basal cisterns with some progression through the Sylvian fissures (Fig. 1). In addition, ventricular filling was evident. At 48 hr there was no significant change (Fig. 1).

Because of a mild metabolic acidosis and of the possible interference of Diamox with CSF kinetics, it was discontinued on the fourth hospital day. A re-

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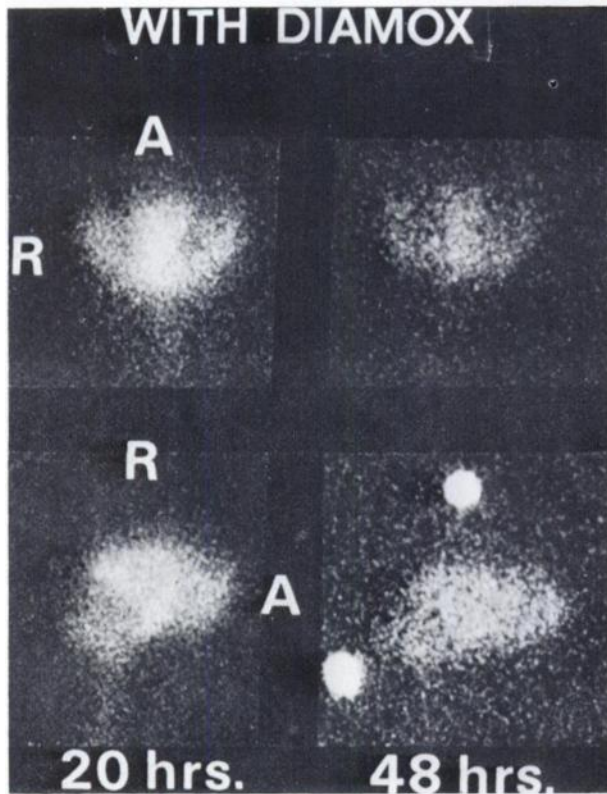


FIG. 1. Radiocisternogram obtained with patient on Diamox. Twenty-hour study shows ventricular filling with a little progression through Sylvian fissure. Forty-eight-hour study is virtually unchanged. (Circular hot spots on 48-hr view are markers.)

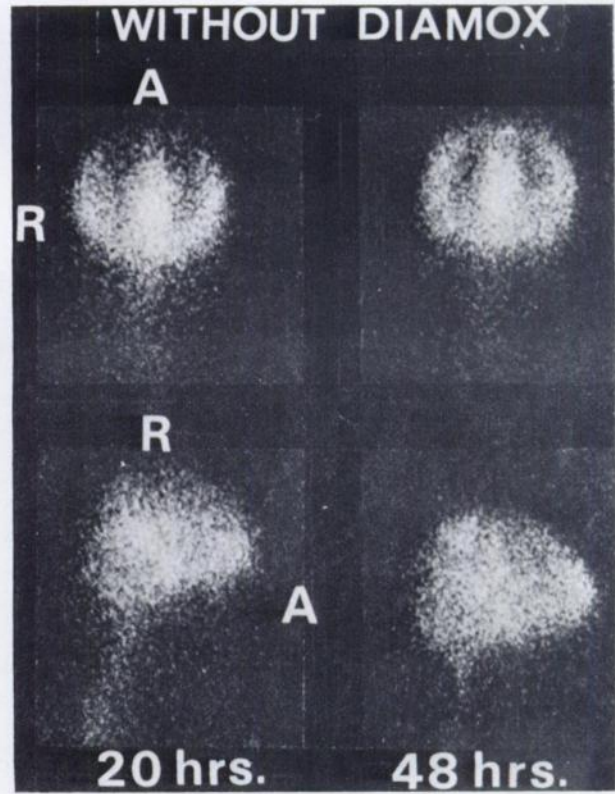


FIG. 2. Repeat examination after Diamox was discontinued. Twenty-hour study shows activity mainly in region of basal cisterns, with only limited ventricular reflux and some migration of tracer cephalad. Forty-eight-hour study shows further parasagittal migration of radionuclide.

peat cisternogram was requested and performed 5 days later. At that time the 4 hr scan again showed activity along the spinal canal only. At 20 hr activity was recorded primarily in the basal cisterns; however, the radionuclide had progressed through the Sylvian fissures (Fig. 2). It then continued to migrate cephalad over the convexities and by 48 hr had reached the superior sagittal sinus (Fig. 2).

DISCUSSION

In the normal individual, after a lumbar subarachnoid injection of a tracer material, the radionuclide ascends to the basal cisterns. Then, by virtue of the net bulk flow of CSF out of the ventricular system and the relative ease of passage through the basal cisterns, the tracer ascends over the cerebral convexities without entering (refluxing into) the ventricles. In patients with presenile or senile dementia, slow ascent of the tracer towards the parasagittal region has been observed, possibly because of slower flow in an enlarged CSF reservoir (1). Some of these patients demonstrate ventricular filling, but this is usually transient and of limited degree.

In patients with normal-pressure hydrocephalus, there is ventricular dilatation with impairment of the

normal CSF flow and absorption pattern. It is postulated that this condition results from a relative obstruction to the flow of CSF, either in the region of the basal cisterns or in the region of the parasagittal venous sinuses (2). A pneumoencephalographic picture showing little or no air over the convexities would support the first mechanism. In these patients secondary absorption sites become important—e.g., the choroid plexuses themselves, the ventricular ependyma, the leptomeninges, and the extradural lymphatics of the cranial and spinal nerves (3). These changes in CSF flow result in a radiocisternogram that characteristically shows both a delay (and/or absence) in the cephalad movement of the tracer to the parasagittal area, and ventricular reflux and stasis of the radionuclide in the ventricles (5).

Although no test procedure has proved completely accurate in identifying patients who will respond favorably to CSF shunting, cisternography has frequently been employed as the most helpful of the several tests available. Its low morbidity and ease of performance further recommend it. However, because of the morbidity and occasional complications of CSF shunting (e.g., serious infections and production of subdural hematomas) it is important that

unnecessary shunts be minimized, that is, that the CSF cisternogram be reliable. The present case illustrates one potential source of an iatrogenically abnormal scan. This patient, placed on Diamox, exhibited an abnormal cisternogram, which returned towards normal on repeat examination after Diamox had been discontinued.

Experimental work in both animals and humans has established that Diamox reduces the rate of CSF formation by 30–50%, by specifically inhibiting the enzyme carbonic anhydrase, which has been implicated in the active formation of CSF by the choroid plexus (4). Studies have not supported any effect of Diamox on the flow or absorption of CSF except as an effect secondary to its inhibition of production (7). There is additional experimental evidence that Diamox may also decrease CSF production by selective vasoconstriction of the choroid-plexus arteries (8). Based on these observations, Diamox has been used with variable success to control neonatal and childhood hydrocephalus, especially where the head is only slowly enlarging (2,3,9,10).

In our patient the administration of Diamox appears to have altered the normal CSF pattern, so that an abnormal cisternographic picture was obtained with both persistent ventricular filling and virtually no parasagittal migration of the tracer. We hypothesize that the reduced CSF production due to inhibition by carbonic anhydrase resulted in a net reflux of tracer into the ventricular system as a consequence of reduced bulk flow of CSF out of the ventricles.

Although there is still considerable controversy regarding the incidence and clinical diagnosis of normal-pressure hydrocephalus, the observation that

Diamox may produce abnormalities on cisternography should reduce further the chances of shunting patients who have little hope for significant improvement.

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