

Is Early Bladder Activity in Radionuclide Cisternography an Indirect Sign of Spontaneous Intracranial Hypotension or Sequence of Lumbar Puncture?

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Abstract: Spontaneous intracranial hypotension (SIH) is characterized by severe postural headache and low cerebrospinal fluid (CSF) pressure. Radionuclide cisternography (RC) is of some value in diagnosing CSF leakage causing SIH. However, the sensitivity of RC is too low to demonstrate the site of leakage. In these cases, the early appearance of the radioactivity in the urinary bladder has also been used as an indirect finding in the diagnosis of SIH. The aim of this study was to evaluate the diagnostic reliability of early urinary bladder activity as an indirect sign of SIH. We investigated early bladder activity in 21 patients with suspicion of normal pressure hydrocephalus. Of the 21 subjects, 13 (62%) showed early bladder activity. We demonstrated that early bladder activity is observed in patients without CSF leakage such as normal pressure hydrocephalus. Therefore, this indirect finding of RC is not a reliable finding in diagnosing SIH.

Key Words: spontaneous intracranial hypotension, early bladder activity, Tc-99m DTPA radionuclide cisternography, normal pressure hydrocephalus

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Spontaneous intracranial hypotension (SIH) is a postural headache associated with low cerebrospinal fluid (CSF) pressure and with no history of previous dural trauma. The characteristic headache comes on or is exacerbated by the upright position and disappears or is alleviated when the patient is in the recumbent position.^{1,2} SIH is thought to result from a dural tear and CSF leakage specifically in the spinal level.

Radionuclide cisternography (RC) is an important tool in diagnosing CSF leakage causing SIH.³ Extradural accu-

mulation of radionuclide in cisternography is direct evidence of CSF leakage and points to the site of leakage.^{4,5} However, the sensitivity of RC is low and sometimes fails to pinpoint the site of leakage.⁶ In such cases, the early appearance of radioactivity in the urinary bladder, which is thought to be an accumulation of radionuclide leakage through the dural defect into the venous system, has also been used as an indirect finding in the diagnosis of SIH.^{4,5,7,8}

In this study, we evaluated the diagnostic reliability of early urinary bladder activity as an indirect sign of SIH. For this purpose, a group of patients who were clinically suspected to have normal pressure hydrocephalus (NPH) was selected to evaluate early urinary bladder activity in RC. We also attempted to uncover some other possible factors causing early bladder activity in these patients.

METHODS AND MATERIALS

Between June 2004 and May 2006, 21 patients (10 males, 11 females; age range, 51–78 years; mean age \pm SD 63.6 \pm 8.4 years) with suspected NPH were referred for RC. The study was approved by the human institutional review board, and informed consent was obtained for each patient. All patients had the clinical triad of NPH with dementia, incontinence, and characteristic gait ataxia. None of these patients had characteristic symptoms of SIH, such as severe postural headache, nausea, vomiting, neck stiffness, and tinnitus.

Radionuclide cisternography was performed after an intralumbar injection of 185 MBq (5 mCi) Tc-99m DTPA (diethylenetriamine-penta-acetic acid) using a 22-gauge needle. During LP, we noted the number of punctures. After 5 minutes of resting, anterior and posterior images of the abdominopelvic region were obtained to visualize bladder activity. Sequential images were obtained at intervals of 2 minutes for 60 minutes in the prone position by using 2 different gamma cameras (ADAC VERTEX-plus dual-headed gamma camera, equipped with low energy high resolution collimators and Siemens Orbiter gamma camera, equipped with a low energy all purpose collimator). Furthermore, delayed images of the skull were obtained at 2, 4, and 24 hours to evaluate ventricular reflux and to confirm activity of the cerebral convexities.

We calculated how frequently early bladder activity is observed in patients with suspected NPH. In the group of

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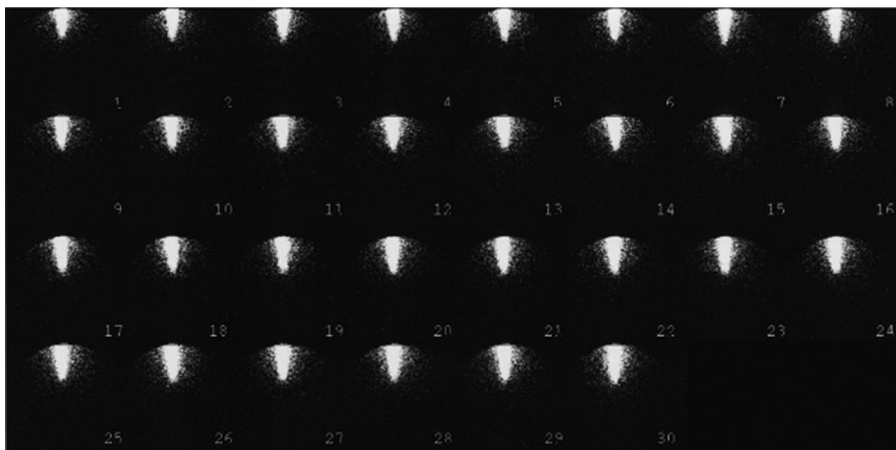


FIGURE 1. Serial Tc-99m diethylene-triamine-penta-acetic acid radionuclide cisternographic images of patient no. 20 in the anterior position. Radioactive accumulation was not observed in the region of the bladder.

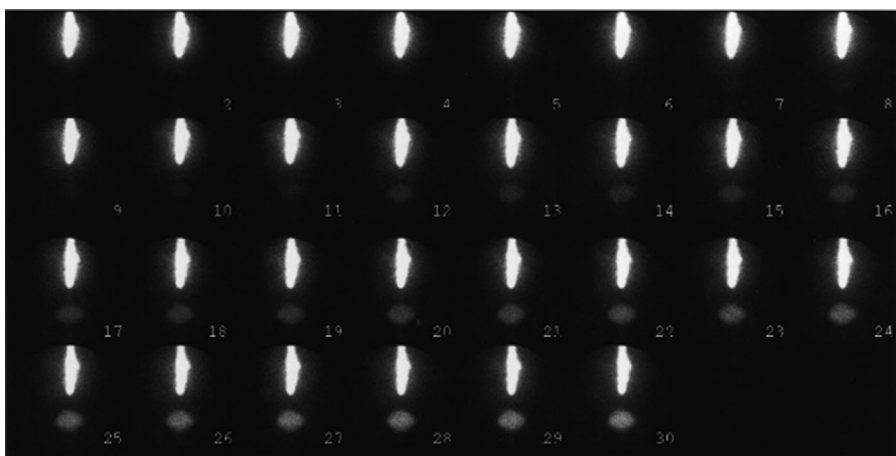


FIGURE 2. Serial radionuclide cisternographic images of patient no. 6 in the anterior position. From 7 images (upper row, 21 minutes) radioactive accumulation was observed in the bladder.

patients with detected early bladder activity, we investigated the association of presence of early bladder activity (response) with age, gender, presence of NPH, and number of puncture (predictors).

In our analysis, we use the statistical software R for Windows version 2.2.0. A P value less than 0.05 was deemed to have statistical significance (for more details on the models and tests performed please see reference 9). First, we fit a logistic regression model in which age, gender, number of punctures, and presence of NPH variables entered as covariates and detection of the early bladder activity as the response variable.

RESULTS

Of the 21 subjects, 13 (62%) showed early bladder activity at varying time points (Figs. 1 and 2). RC revealed NPH in 13 of the patients in our study. Six patients (46%) showed early bladder activity among 13 patients with NPH. Seven patients (87.5%) showed early bladder activity among 8 patients without NPH. The details are given in Table 1.

We found that only the number of punctures exert a significant effect on the probability of detecting early bladder activity ($P = 0.0019$, χ^2 with 1 df). That is, there is a significant association between early bladder activity and the number of punctures. The inclusion of the covariates (gender,

age, NPH, and traumatic puncture factors) does not significantly improve the fit over the final logistic regression model with only the number of punctures as the response variable ($P = 0.4841$ based on the χ^2 with 4 df). In Figure 3, we plot the logit fitted values and the actual values of the detection of early bladder activity against number of punctures. Observe that the probability of a patient at the low end of the distribution of number of punctures (ie, with 1 puncture) has about a 0.3 probability of detection of early bladder activity whereas at the high end of the distribution of number of punctures (ie, with 3 punctures) has about a 0.99 probability of detection of early bladder activity. This is a significantly sizable effect.

DISCUSSION

The pathogenesis of SIH associated with postural headache and low cerebrospinal fluid pressure is not clear, but it is usually considered secondary to occult CSF leakage through a small meningeal defect.^{1,10} CSF leakage also occurs secondary to lumbar puncture, myelography, spinal anesthesia, or head injury.¹¹⁻¹³ The actual cause of spontaneous CSF leaks often remains obscure. However, 2 factors are the most viable suspects: some patients have had previous trivial trauma; and in some patients focal weakness of the thecal sac

TABLE 1. Summary of Patients

Patient No.	Age	Gender	Presence of EBA (min)	Presence of NPH	No. Punctures
1	67	M	No	No	1
2	61	F	No	yes	2
3	73	M	No	yes	1
4	66	F	No	yes	1
5	63	F	Yes (7)	No	3
6	76	F	Yes (19)	No	2
7	59	F	Yes (45)	yes	1
8	71	M	No	yes	1
9	57	F	Yes (21)	No	2
10	54	F	Yes (17)	yes	2
11	53	F	Yes (7)	yes	3
12	52	M	Yes (29)	yes	1
13	51	F	Yes (7)	No	2
14	65	M	No	yes	1
15	68	F	Yes (15)	No	2
16	72	M	No	yes	1
17	75	M	Yes (19)	yes	2
18	58	F	Yes (7)	No	3
19	59	M	Yes (27)	No	1
20	57	F	No	yes	1
21	78	M	Yes (11)	yes	2

EBA indicates early bladder activity; NPH; normal pressure hydrocephalus.

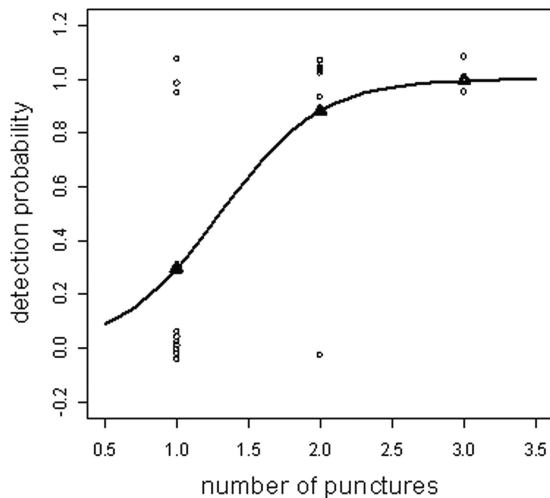


FIGURE 3. Early bladder activity versus number of lumbar punctures. Plotted are the (jittered) raw data (circles), logit fitted values (triangles), and logit prediction line (solid).

likely occur in connection with a connective tissue abnormality such as Marfan syndrome.¹⁴

In most patients, symptoms of SIH are alleviated spontaneously.¹ Conservative medical management is the usual initial treatment for these patients. This approach includes bed rest, oral hydration-over hydration, and caffeine intake. Epidural blood patch is the most common invasive treatment and is probably the treatment of choice, especially in patients who have failed an initial trial of the conservative approach.¹⁵

Epidural saline infusion is another treatment choice, but its effectiveness is questionable.¹⁶ In cases with conservative and less invasive approaches, such as epidural blood patch being ineffective, surgical repair of the dural defect can be performed.

The diagnosis of SIH can be made in conjunction with CSF evidence in a patient with typical postural headache and radiologic–cisternographic findings. CSF findings include decreased spinal fluid pressure, normal or high protein concentrations, and normal or increased white cell counts.^{1,17}

Cranial MRI with gadolinium contrast typically shows diffuse meningeal enhancement. But, diffuse meningeal enhancement can be misleading, because this finding also occurs in inflammatory conditions, dural metastases, or in several other abnormalities.^{18–21} Spinal MRI also reveals characteristic findings in SIH patients.²² CT myelography can be used to detect CSF leakage; however, sensitivity of this technique is low.²³

The most common sites of CSF leakage in SIH syndrome are the cervicothoracic junction and thoracic area.⁵ However, CSF leakage from other areas has also been reported.⁶ RC has been shown to localize CSF leakage in SIH and is considered an important method to identify the leakage site in many cases.^{1,3,6,10,24} The accumulation of the tracer in the extra-arachnoid space is a direct sign of CSF leakage. However, the sensitivity of RC in being a direct sign of SIH is low, and in some cases, RC fails to identify a CSF leaking site. In most cases, the site of the CSF leakage is difficult to locate and may never be identified. The low detection rates of direct findings of dural leakages lead to a search for the indirect findings of dural leakage. In such cases, rapid disappearance of spinal activity and early excretion of the tracer into urine (early bladder activity) are considered indirect signs of CSF leakage.^{4–6,25} Takahashi et al²⁶ accepted appearance of the bladder in the first 5 hours as early bladder activity in their study. Radiopharmaceuticals injected intrathecally into the lumbar subarachnoid spaces normally reach the basal cisterns by 1 hour and the Sylvian fissure area in 2 to 6 hours.²⁷ For this reason, in our study, early bladder appearance after 1 hour of radiopharmaceutical injection is accepted as early bladder activity.

First, Ishiara et al²⁸ speculated on whether early bladder activity in cisternography is a pathognomonic sign or not. Recently, Takahashi et al²⁶ reported early bladder activity in 4 out of 5 NPH patients as a control group. They hypothesized that early bladder activity in their NPH patients may be secondary to complications of lumbar puncture procedures. In our study, 6 patients (46%) showed early bladder activity in thirteen patients with NPH in whom no clinical or laboratory findings of SIH were observed. The studies mentioned above and our study shows that early bladder activity may not be a reliable finding of SIH.

In our study, there is a statistically significant association between early bladder activity and the number of lumbar punctures. A single successful lumbar puncture is difficult because of low or zero CSF pressure, and multiple lumbar puncture attempts are generally required in SIH patients. Moreover, the lumbar epidural venous plexus is engorged in SIH patients.¹⁰ The necessity for multiple lumbar punctures

resulting in unavoidable trauma to the dura and engorged lumbar epidural venous plexus may cause the commonly seen early bladder activity in SIH patients. Besides, a spontaneous dural tear, multiple iatrogenic dural punctures, and an engorged lumbar epidural venous plexus might cause early bladder activity. It is not possible to assert that the definitive cause of early bladder activity is the spontaneous dural tear or multiple iatrogenic lumbar dural punctures. Therefore, this indirect finding of RC is not a reliable finding in diagnosing SIH. Fluoroscopically guided lumbar puncture and a single attempt have a higher reliability for diagnostic purposes. As a result, if it is known that the lumbar puncture has been made without trauma, early visualization of bladder activity may still be a diagnostic sign of SIH.

A potential limitation of this study is generalizing the current findings from NPH patients to SIH patients. This is because the circulation pattern of CSF in NPH patients differs from the circulation pattern of CSF in SIH patients. For this reason, the findings of this study cannot be generalized totally to SIH patients but they can provide an opinion. More detailed studies larger series are needed on this subject.

CONCLUSIONS

Early bladder activity has been accepted as an indirect sign of SIH in the literature. On the contrary, we demonstrated that early bladder activity is observed in patients without CSF leakage, just as it is evaluated for patients with NPH. Multiple punctures may lead to this visualization. Multiple lumbar puncture attempts resulting in additional tears are generally observed in SIH patients during RC. A spontaneous dural tear and multiple iatrogenic dural punctures might also be the cause of early bladder activity.

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