Annals of Nuclear Medicine Vol. 19, No. 4, 339–343, 2005

Detection of cerebrospinal fluid leakage in intracranial hypotension with radionuclide cisternography and blood activity monitoring

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Radionuclide cisternography is an indispensable examination to detect cerebrospinal fluid (CSF) leakage in patients suspected of having spontaneous intracranial hypotension (SIH). However, it sometimes fails to demonstrate the site of CSF leakage, and in such cases, early bladder visualization is utilized for the diagnosis of SIH as an indirect finding. The aim of this work is to improve the diagnostic ability of radionuclide cisternography and to reevaluate the reliability of early bladder visualization as an indirect finding of CSF leakage. ***Methods:*** We obtained serial images during the first hour after injection as well as the following time points in 4 patients with SIH and 5 with normal pressure hydrocephalus (NPH) as a control. We also performed blood sampling over time to measure blood radioactivity concentrations. ***Results:*** All 4 patients with SIH demonstrated leakage, 2 of 4 within one hour after injection. Bladder visualization was observed falsely in 4 of 5 patients with NPH, considered to be the result of a lumbar puncture complication. In this false bladder visualization, blood radioactivity showed a more rapid raise and fall than in CSF leakage of SIH. ***Conclusions:*** The combination of radionuclide cisternography, including early time points and blood sampling, may enable accurate diagnosis of SIH.

Key words: ^{111}In-DTPA cisternography, spontaneous intracranial hypotension, early bladder appearance, time activity curve

INTRODUCTION

SPONTANEOUS INTRACRANIAL HYPOTENSION (SIH) has been shown to cause symptoms such as headache, vomiting, and vertigo due to insufficient cerebrospinal fluid in patients with no remarkable history of trauma. The pathology is considered to be an occult CSF leakage through a small dural defect.[1] An epidural autologous blood injection at the leakage level and surgical treatment which seals the dural lesion are effective in patients who are resistant to an initial trial of conservative management.[2–4] Thus, radionuclide cisternography is an essential examination to detect such leakage.[5–7]

However, radionuclide cisternography sometimes fails to demonstrate the site of CSF leakage.[8] In such cases, the early appearance of urinary bladder activity, which is thought to be an accumulation of radionuclide leakage through the dural defect into the blood stream, has also been utilized in the diagnosis of SIH as an indirect finding,[9–12] but we often encounter cases in which rapid bladder activity appears in patients without CSF leakage, for example, during examination for normal pressure hydrochephalus (NPH).

In this study, to improve the detection of CSF leakage, we obtained serial images during the first hour after injection, monitored the blood radioactivity concentration, and to reevaluate the diagnostic reliability of the early bladder sign, we compared the blood radioactivity curve and planner images in SIH patients with those of NPH patients as a control.

MATERIALS AND METHODS

Between March 1998 and August 2004, thirty-two

Received January 24, 2005, revision accepted March 28, 2005.

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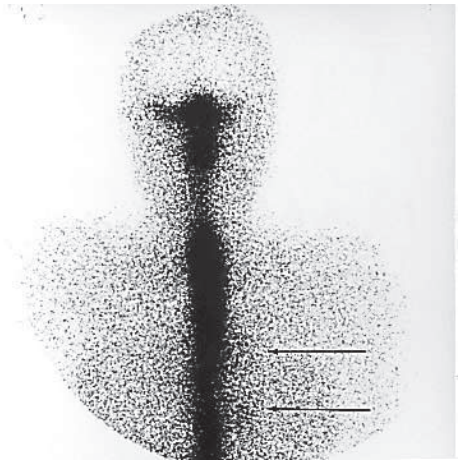
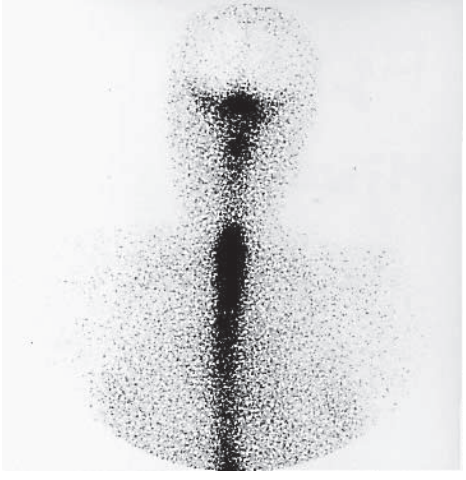
Table 1 The time of the bladder appearance and leakage visualization

patient	bladdar appearance	leakage visualization	
1. SIH	20 min	30 min	shown in Fig. 1
2. SIH	45 min	1 h	shown in Fig. 3 (a) arterial blood sampling
3. SIH	1 h	2 h	shown in Fig. 3 (b) arterial blood sampling
4. SIH	5 h	24 h	
5. NPH	10 min		shown in Fig. 2
6. NPH	20 min		
7. NPH	25 min		shown in Fig. 3 (d) venous blood sampling
8. NPH	30 min		
9. NPH	5 h		shown in Fig. 3 (c) venous blood sampling



a



b

Fig. 1 (a) ^{111}In-DTPA radionuclide cisternography of a patient with SIH. At 30 minutes, the leakages were observed at the left side of the thoracic vertebrae (a). After 1 hour, the leakage could no longer be detected (b).

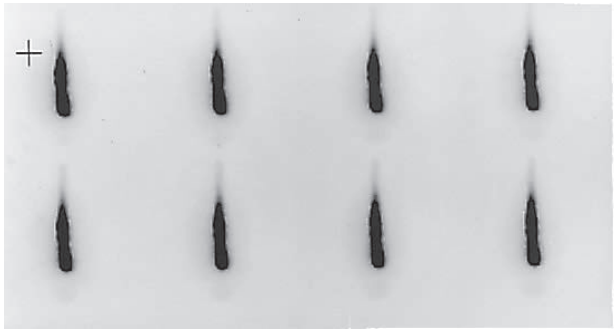


Fig. 2 Serial ^{111}In-DTPA radionuclide cisternography of a patient with NPH, at 10, 15, 20, 25, 35, 40, 45 and 50 minutes. From 10 minutes, radioactivity accumulation was observed in the bladder. This might be attributable to the absorption of radioactivity into the systematic circulation due to unsuccessful lumbar puncture.

patients were referred for radionuclide cisternography due to clinically suspected SIH or NPH. We undertook a retrospective review of 32 scintigraphic scans. Images during the first hour in addition to later images were obtained for 9 patients (6 men and 3 women; mean age 54 ± 15.0 years), among whom 4 were eventually diagnosed with SIH (mean age 42.5 ± 6.6 years), and 5 with NPH (mean age 63.8 ± 12.9). Diagnosis of SIH was based on the characteristic symptoms, such as orthostatic headache, nausea, vomiting, as well as clinical course and CSF leakage on cisternography, while that of NPH was based on the characteristic symptoms, such as dementia, gate apraxia, urinary incontinence, symmetrical bilateral ventricular enlargement on CT or MRI and ventricular reflex on cisternography. In this study, since our patients with NPH had no pathogenic dural defect, we considered them to be a control for SIH.

^{111}In-DTPA at a dose of 37 MBq was administered by lumbar puncture into the subarachnoid space. Images were obtained every 5 minutes during the first hour in the lateral position and at 1, 3, 6, 24 hours in the supine position. Whole body anterior and posterior images were taken using a one-head gamma camera (Starcam 500a GE Medical Systems, Milwaukee, WI) equipped with an intermediate-energy all-purpose collimator 128 × 512 matrix at a speed of 10 cm/min. Radioactive counts lasting 5 minutes in each image were recorded.

Radioactivity concentration in blood was monitored by blood sampling, which was performed for 2 patients with

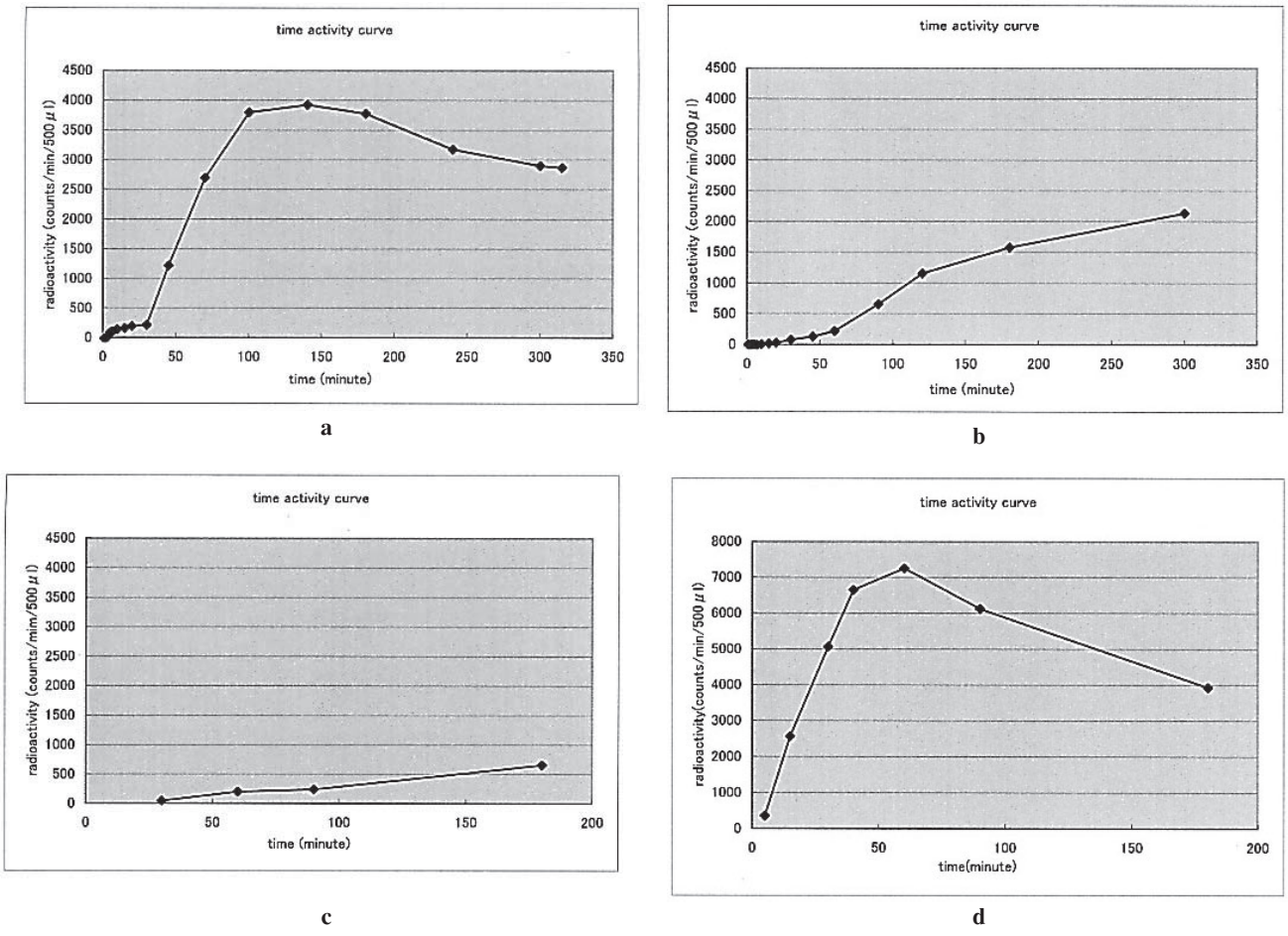


Fig. 3 The blood radioactivity curve of ^{111}In-DTPA radionuclide in 2 patients with SIH (a, b) and in 2 patients with NPH (c, d). (a) The leakage and bladder activity are shown at 1 hour and 45 minutes. (b) The leakage and bladder activity are shown at 2 and 1 hour. (c) No bladder activity was observed until 5 hours at least. (d) The bladder activity was detected at 25 minutes.

SIH through the antecubital artery and for 2 patients with NPH through the antecubital vein. The radioactivity concentration possibly differs in artery or vein; however, our concern in this study was to confirm whether the radiotracer flowed out from subarachnoid spaces into the systemic circulation in the early phase and how the concentration changed with time in each case. From this point of view, the difference in the radioactivity concentration between artery and vein may not be significant enough to need be considered. We informed patients about the aims and potential risks of blood sampling and obtained consent before examinations. Blood sampling started immediately after injection; 17 samples were taken at increasing intervals until 5 hours for 2 patients with SIH, and 4 to 7 samples were taken until 3 hours for 2 patients with NPH.

RESULTS

Four patients with SIH and 5 patients with NPH were included in this study (Table 1). In all patients with SIH, CSF leakage was observed at one or more time points among 30 minutes, 1, 2, and 24 hours. In one patient, leakage was identified at 30 minutes (Fig. 1 (a)), but could not be detected after 1 hour (Fig. 1 (b)). In all patients with NPH, lateral ventricles were shown after 3 or 6 hours. Bladder activity appeared during the first hour in 3 of 4 patients with SIH and 4 of 5 those with NPH. One of the cases which demonstrated the early bladder appearance with NPH is shown in Figure 2.

Blood activity concentration, monitored in 2 of 4 patients with SIH, rose by the time of leakage visualization, and one showed a peak followed by a slow decrease (Fig. 3 (a)), while the other demonstrated a gradual elevation of activity until 5 hours (Fig. 3 (b)). In 2 of 5 patients with NPH, blood activity concentration was monitored. In one patient who did not show early bladder appearance, blood activity remained low until 3 hours (Fig. 3 (c)), whereas the other, who demonstrated early bladder appearance, showed a rapid increase in blood activity (Fig. 3 (d)).

DISCUSSION

Our study showed that early phase images during the first hour were important for the detection of CSF leakage. In the literature, planar images have usually been recommended at 1, 3, 6, 24, and possibly 48, 72 hours.[7] In this study we obtained images at every 5 minutes during the first hour and demonstrated that 2 of 4 SIH patients showed leakage within 1 hour after injection. In one patient, leakage was identified at only 30 minutes and could not be detected after 1 hour. We assume that CSF leakage in SIH is slight and often intermittent, and therefore, early phase images successfully showed the leakage before absorption.

Our study also suggests that image interpretation based on early bladder appearance for the diagnosis of SIH may lead to incorrect readings. So far, bladder appearance has been referred to as an indirect sign for SIH when leakage is not visualized on images. However, in this study, 4 patients with NPH, who had no leakage related to pathogenic dural defect, showed bladder activity within 1 hour. Recent MRI volumetric studies have estimated the cranial CSF volume as 157 ± 59 m*l*.[13] As the rate of CSF production in adults is about 0.35 m*l*/min,[14] CSF is thought to turn over about 2 to 4 times a day. From a different point of view, radiopharmaceuticals injected intrathecally into the lumbar subarachnoid spaces normally reach the basal cisterns by 1 hour, the frontal poles and Sylvian fissure area in 2 to 6 hours, and the cerebral convexities by 12 hours, where the subarachnoid granulations are the primary absorption sites of CSF.[15] Thus, bladder radioactivity, if any, must not appear normally before several hours postinjection in subjects without leakage. Gaucher et al. described that subdural hematoma is a potential complication of lumbar puncture.[16] On this assumption, the early bladder appearance in our patients with NPH may be attributable to the lumbar puncture procedures. In addition, the leakage was unremarkable on images, suggesting that the leakage volume is so slight as not to be demonstrated visually. Leakage caused by lumbar puncture procedures also occurs in SIH patients. Even in the SIH patients whose images do not show the apparent leakage on the puncture site, leakage related lumbar puncture procedures may occur. For the diagnosis of SIH, therefore, early bladder sign should be interpreted with caution.

In the NPH patient who demonstrated early bladder appearance, blood radioactivity curve peaked and then dropped rapidly. The pattern was different from that of the NPH patient who did not show early bladder appearance. Therefore, the pattern of the radioactivity curve is probably one of the characteristic findings seen in the patients whose leakage is caused by the lumbar puncture procedures. One of the SIH patients also showed that the radioactivity curve showed a relatively rapid rise and drop. The combination of early bladder visualization and the early elevation of blood radioactivity may be useful to discriminate the bladder visualization due to CSF leakage from that caused by the puncture procedure. But, to confirm this, we have to investigate a larger number of patients and have to consider the leakage site and the timing of the sharp rising of the radioactivity curve.

CONCLUSION

We reported the successful detection of CSF leakage in SIH with early-phase radionuclide cisternography. Early time points are useful for the detection of CSF leakage as some patients may show leakage sites only in early time points. And this report suggested that early bladder visualization could appear due to traumatic lumbar puncture, and should be interpreted with caution.

ACKNOWLEDGMENTS

We gratefully acknowledge the excellent technical assistance of Tomohiko Saito, Hiroshi Kaibasawa, Syojiro Koyama, Yukihiro Takeuchi, Seiji Kato, Humiaki Ohira, Department of Radiology, The University of Tokyo Hospital.

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