

# Distribution Patterns of Spinal Epidural Fluid in Patients with Spontaneous Intracranial Hypotension Syndrome

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## Abstract

The aim of this study is to clarify the details of distribution patterns of spinal epidural fluid and to establish it as measure of spontaneous intracranial hypotension (SIH) syndrome diagnosis. Magnetic resonance imaging findings of the spine were analyzed in 37 patients, 24 women and 13 men (mean age 46.3 years), with SIH. Detection rate, thickness and patterns of the fluid collection were evaluated at every vertebral level. Follow-up spinal MRI findings were also analyzed for changes in epidural fluid collection and association with clinical symptoms. The MR images of the cervical spine were obtained in 30 patients, the thoracic spine in 36, and the lumbar spine in 17 patients. Epidural fluid collection was detected totally in 36 patients (97%) and was predominantly found at the mid-thoracic vertebrae. The fluid tended to locate dorsal to the dural sac at the thoracic spine and ventral at the cervical and lumbar spine. Patients with shorter duration of illness tended to have thicker fluid in the thoracic spine. In follow-up MRI, the findings of epidural fluid collection has disappeared in 32/36 cases within 3 months after treatment. Although residual fluid collection was found at the thoracic level in 4 cases, clinical symptoms were improved in all patients. This study suggested that the mid-thoracic spine should be chosen as the target of MRI in screening of SIH, and enlarged dorsal epidural space is strongly indicative of SIH.

Key words: epidural fluid collection, intracranial hypotension syndrome, magnetic resonance imaging, spinal epidural space

## Introduction

Spontaneous intracranial hypotension (SIH) syndrome is characterized by orthostatic headache worsening in the upright position and alleviating in the recumbent position, the MRI findings of diffuse dural enhancement, and low cerebrospinal fluid (CSF) pressure.<sup>1–5)</sup> The SIH is not rare as thought before, and reports have been markedly increasing with advent of MRI. The commonly used diagnostic criteria for SIH are mainly based on the postural features of headache, typical radiological findings and low CSF pressure, as well as the resolution of symptoms after epidural blood patch (EBP).<sup>6)</sup> However, headache does not

invariably occur within short time after taking an upright posture, as many different patterns of headache have been reported such as non-positional headache, exertional headache, and second-half-of-the-day headache.<sup>3–5,7)</sup> The CSF pressure is not always below the normal range,<sup>8)</sup> and diffuse dural enhancement is not uniformly visualized on MRI. The diagnostic uncertainty leads overlooking of SIH resulting misdiagnosis as migraine, psychosomatic symptoms, or meningitis.<sup>9)</sup> Further, the diagnostic confusion may lead invasive or inappropriate examinations.<sup>10)</sup>

Spontaneous intracranial hypotension syndrome is mainly thought to be caused by a CSF leak from the spinal dural sac, although the reason of the leak remains unknown. Therefore, demonstration of leaked fluid is straightforward in the diagnosis of SIH. According to a recently proposed criteria, demonstration of spinal CSF leak, i.e., the presence of extrathecal CSF, is sufficient to diagnose SIH

Received November 27, 2017; Accepted February 26, 2018

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regardless of other findings, although the conclusive diagnostic methods have not been developed.<sup>5,11–13</sup> Epidural fluid collection with shrunken dural sac shown on spinal MRI is commonly seen in SIH,<sup>10,14,15</sup> however, MRI of the whole spine is time consuming and is not adequate for the screening of this disorder among patients complaining of long-lasting headache. In this study, to clarify the distribution of epidural fluid accumulation in patients with SIH and to establish whether this is correlated with clinical diagnosis, symptoms and/or treatment success, spinal MRI findings in patients with SIH were retrospectively investigated and patterns of epidural fluid collection was analyzed in detail.

## Materials and Methods

### Subjects

Patients with overt intracranial hypotension syndrome who were treated in the Department of Neurosurgery, University Hospital of Yamanashi, between 2002 and 2012 were initially enrolled in this study. All patients fulfilled the diagnostic criteria for headache caused by low CSF pressure as described in the International Classification of Headache Disorders (ICDH)<sup>6</sup> or the criteria for spontaneous spinal CSF leaks and intracranial hypotension proposed by Schievink.<sup>5</sup> Patients who did not undergo the spinal MRI or patients with poor imaging quality were excluded.

There were 13 men and 24 women with aged from 26 to 68 years old (mean 46.3 years). Typical orthostatic headache worsening within 15 min in the standing position was observed in 36 patients, associated with hearing impairment or tinnitus in 22 patients, nuchal pain in 13, nausea and vomiting in 9, disturbance of consciousness in 3, and photophobia in 2 patients. Most of the patients were diagnosed within 2 months of the onset (mean 30.7 days). Among 29 patients who underwent CSF study, low CSF pressure below 60 mm H<sub>2</sub>O was detected in 22 patients, and increased CSF levels of white blood cells and protein were confirmed in 22 patients. Diffuse dural enhancement on MRI of the brain was obvious in 28 patients, but equivocal in 6 and not visualized in 3 patients. Sagging of the cerebellar tonsil below the foramen magnum in sagittal MRI images was demonstrated in 12 patients, and subdural fluid collections or subdural hematoma at the cranial convexity was detected in 19 patients. Twenty-seven patients underwent radionuclide cisternography and leak point was defined the vertebral level of most prominent extrathecal accumulation of radionuclide tracer along with the nerve roots. Consequently, leak point was estimated

at the cervical level in 3, thoracic level in 15 and was undetermined in 9 patients.

Five healthy volunteers (5 men, mean age 31.6 years, age range 27–42 years) were selected for the control group. The data are presented as the mean  $\pm$  S.D. The statistical difference was determined by two-sided Student's *t*-test. Difference of  $P < 0.05$  was considered significant.

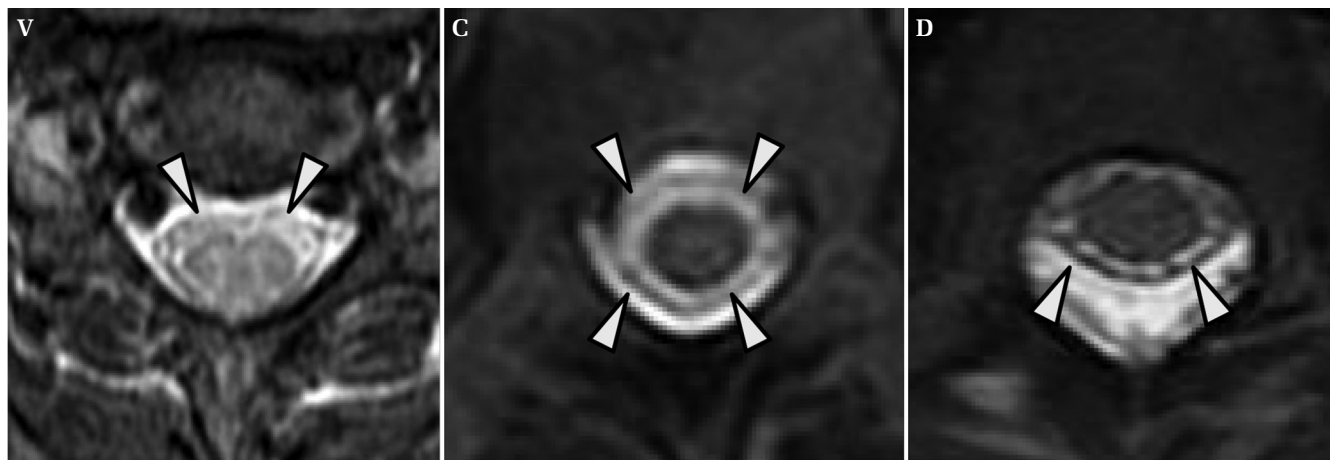
### Magnetic resonance imaging of the spine

Spinal MRI used the protocols for T1-weighted images (TR/TE = 400/10 ms), T2-weighted images (TR/TE = 2600/80 ms), and fat suppression T2-weighted fast spin echo images (TR/TE = 3000/70 ms) as described elsewhere.<sup>16</sup> The images were taken using a 1.5-T MR scanner (GE Medical Systems, Milwaukee, WI) in all patients and the normal volunteers.

Spinal epidural fluid collection was analyzed on the fat-saturated axial MRI and was defined as high intense area outside the dural sac which is visualized as a low intense ring with thin and homogenous thickness. Low intense area in the epidural fluid shown on fat suppression images was regarded as floating epidural fat. Flow void of CSF seen as an irregular low intense area in the dural sac was carefully differentiated. Patterns of epidural fluid collection was classified into three types based on the relation to the dural sac: type V, fluid was mainly located ventral to the dural sac; type C, fluid was circularly surrounding the dural sac; and type D, fluid was mainly located dorsal (Fig. 1). Widest thickness of the epidural fluid was measure in the mid-line at each vertebral level. Horizontal level at the upper part of the vertebral body was selected for the measurement to avoid measurement error due to the preexisting fat tissue between the vertebral laminae and the basivertebral vein locating mid-vertebral body. The MR images were reviewed independently by two investigators and the findings were determined by agreement between them. Existence, thickness, and pattern of fluid collection were evaluated at every vertebral level, and relationship between the MRI findings and the clinical characteristics were investigated. The study protocol was approved by the Institutional Review Board of University of Yamanashi.

### Treatment protocol

After SIH was diagnosed, patients were advised to take bed rest for a few weeks at home or a week in the hospital. If this failed to cure the symptoms, radionuclide cisternography and EBP was performed. For patients with a leak point at the cervical or upper thoracic spine, approximately 20 ml of autologous venous blood mixed with iodine contrast material



**Fig. 1** Classification of epidural fluid collection. V, fluid was located ventral to the dural sac; C, fluid was circularly surrounding the dural sac; D, fluid was located dorsally. *Arrow heads* represent the dural sac.

was injected in the epidural space close to the leak point. For patients with a leak point at the lower thoracic spine or with an undetermined leak point, 25–45 ml of blood was injected at L1/2 or 2/3 level. Patients were requested 3 more days of bed rest and were discharged. Outcome was evaluated at discharge and 1 month after the treatment. If the symptoms of SIH remained, the repeated EBP with an interval of at least a month was considered. Associating intracranial chronic subdural hematoma was treated, if headache was worsened and became continuous after EBP. Magnetic resonance images were obtained within 2 months after EBP, and persisting abnormal findings on MRI were followed-up as long as possible, if exited.<sup>16)</sup>

## Results

### Clinical outcome

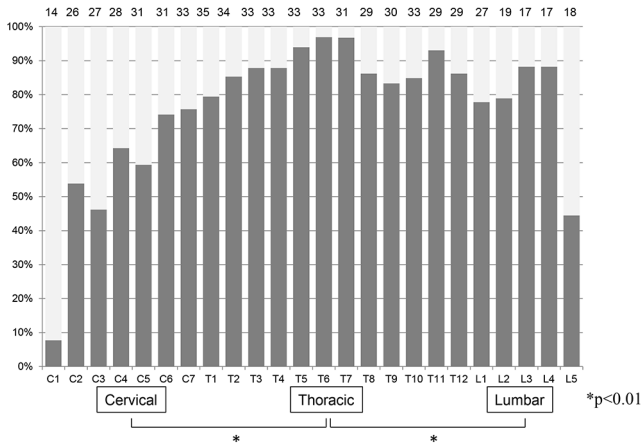
Of 37 patients, 9 patients showed improvement of the symptoms with bed rest, and 28 patients were treated with EBP. Repeated EBP was necessary in 2 patients and evacuation of intracranial subdural hematoma was additionally performed in 5 patients. In 29 (81%) of 37 patients, symptoms were completely disappeared. Eight patients had remission of orthostatic headache but complained of heaviness of the eyes or sporadic dull headache at the time of follow-up.

### Magnetic resonance imaging findings of the spine before treatment

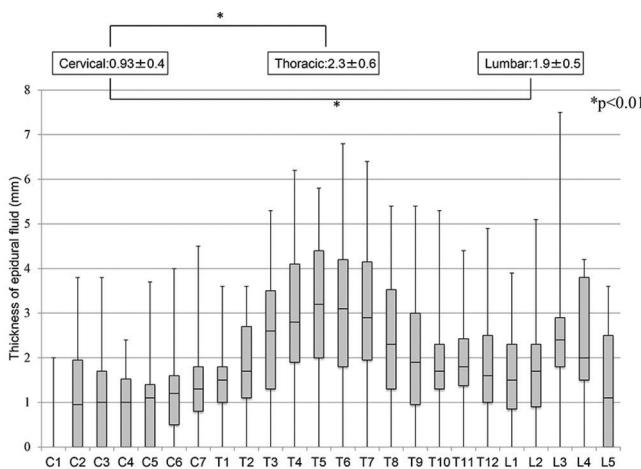
Initial spinal MR images were obtained 3–120 ( $37.7 \pm 24.5$ ) days after the onset of symptoms. The cervical spine was included in the imaging in 30 patients, the thoracic spine in 36, and the lumbar

spine in 17. Magnetic resonance imaging showed fluid collection in the spinal epidural space in 36 patients (97%), but not in one with multiple dural pouches at the lower thoracic and lumbar spine. This patient showed diffuse dural enhancement and bilateral intracranial subdural effusions and was successfully treated with EBP.

Distribution of the epidural fluid was widespread and most prominent in the mid-thoracic spine. Mean detection rate was 57% at the cervical spine, 89% at the thoracic spine and 76% at the lumbar spine, with highest rate of 97% at T6–7 (Fig. 2). The detection rate of the thoracic spine level is significantly higher than that of the cervical spine ( $P < 0.01$ ) and the lumbar spine ( $P < 0.01$ ). Mean and standard deviation of the thickness was  $0.93 \pm 0.4$  mm at the cervical spine,  $2.3 \pm 0.6$  mm at the thoracic spine and  $1.9 \pm 0.5$  mm at the lumbar spine. The average thickness of epidural fluid in the thoracic level was significantly thicker compared to that in the cervical level ( $P < 0.01$ ). The fluid was thickest as over 3 mm at the T5–6 (Fig. 3). Distribution pattern was predominantly dorsal at the mid-thoracic level, ventral at the cervical and lumbar spine, and circular at the junction levels (Fig. 4). The thickness and patterns were not different between patients whose spinal images were obtained within 30 days after the onset and those with longer interval, or between patients who responded to bed rest treatment and those did not (Fig. 5). However, the patients undergoing earlier MRI tended to have thicker epidural fluid at T1–5 and thinner at L1–L4 than those with longer period although significant difference was not proven at each levels. Three patients with a leak point at the cervical spine showed higher detection rate of epidural fluid collection in the cervical spine than the other



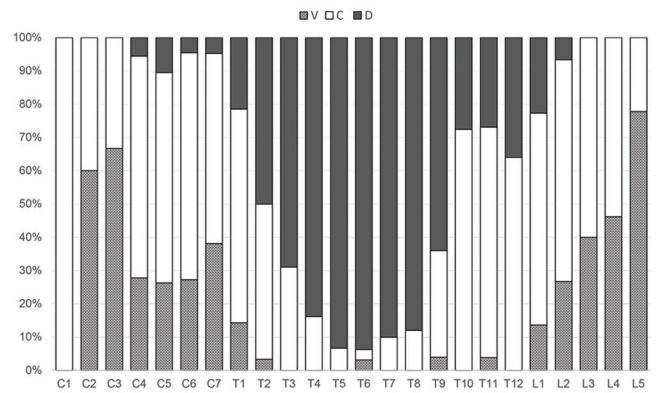
**Fig. 2** Detection rate of epidural fluid in each vertebral level. Digits on the top of the graph are number of examined cases at each vertebral level. Dark areas represent rate of positive finding. The detection rate of the thoracic spine level is significantly higher than that of the cervical spine ( $P < 0.01$ ) and the lumbar spine ( $P < 0.01$ ).



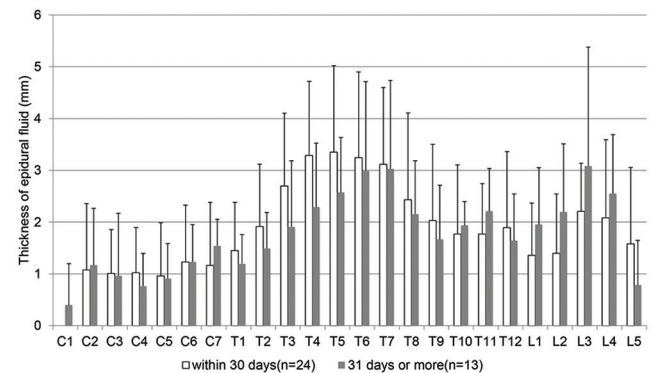
**Fig. 3** Thickness of epidural fluid in each vertebral level. The bottom and top of the box are the 25th and 75th percentile, and the band near the middle of the box is the 50th percentile (the median). The ends of the whiskers represent the maximum and minimum values. The average thickness in the thoracic spine was significantly thicker in comparison with that of cervical spine ( $P < 0.01$ ), but no significant difference in comparison with that of lumbar spine level.

patients; however, the difference was not significant probably due to small number of the patients.

In the healthy volunteers, epidural fluid collection could not be detected, and thickness of epidural space could not be measured because the dural sac and inner surface of bony spinal canal were not distinguished.



**Fig. 4** Types of epidural fluid collection in each vertebral level. The graph shows percentage of each type shown in Fig. 1.



**Fig. 5** Thickness of epidural fluid and timing of spinal MRI. White columns show thickness of epidural fluid in patients whose spinal MR image was obtained within 30 days of initial onset, and light gray columns show those with longer period than 30 days. There is no significant difference between the two groups. Bars indicate standard deviation.

**Changes in spinal MRI findings after treatment**

Follow-up MRI was performed in 36 patients at 2 days to 13 months (mean 3.8 months) after the treatment. In 24 cases out of 36 patients, the dural sac was no longer differentiated from the inner surface of the spinal canal or epidural fat and epidural fluid was not detected at any vertebral levels. However, epidural fluid was still delineated in 12 patients on the initial follow-up images obtained at 2 days to 2 months after treatment. Eight patients showed resolution of the collection within a few months, and subsequently, the epidural fluid was seen partly at the mid-thoracic level in 4 patients at 6, 7, 10, and 12 months after treatment, respectively. Thickness of the fluid was around 1 mm and was located ventral to the dural sac in 3, partly ventral and partly dorsal in 1. One of these

4 patients complained of occasional dull headache, but the 3 other patients had no complaints.

## Discussion

Epidural fluid collection, dural enhancement, dilated epidural vein or venous plexus, high T2 signal between the spinous process of C1–C2 are known as the spinal MRI findings of SIH.<sup>10)</sup> Among them, the fluid collection is the most common findings shown in 67–100% of patients.<sup>10,12,14–17)</sup> In our series, spinal epidural fluid was detected in 97% of the SIH patients. One exceptional case had well-developed dural pouches at the thoracic and lumbar spinal roots. If CSF leak in this case occurred at the tip of a pouch, leaked fluid may have spread in the loose connective tissue around the nerve root instead of epidural space of the spinal canal, although such phenomenon was not evident on MRI. Our result indicates that the MR finding of spinal epidural fluid collection has a sensitivity of 97% to diagnose SIH as far as patients diagnosed based on ICDH or Schievink's criteria. Recently, the detection rate of epidural fluid has been increased by newly introduced imaging techniques such as heavy T2-weighted imaging, fat suppression, and T1–T2 subtraction method.<sup>10,14–16)</sup> However, gross detection rate has only been focused in the previous studies, and the distribution or pattern of the collection has rarely been discussed.

In this study, presence, pattern, and thickness of the fluid collection were evaluated at every vertebral level. The measurement was done strictly in the bony spinal canal at the upper part of the vertebral body, so that the soft tissue between C1 and C2 laminae at which high signal is sometimes seen was not investigated. Furthermore, the sacral vertebra which contains wide epidural fat tissue was excluded from the analysis. As a result, the thoracic spine was found to be the most prominent portion of the fluid collection consisting to the previous report that 16 of 17 patients showed fluid collection at the thoracic spine, whereas 13 of 17 at the cervical and lumbar spine.<sup>14)</sup> The present study also implies that location of leak point may partly affect on the fluid distribution, since the patients with a leak from the cervical spine tended to show high detection rate of fluid at the cervical spine, although the fluid was constantly thickest at the thoracic spine even in these patients.

Distribution pattern of the fluid shown in this study was characteristic. The fluid was predominantly located dorsal at the mid-thoracic level, ventral at the cervical and lumbar spine, and circular at the junction levels. Because no difference in distribution

was found between the patients with shorter duration of illness and those with longer one, the distribution pattern appears not to be influenced by time course of illness, and possibly by resting posture. This pattern implicates that collapsed dural sac uniformly moves to the inside of the curvature given the anatomical structure of the spine. This may be the reason why the mid-thoracic spine which has steep curve shows the widest fluid collection. Interestingly, the patients with a shorter duration of illness had thicker fluid collection at the upper thoracic levels than those with longer duration. The reason was not clear; however, this difference may reflect change of leak rate by time resulting in decrease of epidural fluid. Potentially wide epidural space of the thoracic spine may easily expand or shrink depending on change of intrathecal fluid volume or pressure. For the understanding, we should aware that the finding we called epidural fluid collection presents decreased volume of the dural sac rather than epidural fluid accumulation, since the epidural space does not exclusively contains leaked fluid but actually fat and dilated venous structure. From this point of view, a term “floating dural sac sign” has also been proposed in a previous study.<sup>18)</sup>

In this study, follow-up MR images of the spine after treatment were also investigated. At the final follow-up, most of the patients but 4 showed no epidural space at every vertebral level. If this is regarded as normalized, epidural space does not normally exist in the levels of upper part of vertebral body. Consequently, finding of the epidural fluid collection is thought to be very specific to SIH. Flow void artifact shown as low intense area in CSF appeared to be minimal in the condition of CSF depletion, and became prominent after regaining CSF volume. Though this artifact sometimes shows finding similar to the dural sac on post-treatment MRI, it was usually irregular and wider than the dural sac and was easily distinguished by careful observation of consecutive sections.<sup>19)</sup>

The present study showed that epidural fluid remained in some even after successful treatment as shown in other studies.<sup>12,16,17)</sup> This is an evidence of continuing CSF leakage from the dural sac and indicates failure of treatment. Persisting fluid collection tended to locate mainly in the ventral to the dural sac. This may because of dorsal distribution of injected blood in EBP.<sup>20)</sup> Even if EBP fails to obliterate the leak point, adhesion in the dorsal and dorsolateral epidural space may result in prevention of spreading leaked CSF, and as a result, the clinical symptoms are mitigated even after incomplete EBP.<sup>16)</sup>

One limitation of this study is that the imaging range of spinal MRI is not uniform due to retrospective study.

In addition, in order to obtain accurate specificity of this MRI finding, it is also necessary to examine in headache patients other than SIH. Therefore, to further prove the usefulness of these findings, a prospective study with more cases is necessary.

### Conclusion

This article demonstrated that the MR finding of spinal epidural fluid collection is highly sensitive to SIH, and imaging of mid-thoracic spine is recommended for screening of the disorder among patients with headache. It may particularly be important for cases of SIH requiring immediate diagnosis and treatment, since SIH has been reported to cause life-threatening coma or death.<sup>21,22)</sup>

### Conflicts of Interest Disclosure

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial or non-financial interest in the subject matter or materials discussed in this manuscript. All authors have registered online self-reported COI Disclosure Statement Forms through the website for The Japan Neurosurgical Society members.

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