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DIAGNOSTIC VALUE OF CONTRAST-ENHANCED T2-WEIGHTED FLAIR WITH FAT SATURATION IN LEPTOMENINGEAL METASTASIS

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ABSTRACT – *Objective:* It is well-established that the fluid attenuated inversion recovery (FLAIR) sequence is superior for visualizing leptomeningeal lesions. However, in clinical practice, contrast-enhanced T1-weighted imaging (T1WI) is routinely used to image leptomeningeal metastasis (LM) because of its greater sensitivity and specificity. Potential misestimation may arise from interference by adjacent fat tissues. In this study, we aimed to compare the diagnostic efficacy of contrast-enhanced T1WI-Fat saturation (T1WI-FS) *vs.* contrast-enhanced T2WI-FLAIR-FS for detecting LM.

Patients and Methods: Patients diagnosed with LM by either clinical evaluation or cerebrospinal fluid (CSF) cytology were included. Contrast-enhanced T1WI-FS and T2WI-FLAIR-FS were performed sequentially in all cases.

Results: Contrast-enhanced T2WI-FLAIR-FS demonstrated superior LM visibility ($p < 0.0001$) and depicted lesions more clearly ($p < 0.0001$) than contrast-enhanced T1WI-FS.

Conclusions: Contrast-enhanced T2WI-FLAIR-FS demonstrated superiority over contrast-enhanced T1WI-FS for LM imaging.

KEYWORDS: Enhanced scans, Fat saturation, Fluid-attenuated inversion recovery, Leptomeningeal metastasis.

INTRODUCTION

In recent years, the incidence and mortality rates of cancer have been increasing globally. In China, the cancer incidence rate has reached 293.91 per 100,000 inhabitants, with a mortality rate of 174.55, both significantly higher than the global average[1], posing a great threat to public health[2,3]. Leptomeningeal metastasis (LM) is one of the most severe complications of cancer. It is rather difficult to estimate the incidence of LM as the condition could be easily underdiagnosed[4]. Melanomas (23%), lung cancer (9-25%) and breast cancer (5%) are the tumors most likely to develop LM[5]. Once they enter the cerebrospinal fluid, tumor cells spread along the surface of the meninges and migrate throughout the central nervous system. They implant randomly and grow, forming secondary leptomeningeal metastatic deposits. If left untreated, the time from diagnosis to death is approximately 4-6 weeks[6,7]. Therefore, early detection of LM is crucial for prolonging survival and preserving neurological function.

Currently, contrast-enhanced T1WI is routinely used to image LM in clinical practice. However, this approach may lead to missed diagnoses due to excessive vascular enhancement, poor image contrast, and inflow enhancement effects[8]. By contrast, the fluid-attenuated inversion recovery (FLAIR) sequence suppresses signals from adjacent cerebrospinal fluid (CSF) without enhancing normal cortical vessels, thereby highlighting leptomeningeal lesions by allowing their magnetization to recover. Contrast-enhanced FLAIR imaging has long been considered highly sensitive for detecting infectious meningitis[9,10]. Accordingly, it has been proposed that contrast-enhanced

FLAIR could have greater sensitivity than contrast-enhanced T1WI for the detection of LM. Nevertheless, Singh et al[11] found that contrast-enhanced T1WI had greater sensitivity and specificity than contrast-enhanced FLAIR. Given the proximity of the leptomeninges to the skull, which contains yellow bone marrow, we hypothesized that fat tissue might cause interference. Fat produces high signal intensity on both sequences, similar to that of leptomeningeal lesions, which can mask the lesions and potentially exacerbate motion artefacts. To address this issue, we added a fat-saturation (FS) technique, which can further improve image resolution and better highlight any differences between the two sequences. Therefore, in the present study, we aimed to compare the diagnostic value of contrast-enhanced T1WI-FS versus contrast-enhanced T2WI-FLAIR-FS for LM detection.

PATIENTS AND METHODS

Patients

We included patients with confirmed LM who were treated at our hospital from April 2017 to November 2023. LM diagnosis was based either on positive CSF cytology or on clear clinical signs of central nervous system involvement that showed marked improvement after whole-brain radiotherapy combined with relevant targeted therapy (if available)[12,13]. All subjects provided written informed consent for inclusion before they participated in the study. This study was conducted in accordance with the Declaration of Helsinki of 1975 (as revised in 2013), and the protocol was reviewed and approved by the Institutional Review Board of Changzhou Cancer Hospital (2017KY-018-01) on 7 April 2017.

Imaging procedures

All enrolled patients underwent a contrast-enhanced T1WI-FS scan followed by a contrast-enhanced T2WI-FLAIR-FS scan. Scans were performed using a Siemens Verio 3.0 T superconducting MRI scanner (Siemens Healthineers, Erlangen, Germany) with a head coil. Gadopentetate dimeglumine (0.2 mmol/kg) was administered intravenously as the contrast agent. Scan parameters were as follows: for T1WI, repetition time (TR) = 1200 ms and echo time (TE) = 9.5 ms; for T2WI, TR = 4000 ms and TE = 76 ms; for T2WI-FLAIR-FS, TR = 8500 ms, TE = 108 ms, and inversion time (TI) = 2400 ms. The field of view (FOV) was 230 × 230 mm, with a slice thickness of 6 mm and an inter-slice gap of 1.2 mm. The contrast-enhanced scans used the same parameters as the non-enhanced scans.

Evaluation Procedures

Images were independently evaluated by two senior neurologists who were blinded to patient identities and outcomes. They graded LM visibility on a 0-3 scale: 0 = not visible; 1 = visible; 2 = moderately visible; 3 = clearly visible. In cases of disagreement, a third senior physician determined the final grade by majority opinion. We also measured the signal intensity of the leptomeningeal lesions and adjacent white matter. The ratio of lesion intensity to adjacent healthy tissue intensity was defined as the signal intensity ratio (SIR). A higher SIR indicates stronger contrast and better detectability. Measurements were performed using a Picture Archiving and Communication System (PACS).

Statistical Analysis

Data are presented as counts or mean ± standard deviation. The visibility grades of leptomeningeal lesions were compared using a chi-square test, and SIR values were compared using paired *t*-tests. GraphPad Prism 9 (GraphPad Software, San Diego, CA, USA) was used for all statistical analyses. A two-tailed p-value < 0.05 was considered statistically significant.

RESULTS

Clinical Characteristics

A total of 98 patients were enrolled (45 males and 53 females), with ages ranging from 43 to 79 years (mean age 65 years). The majority of patients (74/98) had lung cancer. Detailed information is provided in the Supplementary Table 1. Most patients presented with symptoms of raised intracranial pressure, such as dizziness, headache, nausea, and vomiting. Other symptoms included diplopia, facial paralysis, gait difficulty, ptosis, visual field defects, seizures, altered consciousness, and cognitive impairment.

Evaluation of LM's Visibility Using Two Sequences

The distribution of lesion visibility grades for the two sequences is shown in Table 1. Eleven cases had Grade 0 (not visible) lesions on contrast-enhanced T1WI-FS, whereas none were Grade 0 on contrast-enhanced T2WI-FLAIR-FS. With T1WI-FS, 35 cases were graded 1, whereas only 13 cases were graded 1 with T2WI-FLAIR-FS. For Grade 2 lesions, there were 42 cases on T1WI-FS *vs.* 37 on T2WI-FLAIR-FS. At Grade 3, there were 10 cases on T1WI-FS compared to 48 on T2WI-FLAIR-FS. Overall, the lesion visibility was significantly higher with T2WI-FLAIR-FS than with T1WI-FS ($p < 0.0001$). In 88 patients (90%), lesions were assigned a higher visibility grade on T2WI-FLAIR-FS than on T1WI-FS. Inter-rater agreement was very high for both sequences. For T1WI-FS, exact agreement was 95.9% ($\kappa = 0.94$, 95% CI: 0.88-0.99; weighted $\kappa = 0.97$, 95% CI: 0.94-0.99). For T2WI-FLAIR-FS, exact agreement was 99.0% ($\kappa = 0.98$, 95% CI: 0.95-1.00; weighted $\kappa = 0.99$, 95% CI: 0.97-1.00). Representative images are shown in Figures 1-3.

Table 1. Comparison of leptomeningeal lesion visibility in 98 patients using contrast-enhanced T1WI-FS and contrast-enhanced T2WI-FLAIR-FS.

Grade	Contrast-enhanced T1WI-FS	Contrast-enhanced T2WI-FLAIR-FS
0	11	–
1	35	13
2	42	37
3	10	48

T1WI-FS: T1-weighted imaging-Fat Saturation; T2WI-FLAIR-FS: T2-weighted imaging-Fluid Attenuated Inversion Recovery-Fat Saturation.

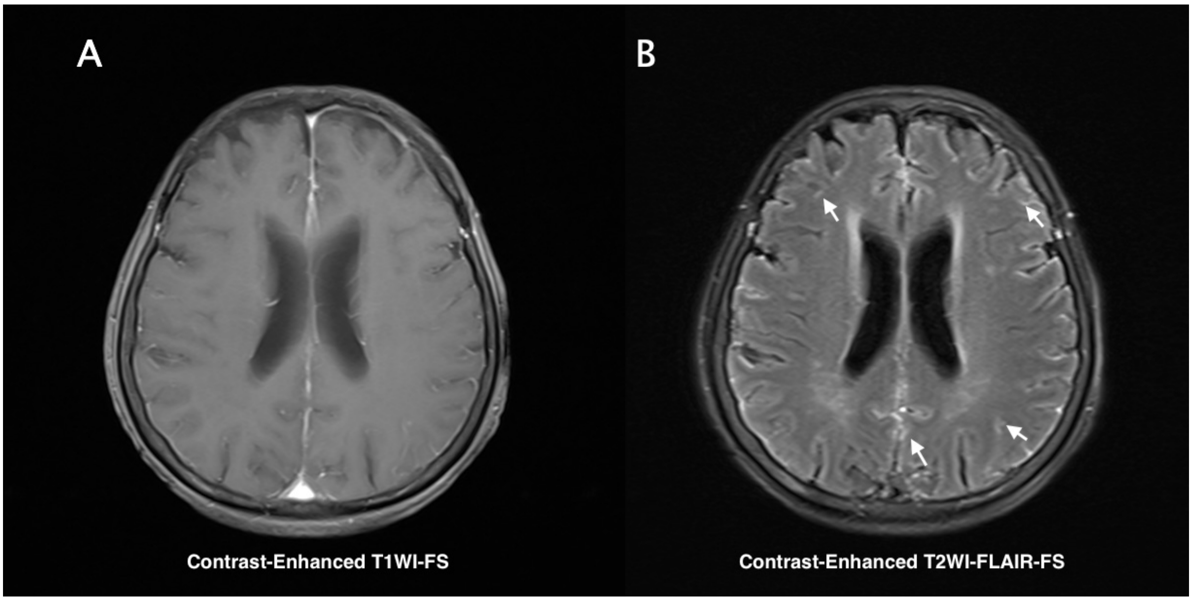

Figure 1. Representative MRI images of the patient classified as Grade 0 using contrast-enhanced T1WI-FS but as Grade 1 with contrast-enhanced T2WI-FLAIR-FS. *A*, No evident abnormal enhancement in T1WI-FS image. *B*, Fine linear enhancement within the cerebral sulci of frontal and parietal lobes in the same level image using T2WI-FLAIR-FS.

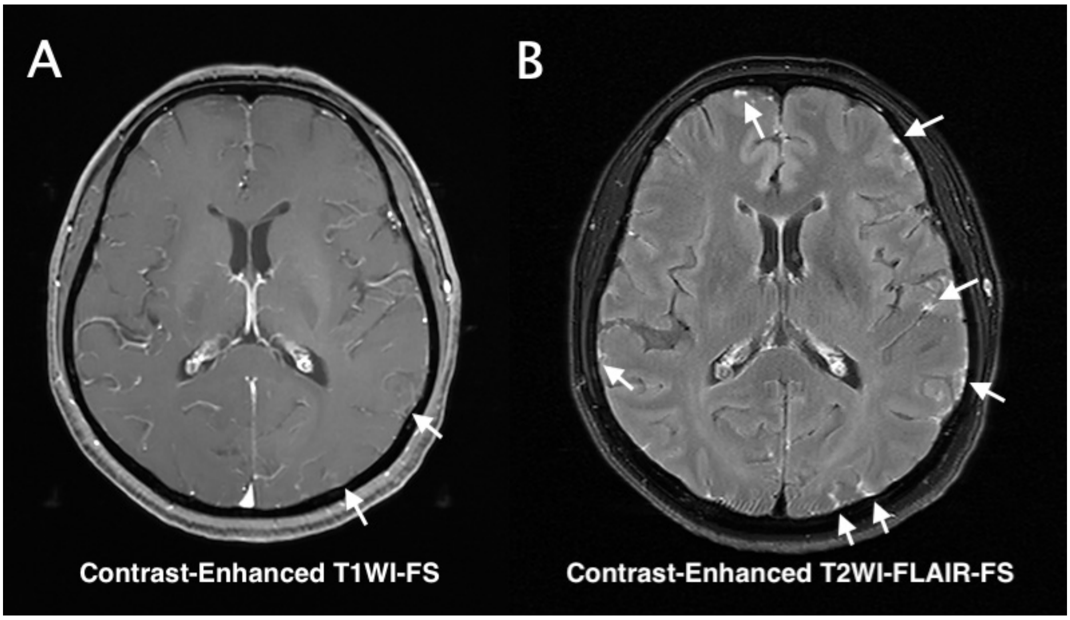

Figure 2. Symbolic MRI images of the Grade 1 patient based on contrast-enhanced T1WI-FS whose lesion was categorized as Grade 2 when adopting contrast-enhanced T2WI-FLAIR-FS. *A*, Linear enhancement within the sulci of the left fronto-occipital lobe in T1WI-FS image. *B*, Linear and nodular enhancements within the cerebral sulci of both hemispheres displayed in the T2WI-FLAIR-FS image, with more pronounced and extensive enhancements on the left side compared to that in T1WI-FS.

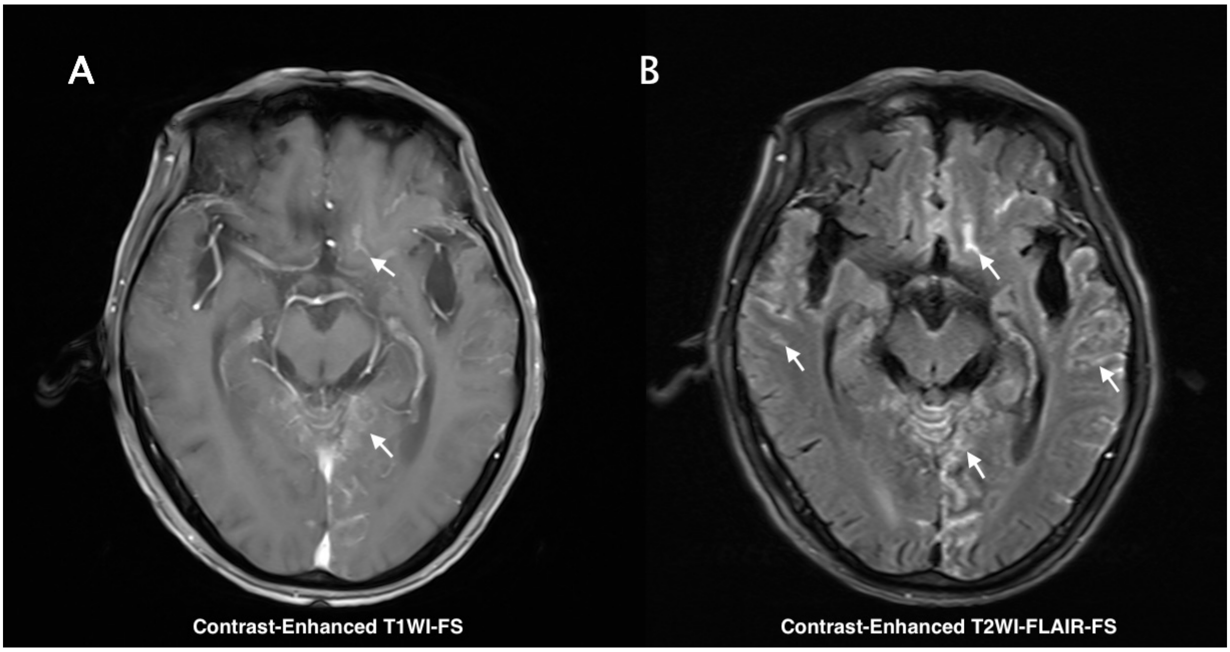

Figure 3. Typical MRI images of the Grade 2 ranked lesion displayed by contrast-enhanced T1WI-FS but considered Grade 3 employing contrast-enhanced T2WI-FLAIR-FS. *A-B*, Linear and small nodular enhancements in the cerebellum and the sulci of the bilateral frontal, temporal, and occipital lobes in images with T1WI-FS or T2WI-FLAIR-FS, but clearer, more pronounced, and larger enhancements using T2WI-FLAIR-FS.

Evaluation of LM's Contrast Against Healthy Tissues Using Two Sequences

For T1WI-FS, the mean signal intensity of LM lesions was 698.51 ± 135.21, whereas that of adjacent white matter was 621.94 ± 84.35, yielding an SIR of 1.13 ± 0.20. For T2WI-FLAIR-FS, the mean lesion intensity was 566.65 ± 146.24, and adjacent healthy tissue intensity was 334.24 ± 71.02, giving an SIR of 1.72 ± 0.39. T2WI-FLAIR-FS images showed significantly higher lesion-to-normal contrast ($p < 0.0001$). Subgroup analysis showed a higher SIR for T2WI-FLAIR-FS compared to T1WI-FS in both lung cancer patients (1.12 ± 0.18 *vs.* 1.69 ± 0.37, $p < 0.0001$) and breast cancer patients (1.186 ± 0.14 *vs.* 1.85 ± 0.40, $p = 0.011$). Detailed data are provided in Supplementary Table 1.

DISCUSSION

LM is a life-threatening complication of cancer. It leads to severe central nervous system dysfunction, and many drugs have limited efficacy because the brain acts as a pharmacological sanctuary. Thus, early diagnosis of LM is crucial in order to initiate treatment promptly, slow cancer progression, and prevent neurological deterioration. Imaging plays an increasingly important role because it is non-invasive, and CSF examinations can yield false-negative results. Therefore, identifying the most effective imaging strategy is of great clinical significance. In the current study, we demonstrated that contrast-enhanced T2WI-FLAIR-FS has greater sensitivity for LM compared to contrast-enhanced T1WI-FS. These findings highlight the practical value of FLAIR in detecting LM and suggest an added benefit from incorporating FS.

The meninges, from innermost to outermost, consist of the pia mater, arachnoid mater, and dura mater. The pia mater closely adheres to the brain surface, extending into sulci, cisterns, and fissures. Normally, the pia mater does not enhance after gadolinium administration. However, in LM, vascular dilation, lesion congestion, and blood-brain barrier disruption can lead to abnormal enhancement.

On MRI, LM typically appears as meningeal thickening with linear or nodular enhancement extending into adjacent sulci, cisterns, and fissures. These enhancements can be focal or diffuse and may be asymmetrical or symmetrical. Contrast-enhanced T1WI is routinely used to detect LM, but it has several limitations, including excessive vascular enhancement, poor contrast between CSF and lesions, and inflow enhancement artefacts, all of which can result in missed diagnoses[14]. In contrast, the FLAIR sequence (with an appropriate inversion time) reduces interference from CSF signals, thereby highlighting areas of LM[15]. FLAIR exploits differences in tissue T1 relaxation times. It uses a 180° inversion pulse followed by a 90° excitation pulse, with a specific inversion time between them. At this inversion time, the longitudinal magnetization of CSF is 0, so CSF produces no signal. In contrast, tissues with shorter T1 (such as brain parenchyma) have almost fully recovered their magnetization and can produce a signal. Thus, it was somewhat surprising that Singh et al[11] reported contrast-enhanced T1WI to be superior to contrast-enhanced FLAIR.

The leptomeninges are adjacent to the skull. After about age 30, the skull's bone marrow is primarily yellow marrow, consisting of approximately 15% water, 5% protein, and 80% fat. Consequently, it appears hyperintense on both contrast-enhanced T1WI and T2WI-FLAIR, mimicking LM and reducing image contrast. Moreover, fat can contribute to increased motion artefacts. This interference could be even more pronounced in the presence of other nearby high-intensity tissues. Therefore, we incorporated an additional FS technique, which exploits the chemical shift between fat and water. This technique primarily suppresses signals from fat with minimal effect on other tissues, and it can be applied on high-field MRI units[16,17]. Unlike the findings of Singh et al[11], our results demonstrated that contrast-enhanced T2WI-FLAIR-FS provides higher diagnostic accuracy and allows visualization of a broader range of lesions than contrast-enhanced T1WI-FS. This advantage was also evident in the lung cancer and breast cancer subgroup, suggesting the value of contrast-enhanced T2WI-FLAIR-FS in this specific cancer type. We propose that the discrepancy between our study and Singh's may be due to the presence of fat, which can degrade image quality and obscure the true benefits of T2WI-FLAIR.

The improved diagnostic performance of contrast-enhanced T2WI-FLAIR-FS could help clinicians manage patients more effectively. In our cohort, 11 cases were misdiagnosed when using contrast-enhanced T1WI-FS. The higher sensitivity of T2WI-FLAIR-FS means that subtle disease manifestations can be detected earlier, allowing prompt initiation of therapy. Our results also showed more lesions and greater clarity on contrast-enhanced T2WI-FLAIR-FS. The number of metastatic brain lesions is a critical factor in deciding treatment: patients with a single metastasis are often treated with surgical resection plus targeted radiotherapy, whereas multiple metastases (>3) typically warrant whole brain radiotherapy[18]. Yuh et al[19] reported that up to 50% of patients with brain metastases may have only a single lesion visible on routine imaging, so improved detection of occult metastases is necessary for optimal treatment planning. Another benefit of T2WI-FLAIR-FS was the clearer delineation of lesion margins. This could help neurosurgeons achieve more complete resections and assist radiation oncologists in accurately targeting the tumor while sparing normal tissue.

Limitations

However, our study has limitations. All patients underwent T1WI-FS followed by T2WI-FLAIR-FS in a fixed sequence order. Nevertheless, both sequences were acquired approximately 10 minutes after contrast administration, with only about a 1-minute interval between them. Given the relatively stable enhancement phase at that time[20], this fixed sequence order is unlikely to have introduced significant bias in lesion conspicuity or detection. Further research is needed to clarify the impact of timing and sequence order on lesion detection.

CONCLUSIONS

Our findings indicate that contrast-enhanced T2WI-FLAIR-FS offers superior accuracy and lesion detection compared to contrast-enhanced T1WI-FS. Adopting this sequence could reduce the risk of missed diagnoses and ensure a prompt, accurate evaluation of the disease, which in turn should improve patient outcomes and quality of life.

Conflict of Interest:
The authors declare they have no conflict of interest.

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Author contributions:
Jin Zhang and Hua Chao designed the study. Hua Chao contributed mainly to data collection with Wenwen Chen assiatance. Huijuan Rui analyzed and interpretated the data. Jin Zhang, Hua Chao and Tiecheng Xiao drafted the article. All the authors approved the final the version of the article to be published

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Data Availability :
All data generated or analyzed during this study are included in this published article and its supplementary material.

REFERENCES

1. Chen W, Zheng R, Baade PD, Zhang S, Zeng H, Bray F, Jemal A, Yu XQ, and He J. Cancer statistics in China, 2015. CA Cancer J Clin 2016; 66: 115-132.
2. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, and Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. Int J Cancer 2010; 127: 2893-2917.

3. Grant WB. A multicountry ecological study of cancer incidence rates in 2008 with respect to various risk-modifying factors. Nutrients 2013; 6: 163-189.
4. Gauthier H, Guilhaume MN, Bidard FC, Pierga JY, Girre V, Cottu PH, Laurence V, Livartowski A, Mignot L, and Diéras V. Survival of breast cancer patients with meningeal carcinomatosis. Ann Oncol 2010; 21: 2183-2187.
5. Thakkar JP, Kumthekar P, Dixit KS, Stupp R, and Lukas RV. Leptomeningeal metastasis from solid tumors. Journal of the Neurological Sciences 2020; 411: 116706.
6. Lee SJ, Lee J-I, Nam D-H, Ahn YC, Han JH, Sun J-M, Ahn JS, Park K, and Ahn M-J. Leptomeningeal Carcinomatosis in Non–Small-Cell Lung Cancer Patients: Impact on Survival and Correlated Prognostic Factors. Journal of Thoracic Oncology 2013; 8: 185-191.
7. Pennisi G, Burattini B, Gessi M, Montano N, Perna A, Silvestri G, and Papacci F. Unusual case of long survival patient with leptomeningeal carcinomatosis from breast cancer. British Journal of Neurosurgery 2023; 37: 1839-1842.
8. Le Rhun E, Weller M, Brandsma D, Van den Bent M, de Azambuja E, Henriksson R, Boulanger T, Peters S, Watts C, Wick W, Wesseling P, Rudà R, and Preusser M. EANO-ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up of patients with leptomeningeal metastasis from solid tumours. Ann Oncol 2017; 28: iv84-iv99.
9. Parmar H, Sitoh YY, Anand P, Chua V, and Hui F. Contrast-enhanced flair imaging in the evaluation of infectious leptomeningeal diseases. Eur J Radiol 2006; 58: 89-95.
10. Splendiani A, Puglielli E, De Amicis R, Necozione S, Masciocchi C, and Gallucci M. Contrast-enhanced FLAIR in the early diagnosis of infectious meningitis. Neuroradiology 2005; 47: 591-8.
11. Singh SK, Leeds NEGinsberg LE. MR imaging of leptomeningeal metastases: comparison of three sequences. AJNR Am J Neuroradiol 2002; 23: 817-21.
12. Le Rhun E, Taillibert SChamberlain MC. Carcinomatous meningitis: Leptomeningeal metastases in solid tumors. Surg Neurol Int 2013; 4: S265-88.
13. Barbour AB, Zaki P, McGranahan TM, Venur V, Vellayappan B, Palmer J, Halasz LM, Yang JT, Blau M, Tseng YD, Chao ST, Suh JH, Foote M, Redmond KJ, Combs SE, Chang EL, Sahgal A, and Lo SS. Emergent radiotherapy for brain and leptomeningeal metastases: a narrative review. Annals of Palliative Medicine 2023; 12: 1405-1419.
14. Ahmad A, Azad SAzad R. Differentiation of Leptomeningeal and Vascular Enhancement on Post-contrast FLAIR MRI Sequence: Role in Early Detection of Infectious Meningitis. J Clin Diagn Res 2015; 9: Tc08-12.
15. Azad R, Tayal M, Azad S, Sharma G, and Srivastava RK. Qualitative and Quantitative Comparison of Contrast-Enhanced Fluid-Attenuated Inversion Recovery, Magnetization Transfer Spin Echo, and Fat-Saturation T1-Weighted Sequences in Infectious Meningitis. Korean J Radiol 2017; 18: 973-982.
16. Essig M, Knopp MV, Schoenberg SO, Hawighorst H, Wenz F, Debus J, and van Kaick G. Cerebral gliomas and metastases: assessment with contrast-enhanced fast fluid-attenuated inversion-recovery MR imaging. Radiology 1999; 210: 551-557.
17. Mathews VP, Caldemeyer KS, Lowe MJ, Greenspan SL, Weber DM, and Ulmer JL. Brain: gadolinium-enhanced fast fluid-attenuated inversion-recovery MR imaging. Radiology 1999; 211: 257-263.
18. Terae S, Yoshida D, Kudo K, Tha KK, Fujino M, and Miyasaka K. Contrast-enhanced FLAIR imaging in combination with pre- and postcontrast magnetization transfer T1-weighted imaging: usefulness in the evaluation of brain metastases. J Magn Reson Imaging 2007; 25: 479-487.
19. Yuh WT, Tali ET, Nguyen HD, Simonson TM, Mayr NA, and Fisher DJ. The effect of contrast dose, imaging time, and lesion size in the MR detection of intracerebral metastasis. AJNR Am J Neuroradiol 1995; 16: 373-380.
20. Fan B, Li M, Wang X, Xu Y, Li F, et al. Time-Dependent Changes in the Magnetic Resonance Detection of Brain Metastases Using Single-Dose Gadobutrol. I J Radiol 2018; 15: e66054.