Case Report

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Diffuse Leptomeningeal Glioneuronal Tumor with FGFR1 Mutation in a 29-Year-Old Male

29세 남성에서 발생한 FGFR1 돌연변이를 동반한 미만성 연수막성 신경교종

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This study reports on diffuse leptomeningeal glioneuronal tumor (DL-GNT) in a 29- year-old male. DL-GNT is a rare central nervous system (CNS) tumor mostly seen in children and only few cases have been reported in adult patients. Our patient presented with a chronic headache that lasted for five months. MR imaging showed mild hydrocephalus, multiple rim-enhancing nodular lesions in the suprasellar cistern, diffuse leptomeningeal enhancement in the lumbosacral area, and multiple small non-enhancing cyst-appearing lesions not suppressed on fluid attenuated inversion recovery (FLAIR) images in the bilateral basal ganglia, thalami, and cerebral hemispheres. Under the impression of germ cell tumor with leptomeningeal seeding, the patient underwent trans-sphenoidal tumor removal. DL-GNT was pathologically confirmed and FGFR1 mutation was detected through a next-generation sequencing test. In conclusion, a combination of leptomeningeal enhancement and multiple parenchymal non-enhancing cyst-appearing lesions not suppressed on FLAIR images may be helpful for differential diagnosis despite overlapping imaging features with many other CNS diseases that have leptomeningeal enhancement.

Index terms Brain Neoplasms; Meningeal Neoplasms; Cysts; Magnetic Resonance Imaging; Adult

INTRODUCTION

Diffuse leptomeningeal glioneuronal tumor (DL-GNT) is a rare and recently described central nervous system (CNS) tumor which is characterized by diffuse leptomeningeal tumor spread in the brain or/and spine (1, 2). MR imaging findings of DL-GNT have been described in several case reports (1, 3-5). However, the differential diagnosis based on image findings is not easy to make due to its rare incidence and overlapping features with many other CNS diseases. Theses tumors are commonly seen in children (1, 4, 5). Only a few cases have been reported in adults (3). We present a case of DL-GNT in a 29-year-old male and discuss its MR imaging findings helpful in differential diagnosis.

CASE REPORT

A 29-year-old previously healthy male presented with headache for five months. He had no other neurologic symptoms and no abnormal neurologic examination. Post-contrast T1-weighted images showed several rim-enhancing nodular lesions in the suprasellar cistern (Fig. 1A). Under the suspicion of leptomeningeal tumor seeding, the patient underwent spine MR imaging, which demonstrated diffuse leptomeningeal enhancement in the lumbosacral level (Fig. 1B). MR images obtained at the level of the lower basal ganglia showed multiple small oval or round cyst-appearing lesions in the bilateral basal ganglia, thalami and cerebral hemispheres (Fig. 1C-E). Their signal intensity is hyperintense (i.e., not suppressed) on fluid attenuated inversion recovery (FLAIR) images (Fig. 1D). There were no diffusion restriction or contrast enhancement in these lesions. Mild hydrocephalus was observed. The most probable diagnosis on the radiology report was germ cell tumors in the suprasellar cistern with spinal leptomeningeal seeding.

Cerebrospinal fluid (CSF) analysis showed WBC 7/mm^3, protein 387 mg/dL and no malignant cells observed on cytology. CSF study was all negative for Gram, Acid-Fast Bacillus and fungal staining. Polymerase chain reaction for tuberculosis was also negative.

The enhancing tumors in the suprasellar cistern were surgically removed via endoscopic trans-sphenoidal approach. The mass appeared yellowish and rubbery on gross examination and was removed by piece-meal method. Histological examination revealed a moderately cellular neoplasm composed of relatively monomorphic oligodendrocyte-like cells (Fig. 1F). The tumor cells had uniform, round nuclei with inconspicuous nucleoli and round clear cytoplasm. Neither tumor necrosis nor mitotic activity was noted. By immunohistochemical studies, the tumor cells expressed glial fibrillary acidic protein (GFAP, glial marker) as well as S100 protein and synaptophysin (neuronal marker), suggesting a glioneuronal tumor. The histological features were similar to oligodendroglioma; however, a possibility of oligodendroglioma was ruled out because tumor cells did not show mutation of IDH1 and IDH2 by immunohistochemistry and next-generation sequencing (NGS) test. By FISH tests, chromosome 1p deletion was noted in 12% of tumor cells, but co-deletion of 1p and 19q was absent. KIAA1549:BRAF fusion was not detected by NGS test, whereas FGFR1 K656E missense mutation as well as NF1 R2832Qfs*2 deletion and BRIP1 A1081Cfs*5 truncation mutation was detected.

Given these findings, the patient was diagnosed as having DL-GNT with FGFR1 mutation.

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Fig. 1. Diffuse leptomeningeal glioneuronal tumor with FGFR1 mutation in a 29-year-old male.
A. Axial (left) and sagittal (right) post-contrast T1WIs show several rim-enhancing nodular lesions in the suprasellar cistern (arrows).
B. Sagittal (left) and axial (right) post-contrast T1WIs at the lumbosacral level show diffuse leptomeningeal enhancement in the lumbosacral level (arrows).
C-E. Axial T2-weighted (C), FLAIR (D), and post-contrast T1-weighted (E) images show multiple non-enhancing small oval or round cyst-appearing lesions in the bilateral basal ganglia, thalami, and cerebral hemispheres (arrows). Their signal intensity is hyperintense on FLAIR image. Mild hydrocephalus is observed.
FLAIR = fluid attenuated inversion recovery, T1WI = T1-weighted image

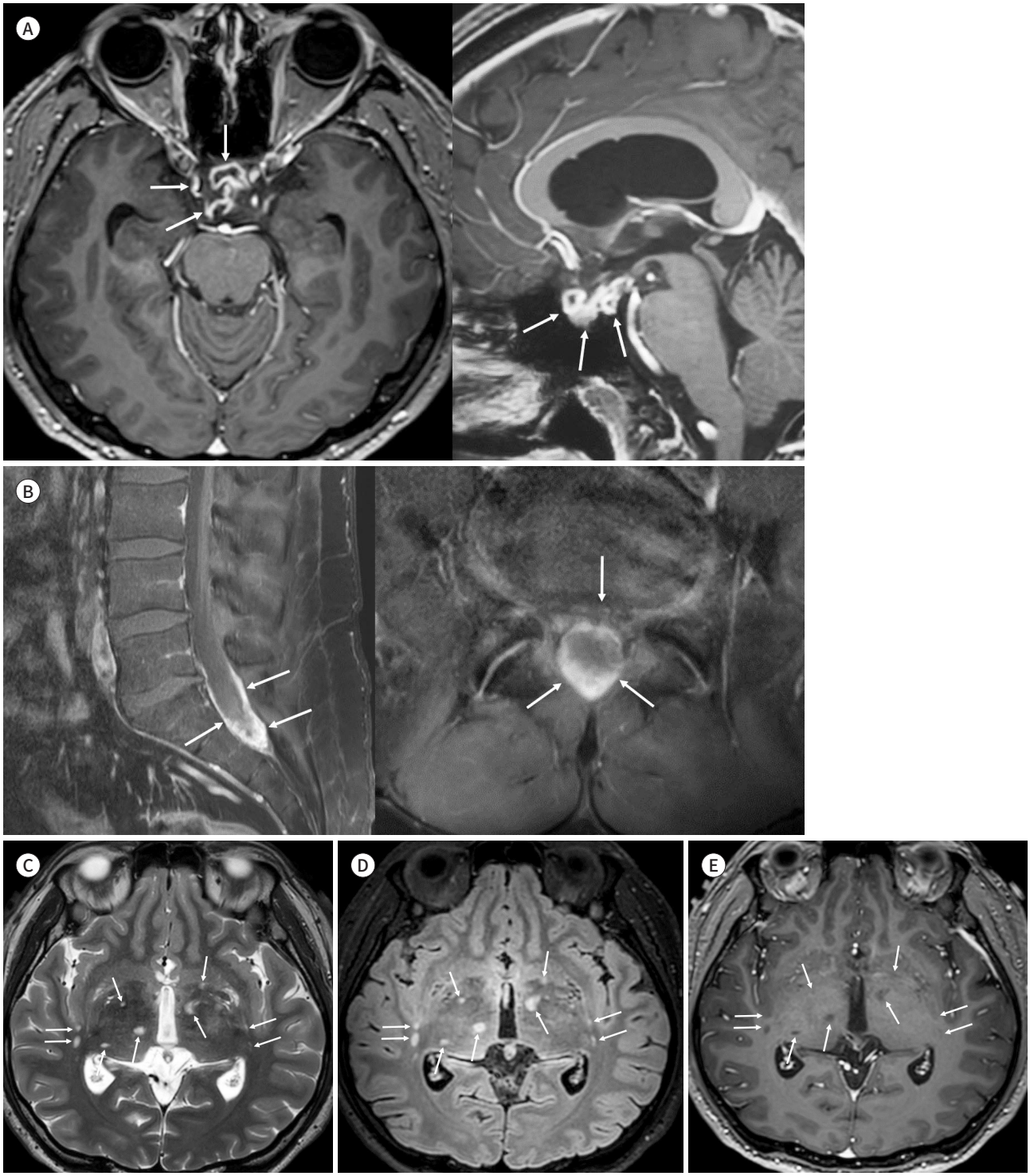
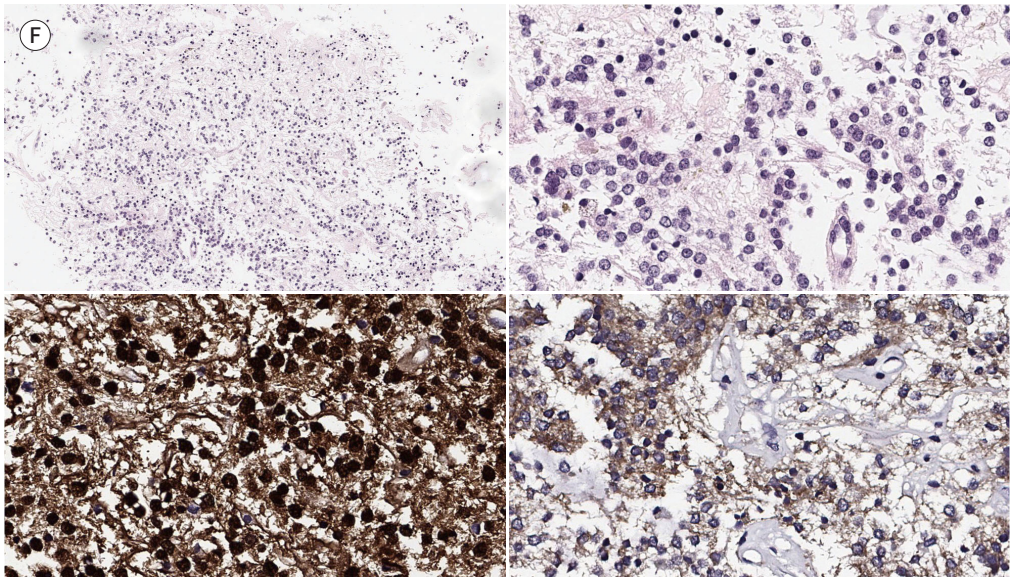


Fig. 1. Diffuse leptomeningeal glioneuronal tumor with FGFR1 mutation in a 29-year-old male.
F. Histopathology shows moderately cellular neoplasm composed of relatively monomorphic oligodendrocyte-like cells (H&E, × 40) (top left). The tumor cells have uniform, round nuclei with inconspicuous nucleoli and round clear cytoplasm. Neither tumor necrosis nor mitotic activity is noted (H&E, × 400) (top right). Immunohistochemistry shows expression of S100 protein (bottom left) and synaptophysin (bottom right) in the tumor cells (× 400).
H&E = hematoxylin and eosin



The patient went on schedule for radiation therapy.

This case report was exempt from the ethical approval in our institution. This study was performed according to the latest ethical principles in the Declaration of Helsinki (2013).

DISCUSSION

DL-GNT is a rare CNS tumor, which is pathologically characterized by diffuse leptomeningeal tumor spread (1, 3-5). They are glioneuronal cells in origin, commonly showing diffuse positivity for GFAP and synaptophysin on immunostaining, sometimes for oligodendrocyte transcription factor (OLIG2) or Neu-N. DL-GNT was first included in the 2016 WHO classification of tumors of the CNS (2). Although its WHO grade has not been yet assigned, most of these tumors are reported to have an indolent clinical course. Stable disease or remission can be achieved with chemotherapy as well as adjunctive radiotherapy (1, 3).

Leptomeningeal enhancement is the most common MR imaging finding of DL-GNT. In our case, nodular or diffuse leptomeningeal enhancement was evident in the basal cistern and in the spine. According to Lakhani et al. (5) with a large number of the literature review, leptomeningeal enhancement was found in 62% of the patients with DL-GNT in the brain and 72% in the spine. These findings, however, are non-specific and can be observed in various diseases including meningitis (e.g., bacterial, viral or fungal), and leptomeningeal dissemination from CNS or extra-CNS tumors (6). Especially in tuberculosis-endemic areas, these findings are prone to being misdiagnosed with Tb meningitis (4).

Hydrocephalus is another frequent MR imaging finding of DL-GNT, which may result from

disturbance of CSF flow by tumor cells. It was seen in 32% of the patients with DL-GNT in Lakhani et al. (5). However, this finding is also non-specific in the differential diagnosis as leptomeningeal enhancement.

Multiple non-enhancing cyst-appearing lesions in the brain is considered as another important MR imaging finding in DL-GNT (5). On FLAIR images, they are hyperintense (i.e., not suppressed), making it possible to differentiate them from normal perivascular spaces. In our case, multiple cyst-appearing lesions were found in the bilateral basal ganglia, thalami, and cerebral hemispheres near the basal cisterns. Similarly, a previous study described that these findings were most commonly seen at the subpial surface of the cerebellum, brainstem, temporal lobes near the Sylvian fissure and within the hippocampi, and medial occipital lobes. The frequency of these multiple cyst-appearing lesions in DL-GNT was reported 42% in Lakhani et al. (5). In terms of the pathogenesis, a previous study (1) suggested that the cyst-appearing lesions are thought to correspond to dilatation of perivascular space as a result of collections of extracellular fluid secondary to progression of the leptomeningeal disease altering normal drainage pathways. The biopsy in their case revealed minimal chronic inflammations with unidentified atypical cells in the perivascular spaces.

However, these multiple non-enhancing cyst-appearing lesions still have differential diagnoses such as neurocysticercosis and cryptococcosis. Non-enhancing multiple cysts can be observed at the vesicular stage of neurocysticercosis. However, hyperintense FLAIR signal of the cysts and the lack of scolex within the cyst in our case is not consistent with the vesicular stage of neurocysticercosis (7). Cryptococcosis can exhibit T2-hyperintense pseudocysts in the perivascular space of the basal ganglia, thalami or midbrain (8, 9). The signal intensity of the pseudocysts on FLAIR image is usually low, but occasionally high. The pseudocysts have no or subtle contrast enhancement at the peripheral rim of the cysts (8, 9). The variability of these imaging findings of cryptococcosis makes it difficult to differentiate from DL-GNT solely based on the imaging characteristics of the cysts. With this one exception for cryptococcosis, we think that a combination of the two findings (diffuse leptomeningeal enhancement and multiple non-enhancing cyst-appearing lesions not suppressed on FLAIR images) could be a radiologic clue for the diagnosis of DL-GNT.

Pathologically, KIAA1549:BRAF fusion is known to be frequent in DL-GNT, but FGFR1 mutation is less common (10). In our case, KIAA1549:BRAF fusion was not detected, whereas FGFR1 mutation was detected. However, there has been no report about the role of FGFR1 mutation in DL-GNT. Further study is needed for the impact of this mutation on the oncogenesis or prognosis of the tumor.

We presented a case of DL-GNT with FGFR1 mutation in an adult patient. Despite the diagnostic difficulty due to its rare incidence, age predilection for children and overlapping image findings with many other CNS diseases, a combination of leptomeningeal enhancement and multiple non-enhancing cyst-appearing lesions not suppressed on FLAIR images may be a diagnostic clue for DL-GNT.

Author Contributions

Conceptualization, K.M., K.J.H.; formal analysis, K.M.; investigation, K.M., K.J.H., L.K.R.; supervision, K.J.H., C.G., H.K.; validation, K.M., L.K.R., H.K.; visualization, K.M.; writing—original draft, all authors; and writing—review & editing, all authors.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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REFERENCES

1. Lyle MR, Dolia JN, Fratkin J, Nichols TA, Herrington BL. Newly identified characteristics and suggestions for diagnosis and treatment of diffuse leptomeningeal glioneuronal/neuroepithelial tumors: a case report and review of the literature. *Child Neurol Open* 2015;2:2329048X14567531
2. Louis DN, Wesseling P, Aldape K, Brat DJ, Capper D, Cree IA, et al. cIMPACT-NOW update 6: new entity and diagnostic principle recommendations of the cIMPACT-Utrecht meeting on future CNS tumor classification and grading. *Brain Pathol* 2020;30:844-856
3. Fiaschi P, Badaloni F, Cagetti B, Bruzzone L, Marucci G, Dellachà A, et al. Disseminated oligodendroglial-like leptomeningeal tumor in the adult: case report and review of the literature. *World Neurosurg* 2018;114:53-57
4. Lee JK, Ko HC, Choi JG, Lee YS, Son BC. A case of diffuse leptomeningeal glioneuronal tumor misdiagnosed as chronic tuberculous meningitis without brain biopsy. *Case Rep Neurol Med* 2018;2018:1391943
5. Lakhani DA, Mankad K, Chhabda S, Feizi P, Patel R, Sarma A, et al. Diffuse leptomeningeal glioneuronal tumor of childhood. *AJNR Am J Neuroradiol* 2020;41:2155-2159
6. Smirniotopoulos JG, Murphy FM, Rushing EJ, Rees JH, Schroeder JW. Patterns of contrast enhancement in the brain and meninges. *Radiographics* 2007;27:525-551
7. Kimura-Hayama ET, Higuera JA, Corona-Cedillo R, Chávez-Macías L, Perochena A, Quiroz-Rojas LY, et al. Neurocysticercosis: radiologic-pathologic correlation. *Radiographics* 2010;30:1705-1719
8. Offiah CE, Naseer A. Spectrum of imaging appearances of intracranial cryptococcal infection in HIV/AIDS patients in the anti-retroviral therapy era. *Clin Radiol* 2016;71:9-17
9. Xia S, Li X, Li H. Imaging characterization of cryptococcal meningoencephalitis. *Radiol Infect Dis* 2016;3:187-191
10. Engelhardt S, Behling F, Beschorner R, Eckert F, Kohlhof P, Tatagiba M, et al. Frequent FGFR1 hotspot alterations in driver-unknown low-grade glioma and mixed neuronal-glial tumors. *J Cancer Res Clin Oncol* 2022;148:857-866

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29세 남성에서 발생한 FGFR1 돌연변이를 동반한 미만성 연수막성 신경교종

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29세 남성에서의 미만성 연수막성 신경교종을 증례 보고한다. 이 질환은 드문 중추신경계 종양으로, 대부분 소아에서 발견되며 성인에서는 소수만 보고되어 있다. 본 환자는 만성 두통으로 내원하여 MRI를 시행하였다. 뇌 MRI에서 경도의 수두증과 다수의 테두리 조영증강을 보이는 병변이 안장위 수조에서 보였으며, FLAIR에서 신호가 억제되지 않는 다수의 비조영증강 낭종성 병변이 양측 기저핵, 시상 및 대뇌에서 관찰되었다. 척추 MRI에서는 요추 및 천추 부위의 미만성 연수막 조영증강이 보였다. 생식세포종양의 연수막 파종을 의심하였고 경접형골 종양제거술을 시행 받았다. 병리학 검사에서 미만성 연수막성 신경교종으로 확진되었고, 차세대 염기서열 검사에서 FGFR1 유전자의 돌연변이가 발견되었다. 결론적으로 연수막 결절성 조영증강과 FLAIR에서 신호가 억제되지 않는 다수의 비조영증강 낭종성 뇌 병변이 함께 관찰될 경우 연수막 조영증강을 보이는 여러 다른 질환들과의 감별 진단에 도움이 된다.

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