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A rare case of diffuse leptomeningeal glioneuronal tumor

Zriedkavý prípad difúzneho leptomeningeálneho glioneuronálneho tumoru

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Conflicts of interest: none.

Major statement
Diffuse leptomeningeal glioneuronal tumor is rare, just recently described as a tumor of the central nervous system, not well known among radiologists and it should be listed in the differential diagnosis for the leptomeningeal processes among children and adolescents.

SUMMARY

Kurčinová S, Mlčák E. A rare case of diffuse leptomeningeal glioneuronal tumor

Diffuse leptomeningeal glioneuronal tumor (DL-GNT) is not a common disease, it has been just lately described as a tumor of the central nervous system. For the first time it was introduced in the 4th edition of WHO classification of CNS tumors in 2014. This type of tumor was categorised into the group of glioneuronal tumors in its current 5th edition of WHO classification of CNS tumors.

The clinical presentation varies according to areas of involvement. The major feature of this tumor as observed in the literature is leptomeningeal involvement with post-contrast enhancement, which secondary may lead to hydrocephalus. Parenchymal components are often not presented. An additional finding is the presence of small subpial cysts, found over the surface of the inferior parts of the supratentorial structures, in the posterior fossa and over the spinal cord.

We present the case of a 19 year old female with leptomeningeal and also pachymeningeal involvement of the spine, with the follow-up also affecting meninges of the brain. What is interesting and worth to mention is that the typical sign of hydrocephalus was not present in our case.

Key words: central nervous system neoplasms, leptomeningeal neoplasms, magnetic resonance imaging.

Hlavné stanovisko práce
Difúzny leptomeningeálny glioneuronálny tumor je zriedkavý, len nedávno objavený tumor centrálneho nervového systému, ktorý ešte nie je dobre známy medzi rádiológmi a mal by byť zahrnutý pri diferenciálnej diagnostike leptomeningeálnych procesov medzi deťmi a mladými dospelými.

SÚHRN

Kurčinová S, Mlčák E. Zriedkavý prípad difúzneho leptomeningeálneho glioneuronálneho tumoru

Difúzny leptomeningeálny glioneuronálny tumor (DL-GNT) nie je také časté ochorenie. Prvý krát bolo zaradené do WHO klasifikácie nádorov centrálneho nervového systému v roku 2014 (4. edícia). V najnovšej WHO klasifikácií nádorov centrálneho nervového systému (5. edícia) je zaradené do zoznamu glioneuronálnych tumorov.

Klinický obraz sa odlišuje podľa miesta postihnutia. Hlavným znakom tumoru popisovaného v literatúre je leptomeningeálne postihnutie s postkontrastným sýtením, čo môže sekundárne viesť k vzniku hydrocefalu. Parenchymálne postihnutie nie je až také časté. Ďalším nálezom môže byť prítomnosť malých subpiálnych cýst v oblasti dorzálnych častiach supratentoriálnych štruktúr mozgu, v oblasti zadnej jamy a pozdĺž miechy.

V našom článku prezentujeme prípad 19-ročnej pacientky s leptomeningeálnym a taktiež pachymeningeálnym postihnutím miechy. S odstupom času sa pridružilo aj postihnutie meningeálnych obalov mozgu. Čo je v našom prípade zaujímavé a dôležité spomenúť je to, že hydrocefalus sa u našej pacientky neobjavil.

Kľúčové slová: nádory centrálneho nervového systému, leptomeningeálne tumory, magnetická rezonancia.

INTRODUCTION

Diffuse leptomeningeal glioneuronal tumor (DL-GNT) is rare, with the true incidence being unknown due to the limited number of cases (1, 2), with fewer than 100 cases reported in the literature since 2012 (3, 4). Due to its rarity and poor knowledge among radiologists, this disease is often wrong and late diagnosed.

These tumors are usually found in children and adolescents, though few cases were found among adults. There appears to be a moderate male predilection (5).

They are considered as low-grade tumors being similar to other WHO grade 2 tumors and those with high-grade features being similar to WHO grade 3 (5).

CASE PRESENTATION

A 19 year old female underwent cervical spine CT in January 2018 for head and neck pain after falling from height of 1.5 metre to exclude traumatic lesions. CT scans revealed no evidence of injury. She also underwent MR scan of the thoracic spine with conclusion of adhesions in the posterior subarachnoid space of Th1–Th12 between spinal cord and dural sac with contrast enhancement. Initially, infection or previous intradural haemorrhage was considered as a cause of adhesions.

She has nearly no symptoms when being clinically assessed. She was treated by a neurologist and infection was excluded.

In October 2020 she had MR scan of the brain for a headache and migrant paraesthesia. There was no suspicious findings in the brain, but whole spine MR scan revealed clear progression of pathologic findings in the thoracic spine. In the posterior subarachnoid space of C7–Th12 were enhancing leptomeningel and pachymeningeal lesions, that at some levels completely covered the posterior aspect of the spinal cord. These changes created the appearance of pseudocystic lesions bounding liquor (Figs. 1, 2). We could also observed less pronounced enhancing lesions on the anterior aspect of the spinal cord, two tiny enhancing lesions on the nerve roots at the level of L3–4 of the lumbar spine.

In differential diagnosis were considered: granulomatous disorders (such as neurosarcoidosis, CNS tuberculosis, granulomatosis with polyangiitis), autoimmune/inflammatory disorders (such as rheumatoid disease, IgG4-related hypertrophic pachymeningitis), also possibility of neoplastic etiology.

A biopsy was suggested, but was several times declined by the patient and her parents. She felt well, there was any clinical progression and every possible laboratory tests were negative (blood and CSF). Meantime she developed temporal hemianopsia. Therefore another follow-up MR scan was performed in December 2020 with the finding of thickened enhancing sheath of the left optic nerve.

On follow-up MR study In June 2023 there were newly diagnosed intracranial pathological findings, leptomeningeal (slightly also pachymeningeal) involvement of the cerebellum, medulla oblongata, quadrigeminal cistern, around the pineal gland and also supratentorially, the most prominent in the area of sulcus lateralis, the temporal lobes and frontobasal areas. The patterns of enhancement varied from thin and linear to thicker, lumpy or nodular (Fig. 3). These findings were significantly better seen on contrast-enhanced FLAIR FS sequence in comparison to contrast-enhanced T1 FS-weighted imaging (Fig. 4). There was slightly progression of enhancing thickened sheath of the left optic nerve (Figs. 3, 4). Patient finally agreed to undergo a biopsy.

Biopsy was performed from the thoracic region of Th10 and just two small pieces with a diameter of 1 mm were taken. Microscopically a low-grade looking lesion was captured, consisting of inconspicuous glial cells of astrocyte appearance, with round nuclei without mitosis, necrosis or microvascular proliferation.

Through an extensive genetic examination the fusion of the GTF2I::BRAF genes were proven in the tumor. The morphology and genetic profile of the lesion were compatible with the diagnosis of Diffuse leptomeningeal glioneuronal tumor (DL-GNT). In the literature the GTF2I::BRAF fusion has not yet been described in this tumor, however, it is an alteration of the MAPK pathway that is typical for this tumor. Other genetic test revealed positivity for GFAP, Olig2, S100, SOX10 and without overexpression of p53, ATRX, IDH1, AE1/AE3, LCA, CD68, synaptophysin, chromogranin and NeuN. 1p deletions were not proven in the analysed materials, though this result has to be taken with caution due to the small pieces of analysed samples.

Our patient currently does not take any medical treatment. As for September 2024 she is feeling well and remained stable after 9-months imaging follow-up.

DISCUSSION

DL-GNT is a rare tumor of the central nervous system, presented especially among children and young adults.

The clinical presentation is not specific, mostly there are some neurological, sensory and motor deficits. Symptoms may be the result of increased intracranial pressure due to the presence of hydrocephalus or mass effect of tumor. In our patient's case symptoms were not specific. Disease was first found accidentally. The main symptoms were headache and migrant paraesthesia. In the meantime she also developed temporal hemianopsia.

Imaging is generally carried out with MRI. The leading finding is of nodular, lumpy leptomeningeal enhancement of lesions, which secondary may lead to hydrocephalus and additional presence of numerous subpial cysts.

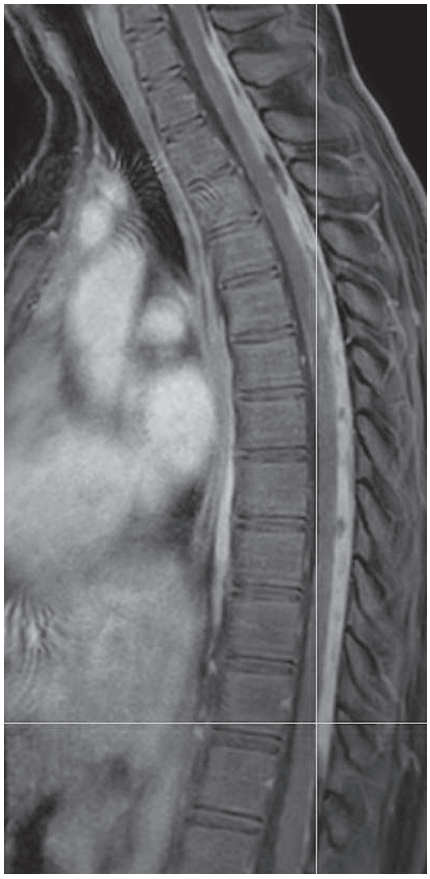
Our patient was diagnosed with leptomeningeal and also pachymeningeal involvement of the spine and on follow-up MRI also meninges of the brain and sheath of the left optic nerve were affected. Hydrocephalus and subpial cysts were not present, just slightly enlarged lateral ventricles.

Although imaging features may suggest the diagnosis, it is impossible to confirm it without a biopsy. A biopsy, which was recommended a number of times, was finally accepted by the patient after the MR scan carried out in June 2023.

When looking at it from a histological view, these tumours appear to be similar to oligodendroglial cells with round nuclei and mimic low grade looking tumors.

Genetically, DL-GNT is often connected with genetic changes, with the most common chromosome arm 1p deletions

1a



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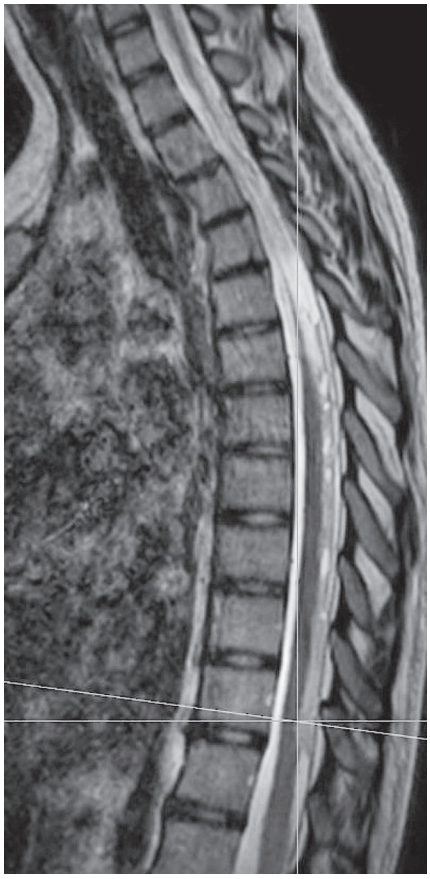

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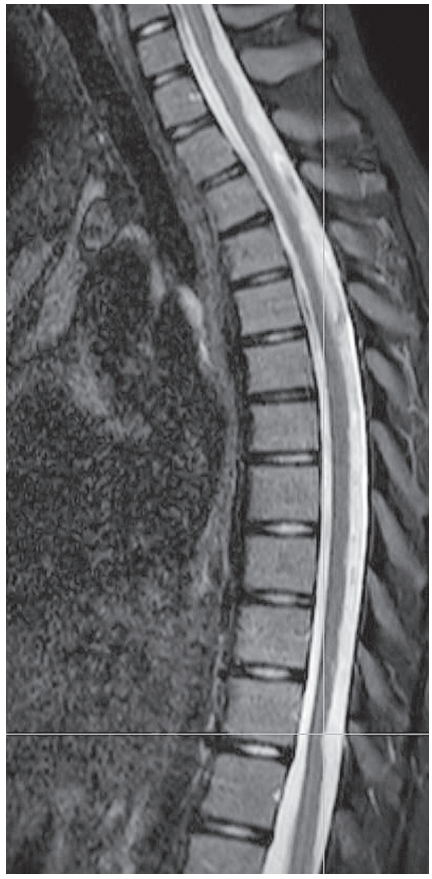

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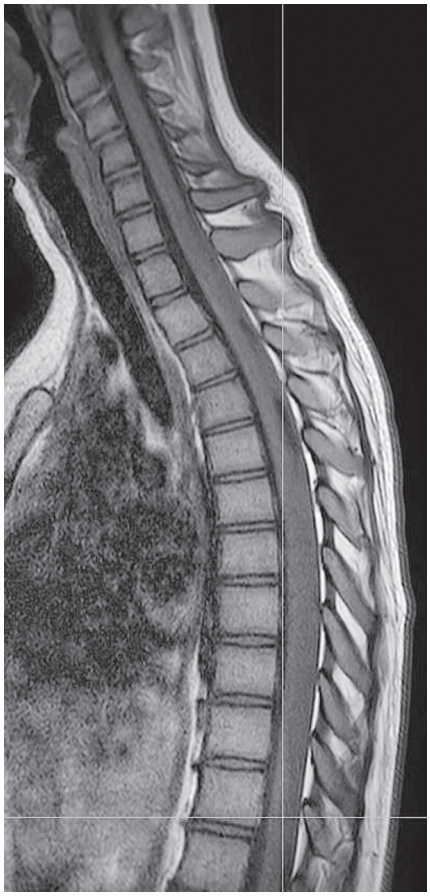

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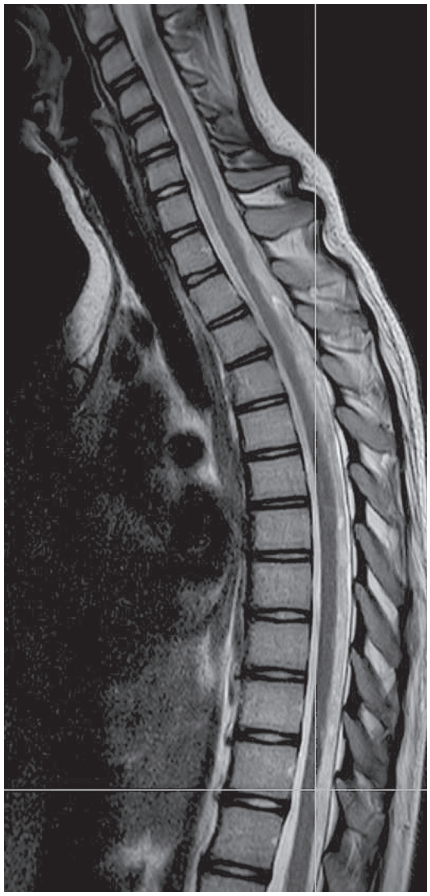

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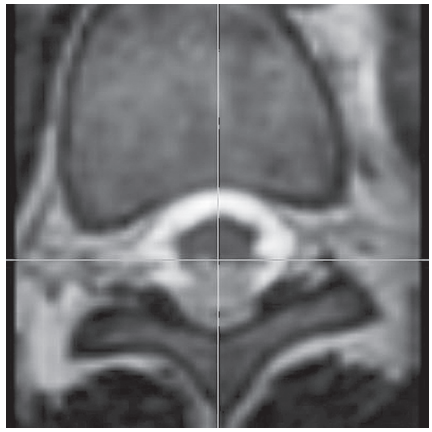

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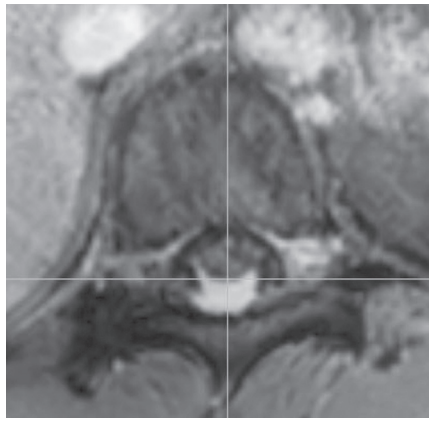
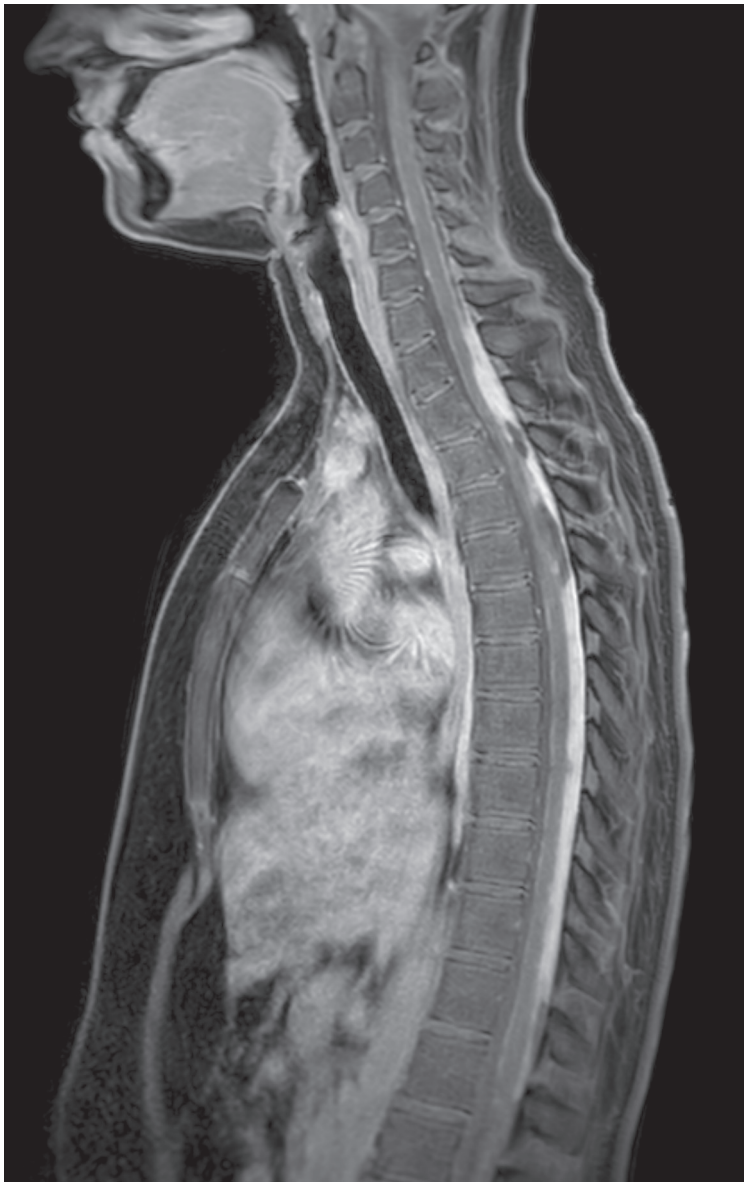




2 **Sagittal contrast-enhanced T1 FS-weighted imaging demonstrating enhancing leptomeningeal and pachymeningeal lesions predominantly in the posterior subarachnoid space, most prominently in C7–Th12**

Sagitálne T1 FS v.o. + GD zobrazuje sýtiace sa leptomeningeálne a pachymeningeálne lézie predominantne v zadnom subarachnoidálnom priestore, najviditeľnejšie v úseku C7–Th12

sometimes with co-deletion of 19q, accounts for its prior name including the term „oligodendroglial-like". In contrast to oligodendrogliomas, diffuse leptomeningeal glioneuronal tumors do not have IDH mutations (5, 6). Other markers are also presented, including KIAA1549-BRAF fusion, OLIG2, MAP2, S-100, GFAP, synaptophysin (5–8). Negative for neurofilament and EMA, and no IDH mutations (5, 6, 9). In our case fusion of the GTF2I::BRAF genes were proven in tumor. The GTF2I::BRAF fusion has not yet been mentioned in this tumor. Other genetic test revealed positivity for GFAP, Olig2, S100, SOX10 and without overexpression of p53, ATRX, IDH1, AE1/AE3, LCA, CD68, synaptophysin, chromogranin and NeuN. 1p deletions were not proven in the analysed materials.

The treatment options include watchful waiting, craniospinal irradiation and, as is strongly suggested by some authors, chemotherapy (4, 10).

Survival varies widely, reported in some instances to be quite low, with an average survival of only 22 months (7), whereas other series have long follow-up (5, 11).

CONCLUSION

DL-GNT is a rare and not completely understood neoplastic disease. Despite its rarity, it is important to think of this disease, which mainly occurs among children and adolescents in the list of the differential diagnosis for the leptomeningeal processes.

Contrast-enhanced FLAIR sequence should be perhaps part of the brain protocol, if a contrast agent is given, especially if leptomeningeal process is suspicious.

This case report adds a further example of the slightly different onset and appearance of this tumor.

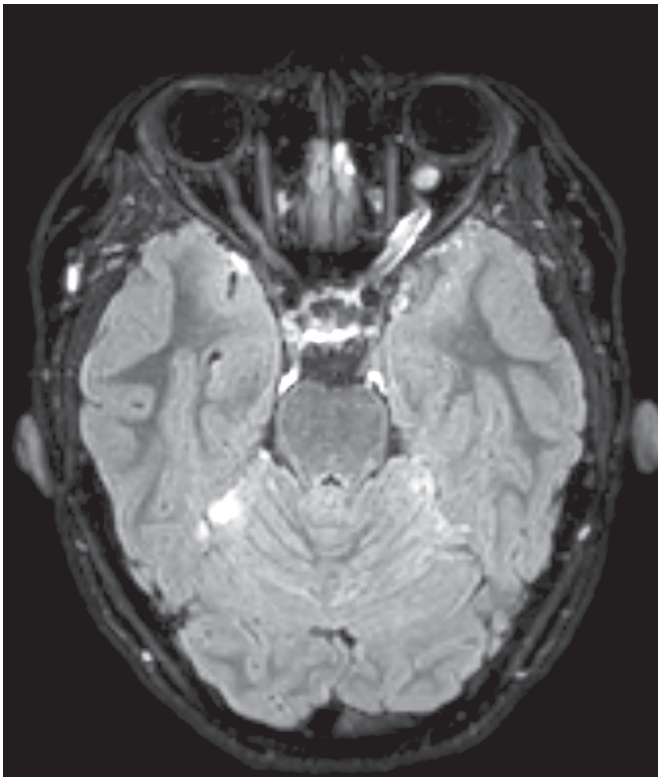
The new genetic alteration (fusion of the GTF2I::BRAF genes) appears to be new and has not yet been described in this tumor. ●

1 **(a) sagittal contrast-enhanced T1 FS-weighted imaging; (b) sagittal T2 iso sequence; (c) sagittal STIR; (d) sagittal T1-weighted imaging; (e) sagittal T2-weighted imaging; (f) axial T2 iso sequence MPR; (g) axial contrast-enhanced T1 FS-weighted imaging**

At C7-Th12 predominantly in the posterior subarachnoid space enhancing leptomeningeal and pachymeningeal lesions, at some levels completely covering the posterior aspect of the spinal cord. These changes created the appearance of pseudocystic lesions bounding liquor.

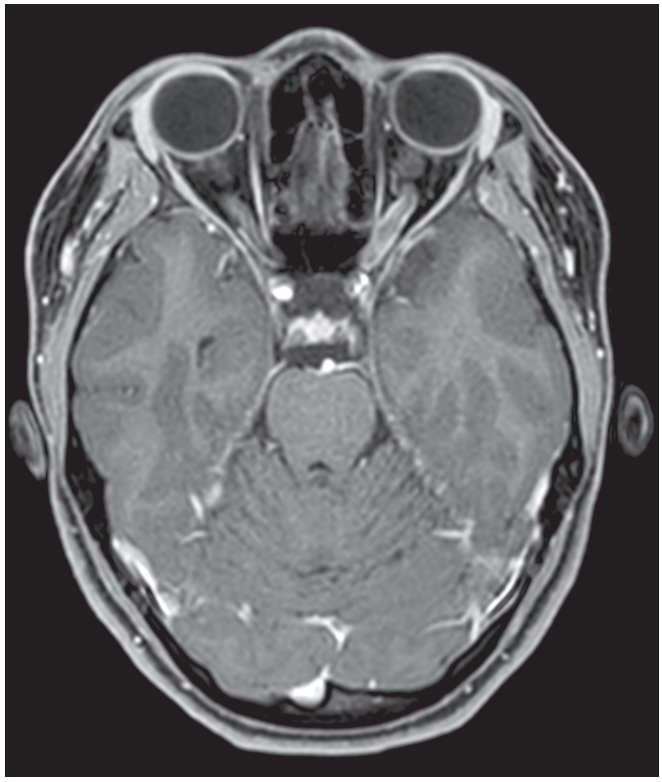
(a) sagitálne T1 FS v.o. + GD; (b) sagitálne T2 iso.; (c) sagitálne STIR; (d) sagitálne T1 v.o.; (e) sagitálne T2 v.o.; (f) axiálne T2 iso. MPR; (g) axiálne T1 FS v.o. + GD

V úseku C7-Th12, predominantne v zadnom subarachnoidálnom priestore sa nachádzajú sýtiace leptomeningeálne a pachymeningeálne lézie, ktoré v niektorej časti kompletne obklopujú zadnú časť miechy. Tieto zmeny vytvárajú vzhľad pseudocystických lézii ohraničujúce likvor.



3 **Contrast-enhanced axial FLAIR FS sequence showed nodular leptomeningeal enhancing lesions and enhancement of thickened sheath of the left optic nerve**

Axiálne FLAIR FS + GD zobrazuje nodulárne sýtiace sa leptomeningeálne lézie a sýtiacu sa zhrubnutú pošvu ľavého optického nervu



4 **Contrast-enhanced axial T1 FS-weighted sequence at the same level. Enhancement of the structures is less prominent than on contrast-enhanced axial FLAIR FS sequence**

Axiálne T1 FS v.o. + GD zobrazuje sýtenie štruktúr, ktoré je menej výrazné v porovnaní s axiálnym FLAIR FS + GD zachytenej v rovnakej lokalite mozgu

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