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Case Report

Diffuse Leptomeningeal Glioneuronal Tumor in Child. Case Report

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Abstract

The manifestation of diffuse leptomeningeal glioneuronal tumor (DLGNT) is unspecific. A timely diagnostic is difficult due to the presence of immune inflammation. An early diagnosis is essential to correct the treatment and reduce the volume of central nervous system damage. We would like to share the clinical case of child with DLGNT.

Keywords: *Diffuse Leptomeningeal Glioneuronal Tumor (DLGNT); Central Nervous System*

Introduction

Diffuse leptomeningeal glioneuronal tumor (DLGNT) is rare pediatric neoplasm. The incidence is not established. Only isolated clinical cases and small series of cases were described in literature [1]. First clinical case of DLGNT was reported in 1940. Since then 90 clinical cases were described. Only a few of them were confirmed by the results of genetic tests [2,3]. Publications about DLGNT are still absent in Russia. This disease is considered to be slowly progressive, however, can be cases of aggressive course with imminent death. Clinical symptoms are not specific [4]. Non-focal neurological symptoms and encephalopathy are noted at the onset, then focal neurological deficit joins. MRI picture is characterized by hyperintensive signal from the meninges of the brain and spinal cord, and cyst-like focus in T2 weight imagine in the brain base, in the posterior fossa and in the spinal cord. Elevated protein level and normal number of cells are found in cerebrospinal fluid (CSF). Tumor cells are rarely identified. KIAA1549-BRAF fusion and deletion 1p or co-deletion 1p/19q with absents mutation IDH may be found during genetic tests [5]. The treatment of DLGNT may include chemotherapy and radiation therapy (according low grade glioma treatment protocols - SIOP LGG 2004) [6]. Some authors reported about effective use valproic acid in therapy DLGNT [7]. There no published case reports, in which intravenous immunoglobulin (IVIg) was used. Targeted therapy with BRAF inhibitors may be recommended in cases of proven.

Clinical Case

A three-year-old boy was examined because of history of continuous vomiting, affective episodes end sleep disturbance. The cardiac deficiency was suggested. Patient was hospitalized in Morozov City Children's Hospital (MCCH) in Moscow. Extensive diagnostic work-up was performed. Two intramedullary nodular lesions on C3-C7 level on T2 weight MRI with minimal accumulation of gadobutrol. Contrast accumulation also in the meninges of the brain stem and craniovertebral region (Figure 1).

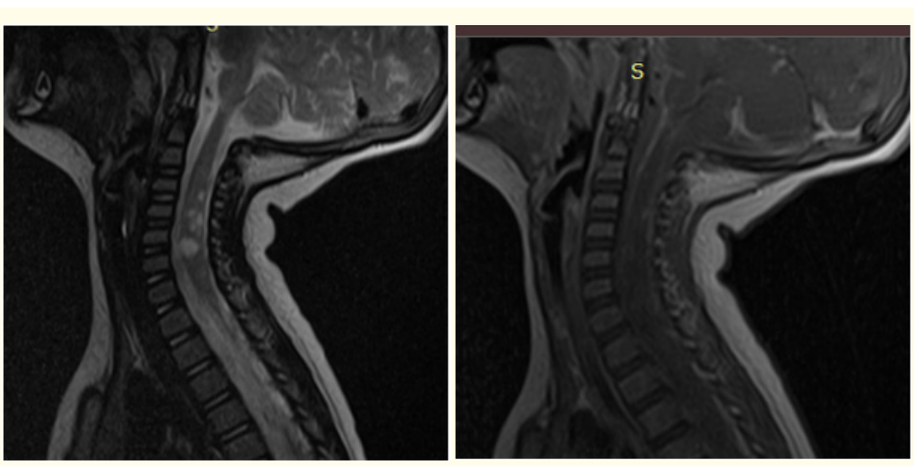

Figure 1: MR-images. Sagittal T2-WI (1), sagittal T1-WI with contrast (2).

CSF analysis revealed high protein level (1.5 g/l), normal cells count and glucose level. Fetal proteins (alpha fetoprotein, chorionic gonadotropin) were within normal. Extra CNS tumors were not founded. Infectious of CNS were excluded. Complete blood count was normal.

MRI findings were suggested with no connection to the clinical presents. Control examination after 3 months was recommended. The patient was treated by gastroenterologist unsuccessfully. The boy was present vomiting, lost weight. Nessen's operation was made. Neurologic examination showed stiff neck and gait disturbance (paraparetic, atactic). Lansky scale index was 80. No progressive disease on MRI scan was revealed after 9 months of surveillance. Patient visited traditional medicine specialists due to desire of parents during that period.

Cyst-like focuses of hyperintensive signal were found in cerebellum (hemisperes and vermis), brain stem and thalamus bilaterally, along the straight gyruses on both sides, parasagittal on the right, in the anterior part of the corpus callosum. The sizes of those focuses differed from minimum to 2,4 x 1,0 x 0,8 cm. Moderate compression of brain structures, without signs of significant perifocal edema, and contrast accumulation were revealed. Two intramedullary nodular lesions on C3-C7 level persisted and new foci appeared on Th2-Th3 level. Accumulation of contrast in the meninges of the brain and spine was more evident on craniovertebral region on control MRI after 9 month of surveillance (Figure 2 and 3).

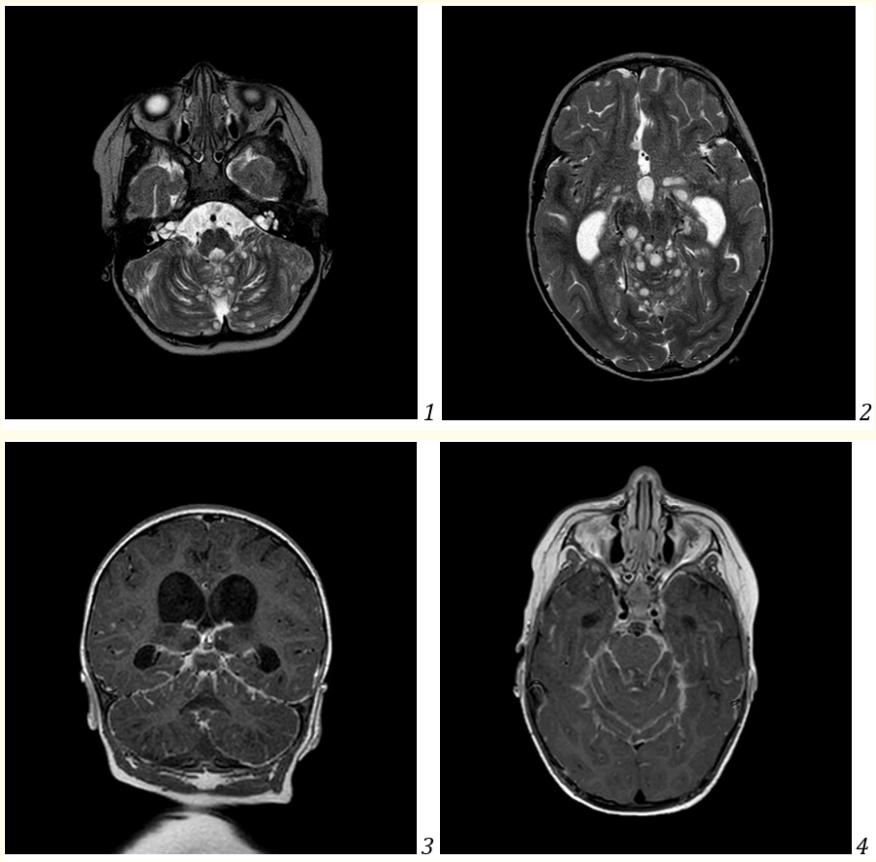

Figure 2: MR-images. Axial T2-WI (1, 2), coronary (3) and axial (4)T1-WI with contrast.

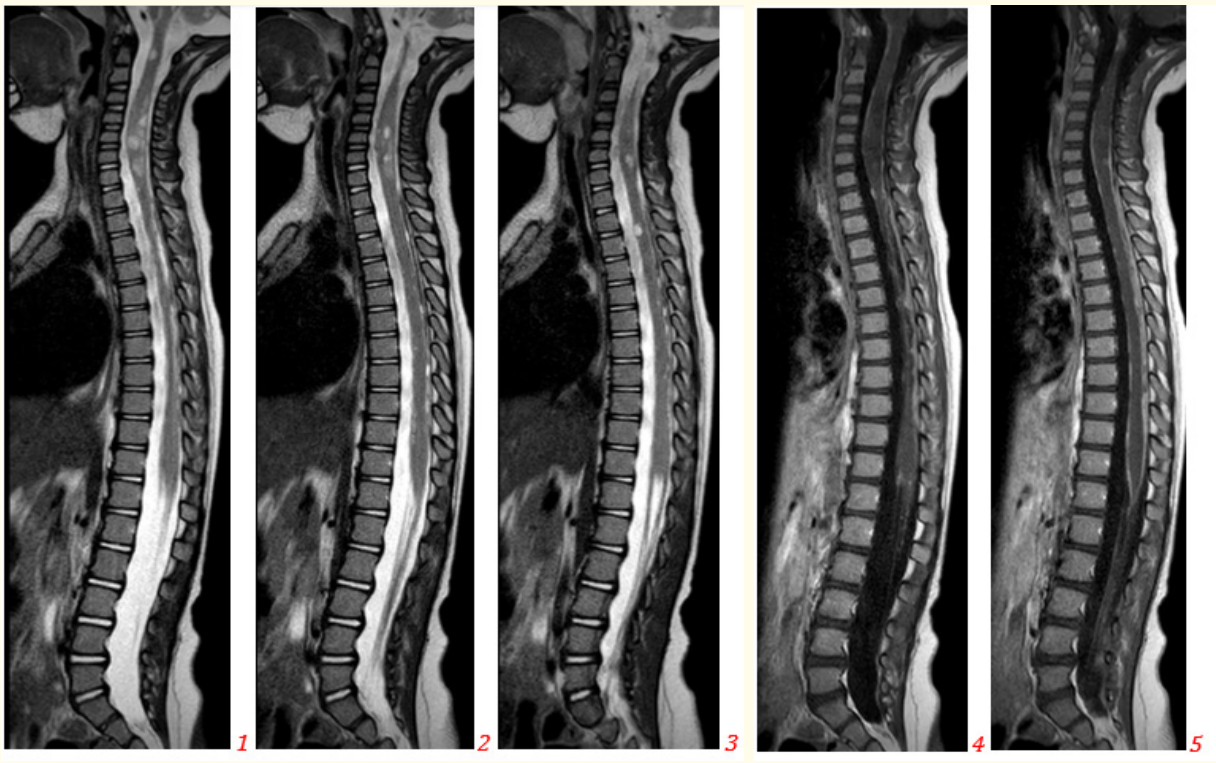

Figure 3: Sagittal MR-images. T2-WI (1, 2, 3), sagittal T1-WI with contrast (4, 5).

Gait disturbance and affective episodes were persisting. Lansky scale index was 70. New extensive diagnostic workup was performed after MRI. Yo-1 antibodies were revealed; elevated protein level (3 g/l) found in CSF again; infections and parasitic invasions were excluded.

Ventriculo-peritoneal shunt (VPS) was implanted due to an obstructive hydrocephaly progression. A biopsy of the meninges and cyst-like foci of the brain was performed. Integrated histomolecular diagnosis was Diffuse leptomeningial glioneuronal tumor with elevated proliferative activity and hints of a BRAF/KIAA1549 fusion, hints for 1p deletion (MCCH; University of Heidelberg, Germany). Chemotherapy was started 26.03.2018 according to protocol SIOP-LGG2004.

Neurocognitive sequelae included meningoencephalopathy, left-side pyramidal signs, severe static and dynamic ataxia, behavioral and emotional disorders (ritual and stereotype behavior).

Behavioral disorders and affective episodes were considered as a result of intensive pain. Lansky scale index was 30. Therapeutic approaches with carbamazepine (without any effect) and amitriptyline (with positive clinical effect) were carried out. Secondary generalized seizure with oral automatisms occurred 2 months after VPS implantation. Dysfunction of VPS was diagnosed and treated minor of surgery.

Valproic acid (VA) was introduced because of size of brain damage, kinematics of a seizure, electroencephalography (EEG) results (peak-wave components in the background inhibition structure) and the presence behavioral disorders (Figure 4). EEG findings - epileptic activity was absent after one month on therapy with VA (Figure 5). Therapy with high dose human intravenous immunoglobulin (IVIg) 2 g/kg/course was started.

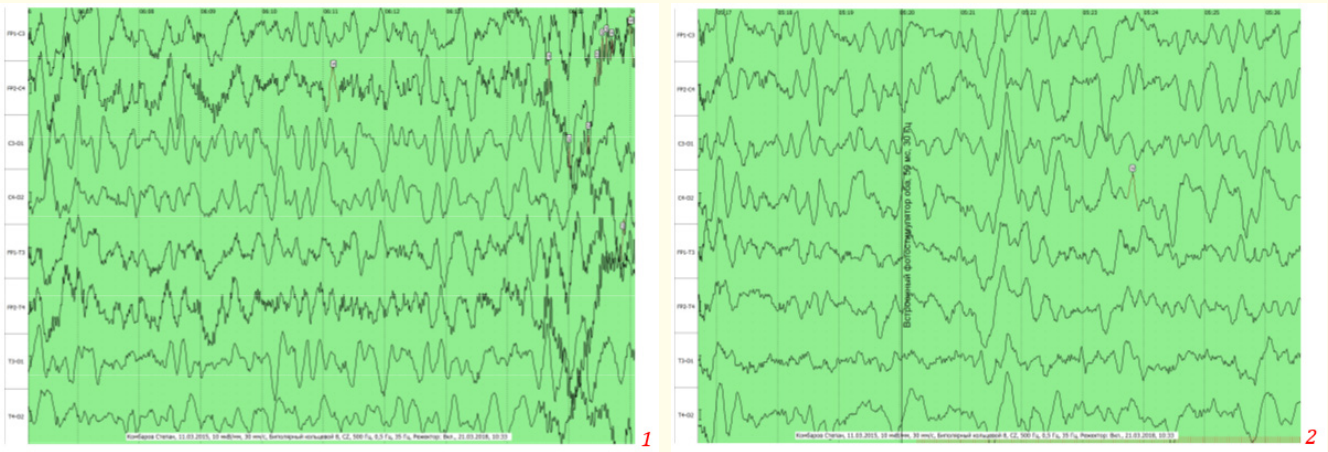

Figure 4: EEG (1,2) comments in the text.

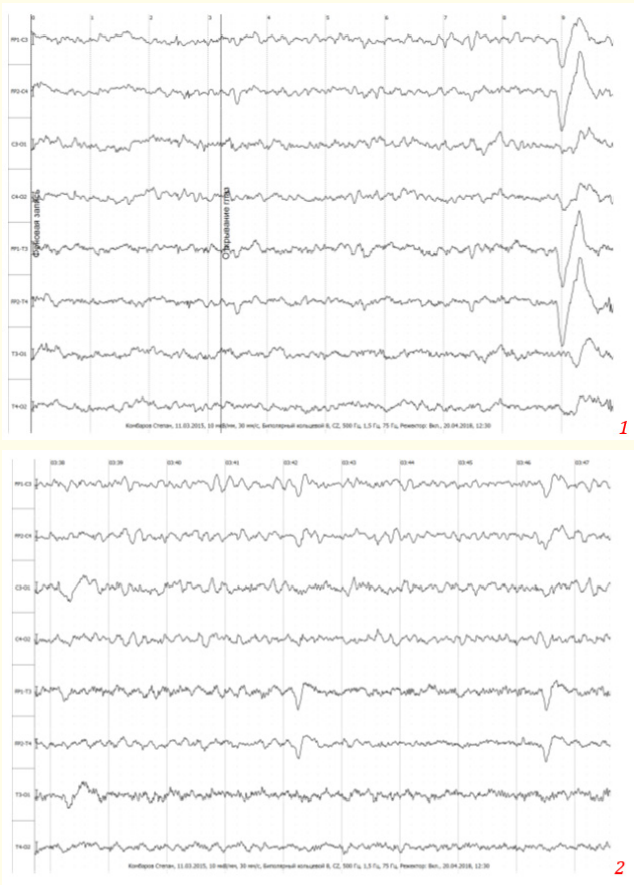

Figure 5: EEG (1,2) comments in the text.

Secondary serial generalized seizure occurred due to dysfunction of VPS 4 month after implantation. The boy was admitted into intensive care unit. Seizures stopped after inhalation of sevoflurane, minor surgery and continuous of VA therapy.

Clinical status of patient improved with chemotherapy and 6 courses of IVIg. Lansky scale index was 80. We saw increasing play, learning and motor activity. The child walked by himself, intentional tremor and dysmetria decreased, affective episodes regressed (amitriptyline was canceled), cognitive functions and social adaptation improved. The number and size of sub- and supratentorial foci decreased. Signal intensity of contrast accumulation on C7 level increased on MRI after 24 weeks of chemotherapy (Figure 6 and 7).

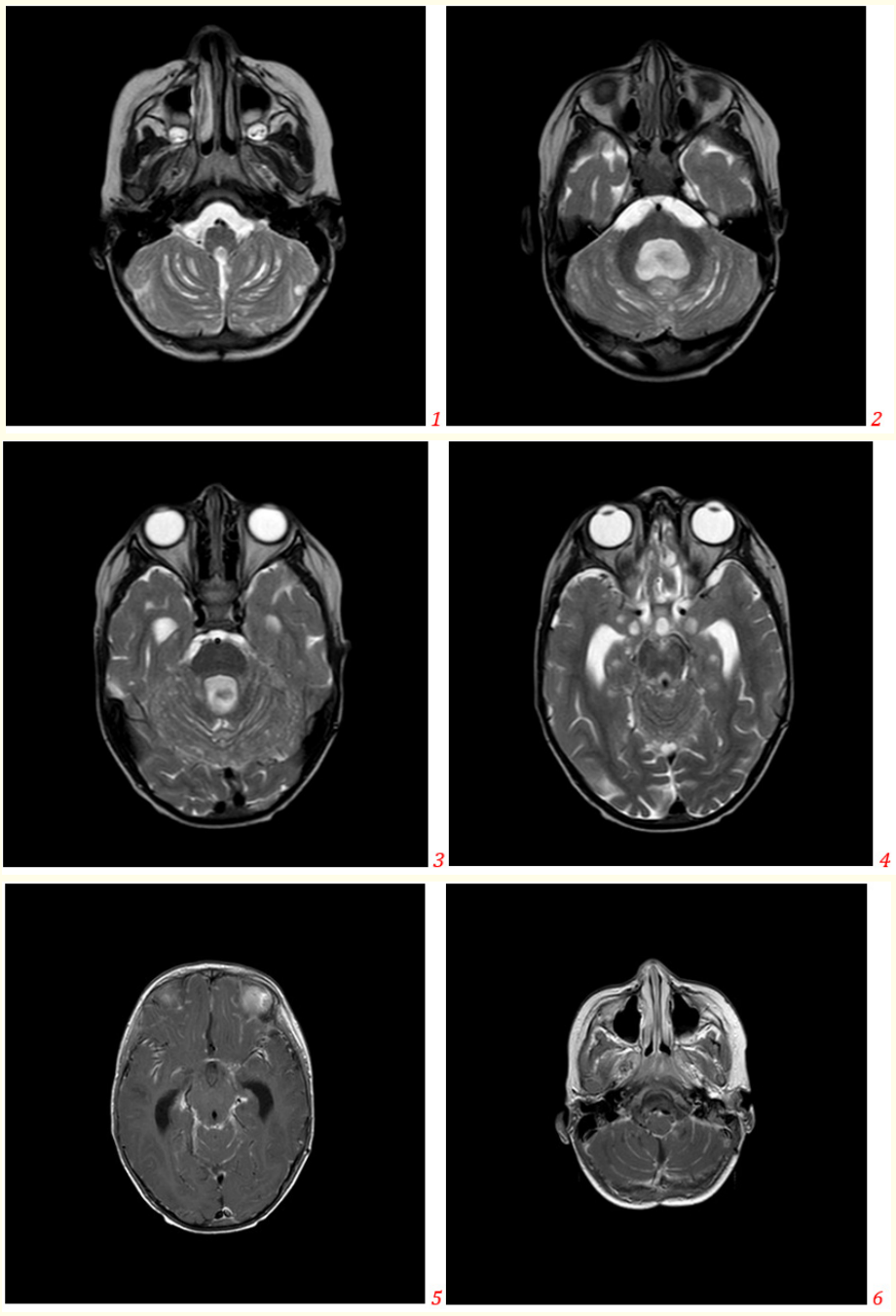

Figure 6: Axial MR-images. T2-WI (1, 2, 3, 4), axial T1-WI with contrast in axial (5, 6).

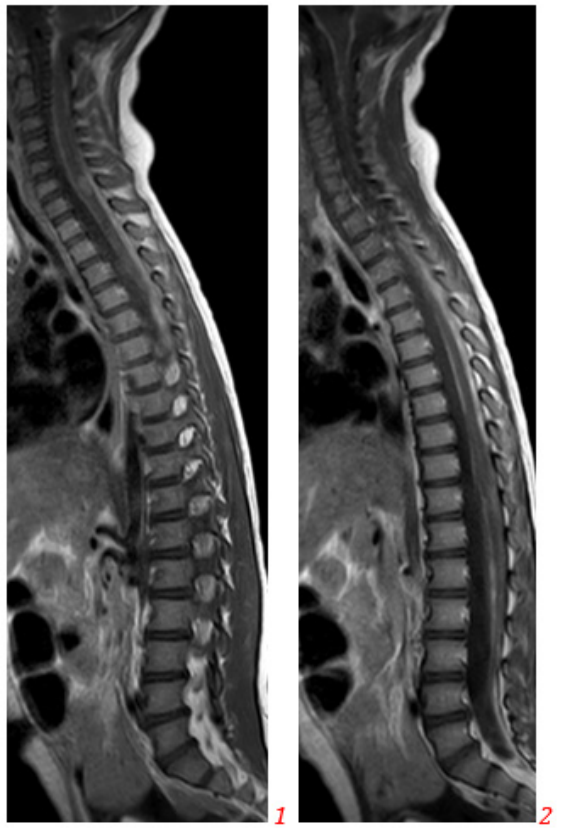

Figure 7: MR-images. Sagittal T1-WI with contrast.

Discussion

This case demonstrated unusual clinical presentation of oncological disease.

There are no published case reports in literature, in which DLGNT was associated with autoimmune process in CNS.

Paraneoplastic syndrome is known fact in patient with oncological diseases. One of the most severe paraneoplastic syndromes are syndrome with involve CNS. Clinical presentation may include ataxia, dizziness, nausea and vomiting, also nystagmus, visual function disorders, affective episodes and seizures. The autoimmune process is an important factor in the pathogenesis of paraneoplastic syndromes [8].

Recommendations on treatment of neurological complications of patients with DLGN are not exist, although in the literature there are descriptions of lethal cases of DLGN from the resulting serious complications of CNS. In our boy Yo-1 antibodies were revealed. This type of antibodies is associated with damage of Purkinje cells in cerebellum. The main in clinical status in our patient was ataxic syndrome. Autoneuronal antibodies and meningoencephalopathy was considered as paraneoplastic syndrome whit involved CNS. In pediatric neurology there are exist recommendation for the use of IVIg in autoimmune encephalopathies [9]. Therapeutic approaches with high dose IVIg was carried out.

The boy was treated in two ways - specific therapy according to protocol SIOP-LGG 2004 and immunotherapy (IVIg). We saw improved of motor and cognitive functions, and social adaptation. Ataxia was decreased. Lansky scale index was increased on 50 points. The number and size of sub- and supratentorial foci decreased.

In this report DLGN is associated with autoimmune meningoencephalopathy. The presence of immune inflammation hided neoplastic process and severed diagnostics. Only biopsy with large immunohistochemistry and molecular genetics studies allowed to make evidence based diagnosis.

Conclusion

DLGN is rare, low-grade, glial or glioneuronal pediatric neoplasm. Recognize distinctive neuroimaging picture it is important for early diagnosis end timely start treatment. Meningoencephalopathy, hyperintensive signal from the meninges of the brain stem and craniovertebral region, and cyst-like focus in T2 WI in spinal cord are noted in the debut of DLGN. These features can be the cause of a long diagnostic search and late diagnosis.

The "gold standard" of therapy DLGN is not exist. Some patients are still on treatment and observation.

Therapy according to SIOP LGG 2004 protocol with VA and IVIg allows to stabilize process with gradual neurological improvement but no to cure the patient. Targeted therapy with BRAF inhibitors should be considered as a future approach to cure such patients.

Perhaps that early search antineuronal antibodies may do immunotherapy timely to reduce the volume of CNS damage.

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