“A diffuse leptomeningeal glioneural tumor (DLGNT) case making hydrocephalus and poliradicupopathy”

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Poster ID: 2345

Disclosure: There is no conflict of interest regarding the subject of this article
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Introduction

• The DLGNT was recognized as a distinguishing entity in 2016 by the WHO classification of tumors of central nervous system (CNS).

• It is a rare primary CNS tumor characterized by diffuse leptomeningeal dissemination of neoplastic glioneural cells.

• The diagnosis based only on clinic-epidemiological aspects is challenging because it has no pathognomonic signs and its clinical presentation and imaging features findings may vary widely. Despite of this, it is most often at young age and show low-growing rate.

• The genetic and epigenetic changes of the DLGNT and its exact biological behavior are not yet fully known.

• Today there is no consensus on DLGNT treatment.
Case report

A 31-year-old-patient sought for medical attention complaining of back pain, urinary and fecal incontinence in addition to weakness, muscle atrophy, paresthesias and hypoesthesias, specially in the lower limbs. About his medical history, he remarked that 14 years ago he had undergone a ventriculoperitoneal shunt surgery due to hydrocephalus which has never had its etiology clarified because he had abandoned the follow-up and investigation workup. At this time, his brain and spine magnetic resonance imaging showed a diffuse contrast enhancement besides multiple infiltrative nodular and cystic lesions in the cranial and spinal subarachnoid space, especially in the basal cisterns, brain ventricles and in the cauda equina (Figures 1, 2 and 4).
Case report

Figure 1. T1-weighted MRI images with gadolinium.
Diffuse leptomeningeal enhancement to the gadolinium injection in the (A) basal cisterns, 4th ventricle and cervical spinal cord, (B) thoracic spinal cord, and (C) lumbar spinal cord and cauda equina.

Figure 2. T2-weighted and FLAIR MRI images.
Hyperintense subpial nodules and cysts in the (A) septum pellucidum, lateral ventricles and 3rd ventricle, (B) thoracic spinal cord, and (C) lumbar spinal cord and cauda equina.
A biopsy of a lesion in the cauda equina was performed and the diagnosis of DLGNT was confirmed (Figure 3, table 1).

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<tr>
<th>Stain</th>
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<th>Characteristics</th>
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<tr>
<td>S100</td>
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<tr>
<td>Neu-N</td>
<td>Positive</td>
<td>Weak</td>
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<td>GFAP</td>
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<td>Synaptophysin</td>
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<tr>
<td>Ki67</td>
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<td>Mutant IDH1</td>
<td>Negative</td>
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Figure 3. Histopathological

(A) Low power examination reveals a diffuse leptomeningeal proliferation of tumor cells with clear cytoplasm; (B) At higher magnification, the nuclei are round and bland. No mitotic figures were seen; (C, D) Tumor cells were diffusely positive for S100 and glial fibrillary acidic protein (GFAP).
Case report

A palliative treatment was proposed and a month later he started to receive three-dimensional conformal radiotherapy to the craniospinal axis (36 Gy in 20 fractions over 4 weeks) with a boost to the sacral tumor (18 Gy in 10 fractions over 2 weeks), adding up to a total dose of 54 Gy. After that, he underwent to 3 courses of conventional PCV chemotherapy (procarbazine, lamustine and vincristine) over 14 weeks without any complications. Despite partial response to the treatment (figure 4) the patient had improvement in pain levels, function and quality of life. Although he still is incontinent and unable to walk without assistance, we consider that his condition of total disability and full dependency (40% on KPS scale) has positively changed to a functional status which he is able to care for most of his needs (60% on KPS scale) and can be included in a rehabilitation program.
Case report

Figure 4. Partial remission of the tumor in response to radiotherapy plus PCV chemotherapy. The nodular and thick gadolinium-enhanced observed on pre-treatment T1-weighted MRI images (A, C and E) became tinner and less intense 3 months after the treatment (B, D and F).
Discussion

- DLGNT is also known as Disseminated Oligodendroglial-like Leptomeningeal Tumor of Childhood.
- Despite its indolent progression, the morbidity and mortality rates are frequently high.
- Its behavior can be more aggressive in adults or elderly people.
- Its clinical manifestations are directly related to the development of hydrocephalus and infiltration of spinal and cranial nerves.
- MRI exams typically shows multiples of thick nodular leptomeningeal enhancement around the basal cisterns and over the surface of the brain. It may extend to the brainstem, posterior fossa, spinal cord and cauda equine. Such lesions usually are T2 hyperintense and has isointense signal on T1. They are commonly associated to hydrocephalus.
- Differential diagnoses: tuberculous meningitis, meningeal carcinomatosis and fungal meningitis.
- Histology: DLGNT has low to moderate cellularity with a biphasic astrocytic (GFAP+) and neurocytes (Synaptophysin+) population. The aspect is monomorphous which consists of oligodendroglial-like cells with clear cytoplasm and rounded nuclei and low mitotic rate. Anaplasia or Ki67 > 4% might predict worse prognosis.
Discussion

- **Immunohistochemistry and molecular findings**: high reactivity to OLG 2, MAP 2 and S-100. Typically **negative** to NeuN, EMA and **mutant IDH1 (R132H)**. All DLGNT carry chromosomal arm 1p deletion as others genetic and epigenetics aberrations that are believed to activate the MAPK/ERK pathway.

- Molecular classes are based on DNA methylation profiling, to know DLGNT-MC-1 and DLGNT-MC-2. **DLGNT-MC-1 class is associated to a lower age of diagnosis, to higher frequency of co-deletion 1p19q and to clinical course less aggressive.**

- **The optimal management of it hasn’t been defined yet.**

- **The current approaches are based on low-grade glioma’s treatment.**

- It is not clear if different combinations of surgery, radiotherapy and chemotherapy can improve clinical outcomes and survival, therefore a conservative or palliative approach must not be ruled out.

- **Our case report suggests that radiotherapy plus PCV chemotherapy can have positive effects on DLGNT treatment and should be considered as a good approach.**
Summary points

- **DLGNT** is an unusual primary CNS tumor characterized by diffuse leptomeningeal dissemination of neoplastic glioneural cells.

- Imaging exams typically shows thick nodular leptomeningeal enhancement around the basal cisterns and over the surface of the brain and spinal cord.

- It is most often at young age and show low-growing rate, nevertheless its behavior can be more aggressive in adults and elderly people.

- Its clinical manifestations are related to development of hydrocephalus and spinal and cranial nerves involvement.

- The optimal management of it hasn’t been defined yet and the current approaches are based on low-grade glioma’s treatments.

- Our case report suggests that radiotherapy plus PCV chemotherapy can have positive effects on DLGNT treatment.