Case Report

**Giant Cell Ependymoma of The Lumbar Spine: Case Report and Review of The Literature**

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**Summary**

Giant cell ependymoma (GCE), is a extremely rare subtype of ependymoma. To date 14 cases have been documented in the literature. Here we present a case of GCE occurring in a 32-year-old patient with a 3-month history of progressively increasing pain in low back and right leg. Magnetic Resonance Imaging demonstrated a well circumscribed and enhancing intramedullar mass extending from L1 to L3. Tumor was totally resected. Histological and immunohistochemical findings were consistent with low grade giant cell ependymoma. This case is the first GCE of a lumbar spinal cord.

All literature related to GCE was reviewed, and the clinic, radiologic, prognostic and histopathologic characteristics associated with such lesions are discussed, based on the presented case.

**Key words:** Giant cell - ependymoma - spinal cord – tumor - spine

**INTRODUCTION**

Ependymomas represent a group of neoplasms derived from the ependymal lining of the central nervous system (CNS). These tumors may occur at any site along the ventricular system and in the intramedullar region of the spinal cord. Ependymomas account for 2-9% of all neuroepithelial tumors and develop in all age groups. In the spinal cord, ependymomas are the most common neuroepithelial neoplasms, comprising 50-60% of spinal gliomas in adults.²,³ Apart from standart ependymomas the 2007 World Health Organization (WHO) classification of CNS tumors incorporates some particular variants, such as cellular, papillary, clear cell and tanycytic ependymoma.⁷
Giant cell ependymoma (GCE) is a extremely rare subtype, first described in 1996.\(^{(17)}\) To date 14 cases have been documented in the literature.\(^{(1,2,4,12,13,15)}\) Only four of these were located in the spinal cord.\(^{(2,5,13,15)}\) Our case is the first example of a lumbar spinal cord GCE. All literature related to GCE was reviewed, and the clinic and histopathologic characteristics associated with such lesions were discussed in this report.

**CASE PRESENTATION**

A 32-year-old man presented with a 3-month history of progressively increasing pain in low back and right leg. Physical examination revealed hyperesthesia at the L1-L5 level. A magnetic resonance imaging (MRI) scan of the spine showed a well circumscribed lumbar intramedullar mass at the L1-L3 level. The tumor was hyperintense on T2-weighted MR imaging, isointense on T1-weighted imaging and contrast enhancing (Fig. 1).

The surgery was performed through a L1 to L2 laminectomy. It was noted to have a clear cleavage between the tumor and the spinal cord. Tumor was totally resected. The tumor was intramedullary, attached the root and slightly vascularized.

The surgical specimen consisted of soft yellow tissue measuring 48x27x15 mm. The parafin sections, stained with hematoxylin and eosin. For immunohistochemistry, antibodies against GFAP, EMA, CD99, Pancytokeratin, S-100, Ki-67/MIB-1, p53 were used.

Histopathologic examination showed dimorphism among the cellular population of neoplastic cells. Some of the cells, with large amphophilic cytoplasm, were oval or round-shaped and vesicular nuclei. Among them multiple giant tumor cells were seen, with bi-multi nuclei. Both areas were occasionally crossed by fascicles of spindle-shaped cells with fibrillary processes. Focally, around vessels, acellular fibrillary background rendered the formation of perivascular pseudorosettes (Fig. 2). Mitoses, necrosis and vascular proliferation were not observed.

Immunohistochemically, neoplastic cells strongly expressed GFAP, CD99 and S-100 protein in the cytoplasm. EMA was positive in disperse strong perinuclear dot-like pattern. No reactivity was detected with anti-cytokeratin antibodies. The Ki-67 labelling index was about 2.4% (Fig. 2). P53 was weakly positive in some giant cells nuclei. As a result the diagnosis of giant cell ependymoma, grade II (WHO, 2007) was established.

Ten months after surgery there is no evidence of residual or recurrent tumor left (Fig. 3).

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**Figure 1:** A magnetic resonance imaging (MRI) scan of the spine showed a well circumscribed lumbar intramedullar mass at the L1-L3 level. A, Sagittal MRI sections, the tumor was hyperintense on T2-weighted MR imaging, isointense on T1-weighted imaging. B, Axial T2-weighted, gadolinium-enhanced, MRI showing a homogeneously enhancing intramedulary tumor.
Figure 2: A, the tumor cells within delicate fibrillary background forming apparently acellular zones resembling perivascular pseudorosettes. H&E, 100X. B, pleomorphic giant tumor cells dispersed between medium-sized cells. H&E, 400X. C, strong immunopositivity for GFAP, 100X. D, immunopositivity for CD99, 100X. E, disperse perinuclear dot-like immunopositivity for EMA, 400X. F, MIB-1 labeling index was 2.4%. Ki-67, 400X.

Figure 3: Postoperative (third month) MRI scan. A, sagittal, T1 and T2 weighted B, axial gadolinium-enhanced MRI showing the complete tumor removal, and absence of recurrence.
Table 1: The review of previously reported giant cell ependymomas including the present case.

<table>
<thead>
<tr>
<th>No</th>
<th>Authors</th>
<th>Age/Sex</th>
<th>Site</th>
<th>Histological features¹</th>
<th>Grade</th>
<th>Follow-up recurrence/mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Zec, et al.</td>
<td>14/M</td>
<td>Filum terminale</td>
<td>V</td>
<td>Low</td>
<td>-/ 35</td>
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<tr>
<td>2</td>
<td>Zec et al.</td>
<td>14/M</td>
<td>Filum terminale</td>
<td></td>
<td>Low</td>
<td>-/ 16</td>
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<tr>
<td>3</td>
<td>Brown et al.</td>
<td>26/M</td>
<td>Supratentorial</td>
<td>M,V,N,</td>
<td>Anaplastic</td>
<td>+/-8</td>
</tr>
<tr>
<td>4</td>
<td>Pimentel et al.</td>
<td>13/F</td>
<td>Supratentorial</td>
<td>M</td>
<td>Anaplastic</td>
<td>-/24</td>
</tr>
<tr>
<td>5</td>
<td>Moritani et al.</td>
<td>50/F</td>
<td>Supratentorial</td>
<td>M, N, R</td>
<td>Anaplastic</td>
<td>+/-7, +/-13, 2nd rec. died</td>
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<tr>
<td>6</td>
<td>Jeon et al.</td>
<td>50/M</td>
<td>İnfratentorial</td>
<td>M,N,R</td>
<td>Anaplastic</td>
<td>+/-8</td>
</tr>
<tr>
<td>7</td>
<td>Fourney et al.</td>
<td>22/M</td>
<td>Spinal cord (cerv)</td>
<td></td>
<td>Low</td>
<td>+/- 6</td>
</tr>
<tr>
<td>8</td>
<td>Pal et al.</td>
<td>24/F</td>
<td>4. ventricle</td>
<td>N,R</td>
<td>Low</td>
<td>+/- 12</td>
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<tr>
<td>9</td>
<td>Cooper et al.</td>
<td>89/M</td>
<td>Post. Fossa</td>
<td></td>
<td>Low</td>
<td>+/- 2</td>
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<tr>
<td>10</td>
<td>Adamek et al.</td>
<td>17/M</td>
<td>Occipital, extraventricular</td>
<td>N,R</td>
<td>Low</td>
<td>+/- 18</td>
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<tr>
<td>11</td>
<td>Sangoi et al.</td>
<td>34/F</td>
<td>Suprasellar</td>
<td>R</td>
<td>Low</td>
<td>+/- 3</td>
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<tr>
<td>12</td>
<td>Barbagallo et al.</td>
<td>25/F</td>
<td>Spinal cord (C2-C5)</td>
<td>R</td>
<td>Low</td>
<td>+/- 18</td>
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<tr>
<td>13</td>
<td>Szpak et al.</td>
<td>28/M</td>
<td>C3 –4 to the 4. ventricle</td>
<td>V,R</td>
<td>Low</td>
<td>+/-12, died</td>
</tr>
<tr>
<td>14</td>
<td>Shamji et al.</td>
<td>67/F</td>
<td>Spinal cord (T8)</td>
<td>R</td>
<td>Low</td>
<td>Died 6 week after (complication)</td>
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<tr>
<td>15</td>
<td>Present case</td>
<td>32/M</td>
<td>Spinal cord (L1-3)</td>
<td>R</td>
<td>Low</td>
<td>+/- 10</td>
</tr>
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</table>

¹ Particulary reported histological features:N, palisading necrosis; M, Brisk mitotic activity; V, vascular proliferation; R, perivascular pseudorosettes.

DISCUSSION

Spinal cord ependymomas represent more than one-half of intramedullary spinal cord tumors. They are often well circumscribed and do not invade adjacent tissue. In the spinal cord, cervical and cervico-thoracic segments appear to represent primary sites. In contrast myxopapillary variant predominantly affects the conus-cauda equina region.²,⁷,¹³ The 2007 WHO classification of CNS tumors recognizes a range of ependymal neoplasms, including cellular, papillary, clear cell and tanycytic variants.⁷ But there are rare examples of other ependymoma variants such as; giant cell type, ependymoma with lipomatous differentiation, ependymoma with extensive tumor cell vacuolation, melanotic type, signet ring cell type,
ovarian ependymoma, ependymoma with neuropil-like islands and ganglioglioma with a tanyctic glial component.\(^{(7)}\)

Ependymomas develop in all age groups, however, peak incidences occur during the first and the fourth decades of life. Ependymomas appear equally distributed between males and females.\(^{(7)}\)

Giant cell ependymoma is very rare. To date fourteen case of GCE have been reported in the literature (Table 1). The patients were 8 men and 6 women. The mean average age was 33.8 years (range 13-89 years). Only four of these were located in the spinal cord.\(^{(2,5,13,15)}\) Our case is the first example of the lumbar spinal cord.

Typically, most examples of ependymomas contain isomorphic cells. Perivascular pseudorosettes are among the most characteristic features of ependymomas, although they are not pathognomonic.\(^{(7,13)}\)

The gigantocellular morphology with marked pleomorphism, necessitate considering not only special variants of ependymoma, such as anaplastic ependymoma, and giant cell ependymoma but also some other possibilities like: subependymal giant cell astrocytoma (SEGA), pleomorphic xantoastrocytoma (PXA) and giant cell glioblastoma, in spite of barely spotted structures resembling true ependymal rosettes and perivascular pseudorosettes. SEGA, PXA and giant cell glioblastoma do not contain rosettes and canals.

SEGA is the most common neoplasm in tuberous sclerosis, typically arising in the wall of the lateral ventricles and composed of large plump cells. Other characteristic of the PXA, such as lipidized giant cells and reticulin-rich architecture, were absent from GCE. The anaplastic features as increased cellularity, brisk mitotic activity, microvascular proliferation, necrosis and the high degree of Ki-67 positivity that, which would be expected in giant cell glioblastoma and anaplastic ependymoma were also absent.\(^{(1,7,12,13)}\)

The three possible diagnosis of GBM, anaplastic ependymoma and giant cell ependymoma could not be differentiated by frozen section. As revealed by routine permanent section with hematoxylin and eosin staining, an abrupt demarcation between the tumor and spinal cord tissue was observed. Intraoperatively, in view of both the surgical anatomical features of the mass and the relatively ease of its dissection off the spinal cord, the neoplasm appeared less infiltrating and less aggressive like the present case.

Giant cells do not carry worse prognosis in other low grade lesions such as SEGA and PXA. The cellular pleomorphism among GCEs has been attributed to degenerative changes with no worse prognosis in the absence of other anaplastic features. Although some authors interpret the giant cells as representing more aggressive pathology.\(^{(6,8,10,12)}\) We agree with Zec\(^{(17)}\), Shamji\(^{(13)}\) and Barbagallo\(^{(2)}\) et al. who attribute cellular pleomorphism to degenerative changes.

According to the WHO grading system, the pathological spectrum of ependymomas might be very wide, including in rare cases a giant cell component.\(^{(7,15)}\)

Histologically, ependymoma corresponds to WHO grade II. Increasing cellularity, brisk mitotic activity, microvascular proliferation and pseudopalisading necrosis are the features which were described by the WHO classification of an ependymoma as anaplastic (grade III).\(^{(7)}\) Of the 14 reported cases of GCE, 4 are graded as anaplastic using variable criteria.\(^{(3,8,10)}\)

Spinal cord ependymomas of classic type are usually classified among slow growing WHO grade II tumors characterized by long–term survival.\(^{(7,15)}\) It has been shown that, the localization and histological classification of ependymoma are a significant predictor of clinical outcome (Table 1).\(^{(15)}\)
Ki-67 is an adjunctive prognostic indicator for ependymoma. Disruptions of the TP53 gene pathway are rare in ependymomas. However, some reports suggested the role of p53 gene mutation or overexpression in anaplastic transformation in ependymoma, which correlated with a poor prognosis and high grade histology. There are two GCE cases available, where overexpression of p53 has been found. Both cases had anaplastic morphology may be involved in the pathogenesis. In our case, the Ki-67 labelling index was about 2.4% and P53 was weakly positive in some giant cells nuclei. These findings are correlated with a good prognosis and low-grade histology.

CONCLUSION
This is the first case report of this unusual variant of ependymoma in the lumbar spinal cord. The biologic behaviour of such rare variant of ependymoma is difficult to predict. Of the 14 reported cases of GCE, 4 are graded as anaplastic using variable criteria. Among Giant Cell Ependymomas, the cellular pleomorphism observing as the existence of giant cells, which are witnessed in the literature with no worse prognosis in the absence of other anaplastic features, has been attributed to degenerative changes. The localization and histological grade of giant cell ependymomas are a significant predictor of clinical outcome. The long term prognosis for the tumor is being questioned, because of the rarity of this tumor.

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