

## Case Report

# Clear Cell Ependymoma Occurring in the Cauda Equina

Dong Joon Kim, M.D.,<sup>1</sup> Tae Wan Kim, M.D.,<sup>1</sup> Yoonjung Kim, M.D.,<sup>2</sup> Kwan Ho Park, M.D.<sup>1</sup>

Departments of Neurosurgery,<sup>1</sup> Pathology,<sup>2</sup> Seoul Veterans Hospital, Seoul, Korea

The authors present a rare case of clear cell ependymoma that developed in the cauda equina. A 54-year-old man was admitted to hospital with intermittent lower back pain. A neurological examination conducted on admission revealed no sensory or motor disturbance. Deep tendon reflexes in both lower extremities were normal. Magnetic resonance images demonstrated a 1.0 cm-sized intradural mass at the filum terminale. Gross total resection was performed via total laminectomy of L1 and L2. The tumor was confirmed to be clear cell ependymoma by histopathologic examination. His symptom was relieved after surgery.

**KEY WORDS :** Clear cell ependymoma · Cauda equina.

## INTRODUCTION

Clear cells are not uncommon in ependymomas, and resemble oligodendroglial cells with round cell bodies and nuclei with a perinuclear halo. Clear cell ependymomas are listed as a pathological entity in the World Health Organization's (WHO) classification of tumors of the central nervous system. Clear cell ependymoma is a subtype of ependymoma, as advocated by Kawano in 1989,<sup>10</sup> and was added to the WHO Classification of Tumors of the Central Nervous System revised in 1993. Clear cell ependymomas are usually encountered in the cerebral and cerebellar hemispheres, and rarely in the spinal cord<sup>1,11,13</sup>; intradural and extramedullary locations are also rare<sup>12</sup>.

Generally, magnetic resonance (MR) images visualize clear cell ependymomas as mildly hyperintense as compared with the normal spinal cord on T1-weighted images and as homogeneously hyperintense on T2-weighted images. In addition, tumors show uniform, marked enhancement<sup>2,9,17,20</sup>.

In the present case, light microscopy showed that the tumor cells possessed clear cytoplasm and round nuclei with a perinuclear halo. Immunohistochemical stainings for glial fibrillary acidic protein (GFAP) and vimentin were positive in

cytoplasm. A search of the English literature failed to unearth any previous report of cell ependymoma of the cauda equina.

## CASE REPORT

A 54-year-old man presented with intermittent lower back pain. A neurological examination revealed no reduction in sensation or motor function, and no bowel or bladder function difficulty. Lumbar MR imaging demonstrated a 1.0 cm-sized intradural mass at the L1-L2 level. The tumor had isosignal intensity on T1-weighted images and high signal intensity on T2-weighted images. In addition, it demonstrated homogeneous contrast enhancement and was well demarcated (Fig. 1).

Total laminectomy of L1 and L2 was performed. After opening the dura, a round, encapsulated mass was noted. The tumor was a pale pink, rubbery, well circumscribed, and attached to the cauda equina. Accordingly, the cauda equina was sectioned, and the tumor was totally excised. The resected tumor was soft and had a volume of approximately 1.0 mL. The tissue sections were stained with hematoxylin and eosin (H & E). Frozen smear findings revealed no evidence of clear cells and suggested a glial tumor. A light microscopic examination revealed that tumor cells had long glial processes, and microphotographs showed characteristic perivascular pseudorosettes, in which tumor cells were arranged radially around blood vessels (Fig. 2A). A high magnification examination revealed that tumor cells had round nuclei with a perinuclear halo; a characteristic of oligodendroglia (Fig. 2B). Relatively, few mitotic figures and no evidence of anaplasia

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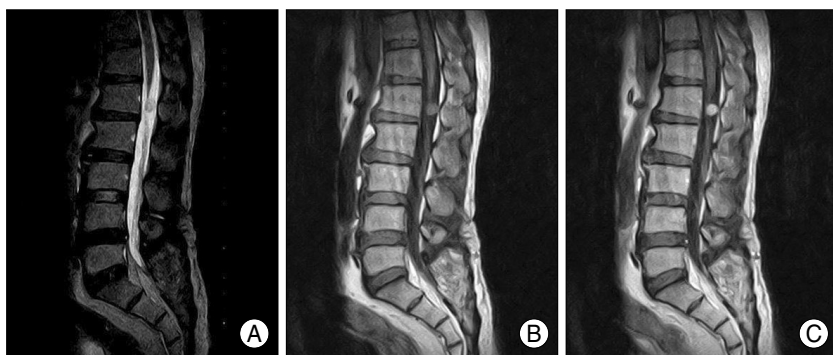
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• Address for reprints : Tae Wan Kim, M.D.

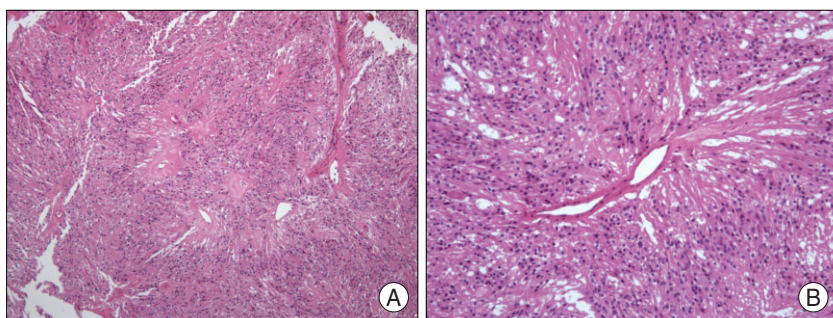
Department of Neurosurgery, Seoul Veterans Hospital, 27 Iljasan-gil, Gangdong-gu, Seoul 134-791, Korea

Tel : +82-2-2225-1363, Fax : +82-2-2225-1366

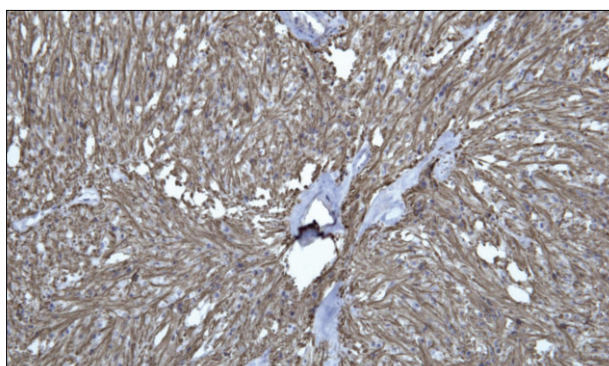
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**Fig. 1.** Preoperative magnetic resonance image shows a mass lesion. A high signal mass on a T2 sagittal image (A), an isosignal mass on a T1 weighted sagittal image (B) and a well enhanced round mass (C).



**Fig. 2.** Microscopic Photomicrograph. Perivascular pseudorosettes, in which tumor cells were arranged radially around blood vessels (H & E,  $\times 100$ ) (A), round nuclei with a perinuclear halo (an oligodendroglioma-like appearance; H & E,  $\times 200$ ) (B).



**Fig. 3.** Immunohistochemically, tumor cells were positive for glial fibrillary acidic protein (GFAP).

were observed. Immunohistochemically, tumor cells were positive for glial fibrillary acidic protein (GFAP) (Fig. 3) or vimentin, but negative for cytokeratin (AE1/AE3). Immunohistochemical staining revealed only rare tumor cell positivity for Ki-67, and equivocal positivity to negativity for S-100 protein. These results were compatible with the characteristics of clear cell ependymoma.

Neither radiotherapy nor chemotherapy was performed postoperatively. Cranial and whole spinal MR image examinations revealed no other tumors. The patient demonstrated a favorable outcome, and there was no evidence of recurrence during a 6-month follow-up (Fig. 4).

## DISCUSSION

Ependymoma arises from the ependymal cells which line the ventricles and central canal of the spinal cord. About 40 percent of spinal canal ependymomas arise within the cauda equina, and most occur in its proximal intradural region. Cauda equina ependymoma has been classified as an intramedullary lesion due to the neuroectodermal origin of the cauda equina. However, it should also be considered an extramedullary tumor from an anatomic and surgical perspective.

The new classification of tumors of the nervous system issued by the WHO (1999) characterizes ependymal tumors as : 1, four subtypes of ependymomas (cellular, papillary, clear cell, and tanyctic); 2, anaplastic ependymoma; 3, myxopapillary ependymoma; or 4, subependymoma. Clear cell ependymomas are predominantly composed of clear cells and usually develop in the

brain. Clear cell ependymoma of the spinal cord has been reported on several occasions,<sup>1,11,18</sup> but no report has been previously issued on clear cell ependymoma of the cauda equina, although Robles et al.<sup>18</sup> reported malignant transformation of intradural extramedullary ependymoma. However, all ependymomas pursued a benign course.

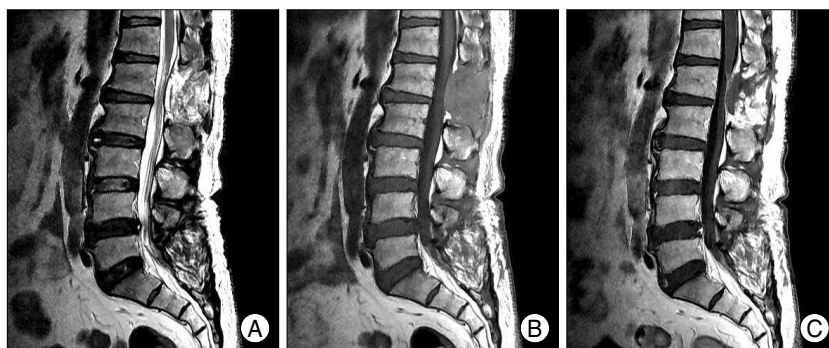
Ependymomas show mildly hyperintensity versus the normal cord on T1-weighted images and homogeneously hyperintensity on T2-weighted images, homogenous and heterogenous contrast enhancement,<sup>17,20</sup> and sharply defined rostral and caudal margins<sup>7</sup>. In clear cell ependymoma, this enhancement pattern is uniform and homogenous<sup>2</sup>. The early recognition of clear cell ependymoma is critical for optimal management, and an MR image examination should be performed as soon as possible to check for a tumor of the cauda equina<sup>19</sup>.

Our microscopic examination of the excised tumor showed characteristic perivascular pseudorosettes, in which tumor cells are arranged radially around blood vessels. High magnification revealed tumor cells with an oligodendroglioma-like appearance, that is, round nuclei with a perinuclear clear halo. The diagnostic electron microscopic hallmarks of clear cell ependymoma are intercellular junctions, surface microvilli, and cilia, and microrosette formation<sup>13,16</sup>. Its differential diagnosis includes central neurocytoma and glioneurocytoma in

addition to oligodendroglioma<sup>16</sup>). Immunohistochemical staining for glial fibrillary acidic protein (GFAP) is positive for tumor cells, which confirms a glial origin. Immunohistochemical stain is also positive for epithelial membrane antigen (EMA) and vimentin, but negative for cytokeratin (AE1/AE3) and synaptophysin<sup>15</sup>). Some authors have reported that clear cell ependymoma tumor cells are positive for S-100, GFAP, and vimentin, but negative for synaptophysin and EMA. The Ki-67 labeling index of tumor cells has been previously reported to be 1%<sup>11</sup>). It is important to realize cytokeratin AE1/AE3 stains glial tumors strongly, and that occasionally it also strongly stains mesenchymal neoplasms that express GFAP (such as schwannomas). In our case, immunostaining was equivocal to negative for S-100 protein, which is compatible with a diagnosis of clear cell ependymoma. S-100 is normally present in cells derived from the neural crest (Schwann cells, melanocytes, and glial cells), chondrocytes, adipocytes, myoepithelial cells, macrophages, Langerhans cells, dendritic cells, and keratinocytes, and it may also be present in some breast epithelial cells. Furthermore, several members of the S-100 protein family are useful markers of epidermal differentiation and certain tumors, for example, S-100 is expressed in melanomas, in 50% of malignant peripheral nerve sheath tumors, and in clear cell sarcomas. In our case, tumor cells were positive for GFAP and vimentin, but negative for EMA, synaptophysin, and S-100 protein, and their Ki-67 labeling index was less than 1%. Furthermore, the presences of a macroscopic cleavage plane, true ependymal rosettes, perivascular pseudorosettes, perinuclear lucency, and GFAP positivity are essential for the diagnosis of clear cell ependymoma<sup>10,11,13</sup>).

Min et al.<sup>16</sup> reported that the biologic behaviors of clear cell ependymomas and other ependymomas are similar, and that a proliferative index must be used to determine malignancy. In our case, Ki-67 was expressed only rarely at low levels in tumor cells, which suggested that the tumor was benign.

Microsurgery is the treatment of choice for ependymoma of the cauda equina. Radical excision using microsurgical techniques enables curative surgery to be undertaken, and this should be the goal of initial surgery<sup>6,8,15</sup>). Furthermore, the extent of tumor resection is the most important prognostic factor of long-term survival in patients with a nonmalignant form of ependymoma, regardless of location. Thus, gross total resection (GTR) is optimal. The surgical results of cauda equina tumors depend on both histologic findings and



**Fig. 4.** Magnetic resonance images taken at 6 months postoperatively revealing no evidence of recurrence. A : T2-weighted image. B : T1-weighted image. C : After enhancement.

tumor size, because large lesions are generally more difficult to remove without causing further neurological damage. Currently, adjuvant therapy is not used after the complete surgical resection of spinal ependymoma<sup>7</sup>). Radiation is used in patients with a residual tumor postoperatively and in those that experience early recurrence, after considering medical condition and neurological status,<sup>14</sup> and can achieve excellent local control and survival. However, radiotherapy of the neuroaxis is reserved when dissemination has been diagnosed before surgery or as a rescue therapy after conventional radiotherapy in cases of late spreading. Chemotherapy has also been recommended<sup>14,5</sup>) in those with a recurrent or intradural extramedullary ependymoma and in those refractory to surgical treatment.

Some authors have reported late recurrence at more than 40 years postoperatively despite radical total resection and postoperative radiotherapy<sup>3</sup>). Accordingly, long-term follow-up is also recommended.

## CONCLUSION

The authors report a rare case of clear cell ependymoma that developed at the cauda equina. Although clear cell ependymoma of the cauda equina is extremely rare, the possibility of occurrence should be considered. A histological diagnosis is crucial when considering postoperative adjuvant therapy for ependymoma of the cauda equina, and long-term follow up is recommended.

## References

1. Akutsu H, Shibata Y, Okazaki M, Hyodo A, Matsumura A : Intramedullary clear cell ependymoma in the cervical spinal cord : case report. *Neurosurgery* 47 : 1434-1437; discussion 1437-1438, 2000
2. Bapuraj JR, Parmar HA, Blaivas M, Muraszko KM : Imaging features of clear-cell ependymoma of the spinal cord. *Pediatr Radiol* 37 : 384-387, 2007
3. Celli P, Cervoni L, Salvati M, Cantore G : Recurrence from filum terminale ependymoma 42 years after 'total' removal and radiotherapy. *J Neurooncol* 34 : 153-156, 1997
4. Chamberlain MC : Etoposide for recurrent spinal cord ependymoma.



- Neurology** 58 : 1310-1311, 2002
5. Chamberlain MC : Salvage chemotherapy for recurrent spinal cord ependymoma. **Cancer** 95 : 997-1002, 2002
  6. Cooper PR : Outcome after operative treatment of intramedullary spinal cord tumors in adults : intermediate and long-term results in 51 patients. **Neurosurgery** 25 : 855-859, 1989
  7. Epstein FJ, Farmer JP, Freed D : Adult intramedullary spinal cord ependymomas : the result of surgery in 38 patients. **J Neurosurg** 79 : 204-209, 1993
  8. Fearnside MR, Adams CB : Tumors of the cauda equina. **J Neurol Neurosurg Psychiatry** 41 : 24-31, 1978
  9. Fine MJ, Kricheff II, Freed D, Epstein FJ : Spinal cord ependymomas : MR imaging features. **Radiology** 197 : 655-658, 1995
  10. Kawano N, Yada K, Aihara M, Yagishita S : Oligodendroglioma-like cells (clear cells) in ependymoma. **Acta Neuropathol** 62 : 141-144, 1983
  11. Kim NR, Chung DH, Lee SK, Ha SY : Intramedullary clear cell ependymoma in the thoracic spinal cord : a case with its crush smear and ultrastructural findings. **J Korean Med Sci** 22 : S149-S153, 2007
  12. Kim SY, Kim SW : Primary intramedullary extramedullary myxopapillary ependymoma. **J Korean Neurosurg Soc** 39 : 382-384, 2006
  13. Kim YJ, Tsunoda S, Yokoyama K, Miyamoto K, Tamai M, Yamauchi M : Clear cell ependymoma with a lipidized component that developed in the thoracic spinal cord. **Neurol Res** 25 : 324-328, 2003
  14. Lin YH, Huang CI, Wong TT, Chen MH, Shiau CY, Wang LW, et al. : Treatment of spinal cord ependymomas by surgery with or without postoperative radiotherapy. **J Neurooncol** 71 : 205-210, 2005
  15. Meneses MS, Leal AG, Periotto LB, Milano JB, Coelho-Net M, Sobral AC, et al. : Primary filum terminale ependymoma : a series of 16 cases. **Arq Neuropsiquiatr** 66 : 529-533, 2008
  16. Min KW, Scheithauer BW : Clear cell ependymoma : a mimic of oligodendroglioma : clinicopathologic and ultrastructural considerations. **Am J Surg Pathol** 21 : 820-826, 1997
  17. Miyazawa N, Hida K, Iwasaki Y, Koyanagi I, Abe H : MRI at 1.5 T of intramedullary ependymoma and classification of pattern of contrast enhancement. **Neuroradiology** 42 : 828-832, 2000
  18. Robles SG, Saldaña C, Boto GR, Martinez A, Zamarron AP, Jorquera M, et al. : Intradural extramedullary spinal ependymoma : a benign pathology? **Spine (Phila Pa 1976)** 30 : E251-E254, 2005
  19. Shimada Y, Miyakoshi N, Kasukawa Y, Hongo M, Ando S, Itoi E : Clinical features of cauda equina tumors requiring surgical treatment. **Tohoku J Exp Med** 209 : 1-6, 2006
  20. Sun B, Wang C, Wang J, Liu A : MRI features of intramedullary spinal cord ependymomas. **J Neuroimaging** 13 : 346-351, 2003