

# A case of recurring spinal ependymoma in 37-years old man after surgery and adjuvant therapy

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## SUMMARY

We present the case of a 39-years old man who underwent three surgeries because of spinal ependymoma located in cauda equina region. He presented at the Oncology Institute of Vojvodina for combined adjuvant chemo- and radiotherapy after the second surgery. An MRI examination performed after six cycles of therapy showed no signs of disease. 26 months later, a follow-up MRI showed recurrence of disease in the form of small drop metastasis. Six months later, the patient underwent the third surgery. The patient is currently receiving another cycle of radiotherapy, and is scheduled for additional cycles of chemotherapy.

Ependymomas are the most common spinal cord malignancy in adults. The symptoms are nonspecific which often causes a delay in diagnosis. An MRI examination of the spine with contrast admission is the study of choice for detecting spinal cord masses. Surgery is the first-line therapy for ependymomas. Recurrence rate is associated with the extent of surgical resection, with *en bloc* and gross-total resection being associated with lower rates of disease recurrence. In children under 3 years, adjuvant chemotherapy is advocated, while older children and adults undergo adjuvant radiotherapy or combined chemo- and radiotherapy in cases of subtotal resection or tumor recurrence.

**KEY WORDS:** ependymoma, adult, spinal, surgery, recurrence, radiotherapy

## INTRODUCTION

Ependymomas are glial tumors that belong to a group of ependymal tumors. There are three histopathological phenotypes, which are classified as ependymoma variants: papillary ependymoma, clear cell ependymoma, and tanycytic ependymoma. Ependymomas are rare, representing between 3 and 9% of all neuroepithelial tumors. They can develop in patients of any age but are more common in children and young adults. In children aged 3 years or less, approximately 30% of all CNS tumors are ependymomas. Ependymomas can arise anywhere in the CNS, as well as at extra-CNS sites, which is extremely rare. In children, they predominantly occur intracranially, as infratentorial ependymomas. In adults (30-40 years of age) spine is the most prevalent location; ependymomas are the most common intramedullary neoplasm in adults. There is no evident gender predilection. According to WHO classification, classic ependymomas are grade II. There is no clear association between grade and biological behavior or survival (1-3).

Ependymomas are slow-growing expanding tumors, they tend to displace adjacent structures rather than infiltrate them. The clinical manifestations depend on tumor localization. Ependymomas of posterior fossa can present with headache, nausea, vomiting, and dizziness. Hydrocephalus is seen in two-thirds of cases of posterior fossa involvement. Cranial nerve deficits, visual disturbances, paresis, and ataxia can occur if cerebellum and brain stem are involved. Supratentorial ependymomas can cause epilepsy and focal neurological deficits (4,5).

Spinal cord tumors can arise in the cervical, thoracic and lumbosacral segment. Spinal ependymomas are usually associated with a history of nonspecific neurologic deficit related to the involvement of afferent or efferent nerve tracts, exiting peripheral nerves and pain correlated to the level of the lesion.

Ependymomas in lumbosacral spine usually present with chronic low back pain, sciatica and lower limb weakness, as well as sensory

dysfunction related to bowel and urinary impairments, progressing over years prior to diagnosis, although rare instances of intratumoral hemorrhage can provoke acute deterioration (4,6).

Due to the nonspecific clinical presentation, especially at the early stage, lower spine ependymomas present a difficult challenge in terms of clinical suspicion and detection. Chronic lower back pain is often considered to be of a self-limiting and non-life-threatening cause; therefore, symptomatic treatment is usually continued, and the underlying cause can be masked and easily mismanaged. Consecutively, the right diagnosis is delayed, which leads to the development of further neurological deficits, increased risk of complications related to surgery, and overall worse morbidity and prognosis.

MRI is the study of choice for cranial and spinal ependymoma, since it allows evaluation of brain and spinal cord for masses and associated findings such as edema, hemorrhage, cyst, hydrocephalus, syringomyelia and atrophy. Spinal ependymoma usually presents with enlarged spinal cord, since they arise from ependymal cells of the central canal, they are usually located in the central portion of spinal cord expanding it symmetrically. They are well-circumscribed, although they don't have a capsule. Cysts are often seen, which can be either tumoral (seen in about 22% of cases) or non-tumoral (present in about 62%). Syringomyelia is seen in 10-50% of cases. Calcification is rare, in contrast to cranial ependymomas. Ependymomas are isointense to hypointense on T1 weighted images, with mixed signal if cysts, hemorrhage and necrosis are present. On T2 weighted images, they are hyperintense, with perifocal edema in about 60% of cases. "Cap sign", a hypointense rim of haemosiderin deposition on T2 weighted images associated with hemorrhage, is seen in about 20-33% of cases. There is a strong enhancement on T1 weighted images obtained after intravenous gadolinium contrast injection (3,7).

For spinal ependymomas, surgery is considered as the first-line treatment with a goal of achieving complete tumor resection. The extent of resection is defined as *en bloc* if all of visible tumor was removed

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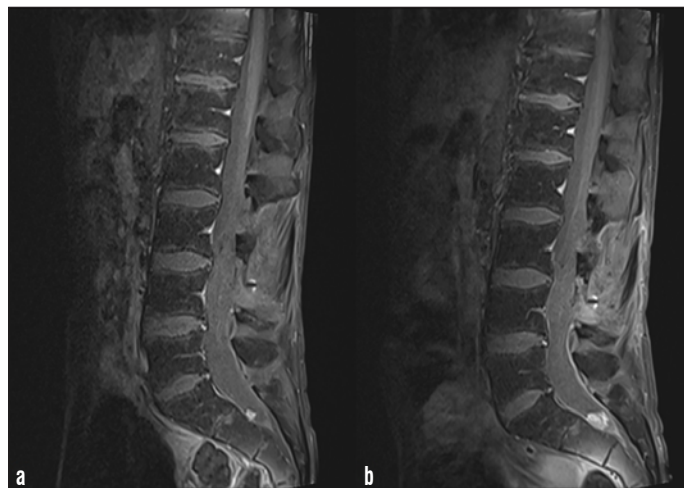
**Figure 1.** A sagittal T1-weighted image (a), a sagittal T2-weighted image (b), and an axial T2-weighted image (c) of the lumbar spine, showing a cylindrical tumoral mass posterior to L3 and L4 vertebral bodies compressing the cauda equina roots against the lateral walls of the spinal canal (September 2015), as well as the abnormal signal intensity of CSF distally, most likely due to high protein content and/or small hemorrhagic events.



**Figure 2.** Sagittal T2-weighted images of the lumbar spine. Follow-up after the first surgery, April 2016 (a), showing an unclear 3 mm formation in the area of the previously present tumor. MRI scan from December 2016 (b) proved the previously seen structure to be a residual tumor. Three additional independent smaller lesions were also described (not shown).



**Figure 3.** A sagittal T2-weighted image (a) and a sagittal T1-weighted image with fat signal saturation of lumbar spine (b) immediately after the conclusion of combined adjuvant chemo- and radiotherapy (July 2017), showing no signs of the disease.



**Figure 4.** Sagittal T1-weighted images with gadolinium contrast of lumbar spine. An MRI follow-up study showing an enlarging contrast enhancing mass (arrows), likely a drop metastasis, posterior to the S2 vertebral body in September 2019 (a) and January 2020 (b); 26 and 30 months after the conclusion of combined adjuvant therapy, respectively.

without violation of its margins, gross-total resection (GTR) if all of the visible tumor is removed, but with tumor violation, and subtotal resection (STR) if a known residual was left at the time of surgery. The GTR rate for spinal ependymoma is high since they expand rather than infiltrate adjacent structures. Postoperative MRI examination should be reviewed to confirm the extent of resection, and resected mass should be sent on pathohistological analysis to evaluate the tumor margins integrity and confirm the diagnosis of ependymoma, its variants or other ependymal neoplasms, although no clear association between grade and biological behavioral or survival has been confirmed. Intraoperative tumoral margin violation is shown to be associated with a higher recurrence rate (1,8,9). Adjuvant treatment of histologically confirmed ependymoma remains an unsettled debate. For children younger than 3 years with intracranial ependymoma, chemotherapy is advocated, while radiotherapy is avoided because of its adverse effects. Combined chemotherapy

includes cisplatin, etoposide, carboplatin (VP-16), vincristine and mechlorethamine, or ifosfamide, carboplatin and etoposide (ICE), but with variable success. In older children and adults, radiotherapy is the standard treatment following resection for most patients with WHO grade II intracranial ependymoma. After subtotal resection with the postoperative residual tumor or early recurrence, radiation is considered based on the individual patient's condition. Typically, fractionated external beam therapy to a dose of 54 Gy is used, which has been shown to improve local tumor control. Progression-free survival (PFS) was significantly prolonged among those who received adjuvant radiotherapy after STR. The use of chemotherapy after both surgery and radiotherapy fail had shown mixed and inconclusive results (6,9-13). Progression-free survival in patients with spinal cord ependymoma is associated with the extent of resection, as multiple studies have shown. Patients with WHO grade II ependymoma in whom GTR is

achieved have a significantly lower recurrence rate compared to patients with STR (6,12).

Neurologic deficits after surgery are common, despite the efforts to preserve neural tissue. Studies have shown that the risk of postoperative neurologic symptoms is best predicted by the patient's preoperative neurologic function. Patients with a good neurologic score prior to surgery are less likely to develop symptoms after surgery for spinal ependymoma (14).

## CASE REPORT

A 39-years old man presented to the Oncology Committee of Oncology Institute of Vojvodina for combined adjuvant chemo- and radiotherapy, after two surgeries for a spinal canal mass at the level of the third and fourth lumbar vertebra. The first symptoms started in April 2015 as a nonspecific dull lower back pain, which later extended to gluteal and thigh regions. Symptomatic therapy helped in the beginning, but after symptoms had worsened, the patient underwent an MRI scan of the lumbar spine in September 2015. The scan showed an intradural neoplasm at the level of L3 and L4 vertebral bodies, which compressed the cauda equina roots against the lateral walls of the spinal canal. MRI characteristics and central position of the mass implied that the neoplasm was most probably an ependymoma originating from terminal filum (Figure 1a, 1b and 1c). The patient underwent surgery two weeks later, and the tumor was histologically identified as cellular ependymoma, a variant that is currently considered to significantly overlap with classic ependymoma and is therefore removed from the newest WHO classification of CNS tumors. The surgery went well, pain and other symptoms subsided and no adjuvant therapy was deemed necessary at the time. Follow-up MRI scan in April 2016 showed an unclear 3 mm formation in the area of the previously resected tumor, which on the MRI scan from December 2016 was proved to be a residual tumor (Figure 2a and 2b). In addition, three more new independent smaller lesions were described in proximity to the previous one. The patient underwent the second surgery in February 2017. The second surgery was described as a reduction of tumor, presumably subtotal resection (STR), since the part of the tumoral mass was found to adhere to the nerves supplying the pelvic floor sphincters, and total surgical resection could not be achieved. Combined adjuvant therapy was advocated. There was no follow-up MRI examination after the second surgery. The patient suffered from postoperative urine retention due to bladder dysfunction that lasted for almost a year before the condition started to gradually improve with treatment and rehabilitation. The patient underwent six cycles of conformal teloradiotherapy combined with simultaneous chemotherapy (vincristine) from March to May 2017. Follow-up MRI examination of endocranium and whole spine after completion of the combined therapy showed no signs of tumor residue nor recurrence. Seven more follow-up MRI examinations of head and spine in three to four-month intervals were done, with no signs of the disease (Figure 3a and 3b). On the ninth MRI examination, in September 2019, 26 months after the first MRI follow-up, a small nodular intradural mass measuring 9 mm in diameter was seen posterior to the S2 vertebral body and reported as a drop metastasis of the ependymoma (Figure 4a). Four months later, in January 2020, an

MRI scan showed enlargement of the aforementioned intradural mass, measuring 16 mm in diameter (Figure 4b). The patient underwent the third surgery in March 2020. Reportedly total surgical resection was achieved with no visible residual. The patient reported no recurrence of symptoms. Follow-up MRI scan showed no signs of the disease.

At the time of reporting the case, the patient is undergoing another cycle of radiotherapy and is scheduled for additional chemotherapy.

## CONCLUSION

Spinal ependymomas are rare but they are still the most common spinal cord malignancy in adults. Nonspecific chronic back pain should not be taken lightly by general practitioners and specialists, and potential cause should be sought for. The MRI examination of the spine is a study of choice since it can usually give a precise diagnosis and lead to the right therapeutic approach. *En bloc* or gross-total resection of an ependymoma should be aimed for, since these two are associated with lower recurrence rate than subtotal resection. In the case of STR or in case of tumor recurrence, adjuvant radiotherapy is advocated. There are only a few studies available about the use of adjuvant chemotherapy in patients with spinal ependymomas, with a small number of participants and they give inconclusive and mixed results.

## Declaration of interests

Authors declare no conflicts of interest.

## REFERENCES

- Louis DN, Ohgaki H, Wiestler OD, Cavenee WK, Ellison DW, Figarella-Branger D, Perry A, Reifenberger G, von Deimling A, editors. WHO Classification of Tumours of the Central Nervous System. Revised 4th ed. Lyon (France): IARC Press; 2016.
- Abdelzaher E. Ependymoma [Internet]. Bingham Farms (MI): PathologyOutlines; 2012 Aug 1 [revised 2019 Nov 22; cited 2020 Feb 6]. Available from: <https://www.pathologyoutlines.com/topic/cnstumorependymoma.html>
- Dahner W. Radiology review manual. 6th edition. Philadelphia: Lippincott Williams Wilkins; 2007.
- Wu J, Armstrong TS, Gilbert MR. Biology and management of ependymomas. *Neuro Oncol* 2016;18:902–13.
- Warren K. Ependymomas [Internet]. Germantown (MD): The Childhood Brain Tumour Foundation. [cited 2020 Feb 6]. Available from: <https://www.childhoodbraintumor.org/medical-information/braintumor-types-and-imaging/item/84-ependymomas>.
- Celano E, Salehani A, Malcolm JG, Reinertsen E, Hadjipanayis C. Spinal cord ependymoma: a review of the literature and case series of ten patients. *J Neurooncol*. 2016 July;128(3):377–386.
- Koeller KK, Rosenblum RS, Morrison AL. Neoplasms of the Spinal Cord and Filum Terminale: Radiologic-Pathologic Correlation. *RadioGraphics*. 2000;20(6):1721–49.
- Wild F, Hartmann C, Heissler HE, Hong B, Krauss JK, Nakamura M. Surgical Treatment of Spinal Ependymomas: Experience in 49 Patients. *World Neurosurg*. 2018;111.

- 9 Abdulaziz M, Mallory GW, Bydon M, Ramos RDLG, Ellis JA, Laack NN, et al. Outcomes following myxopapillary ependymoma resection: the importance of capsule integrity. *Neurosurg Focus*. 2015;39(2).
- 10 Rogers L, Pueschel J, Spetzler R, Shapiro W, Coons S, Thomas T, et al. Is gross-total resection sufficient treatment for posterior fossa ependymomas? *J Neurosurg*. 2005;102(4):629-36.
- 11 Reni M, Gatta G, Mazza E, Vecht C. Ependymoma. *Crit Rev Oncol Hematol*. 2007;63(1):81-9.
- 12 Oh MC, Tarapore PE, Kim JM, Sun MZ, Safaee M, Kaur G, et al. Spinal ependymomas: benefits of extent of resection for different histological grades. *J Clin Neurosci*. 2013;20(10):1390-1397.
- 13 Oh MC, Ivan ME, Sun MZ, Kaur G, Safaee M, Kim JM, et al. Adjuvant radiotherapy delays recurrence following subtotal resection of spinal cord ependymomas. *Neuro Oncol*. 2013;15:208-215.
- 14 Nagasawa DT, Smith ZA, Cremer N, Fong C, Lu DC, Yang I. Complications associated with the treatment for spinal ependymomas. *Neurosurg Focus*. 2011;31:E13.