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Case Report

Unusual location of myxopapillary ependymoma in the sacrum: Case report and review of the literature ☆

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ABSTRACT

Myxopapillary ependymoma, a rare variant of ependymoma, commonly occurs in the conus medullaris or filum terminale. The rarity of these tumors can make their diagnosis and treatment challenging. This case report presents an atypical occurrence of myxopapillary ependymoma within the sacrum in a 68-year-old patient presented with a 3-month history of persistent left-sided low back pain radiating to the legs and fecal dysfunction. The patient underwent a sacral laminectomy and subtotal excision of the tumor, followed by adjuvant radiotherapy with favorable outcomes.

This report highlights the significance of tailored approaches for unconventional tumor locations emphasizes the potential benefits of multimodal treatment strategies and provides insights from a comprehensive literature review on similar cases.

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Introduction

Myxopapillary ependymoma represents approximately 13% of spinal ependymomas, commonly occurs in the conus medullaris or filum terminale [1], but can also manifest in the sacral region, although this is less common [2].

While the exact etiology is not well-established, researchers have identified certain risk factors that may be associated with an increased likelihood of developing ependymoma such as radiation exposure, genetic syndromes like neurofibromatosis type 2 (NF2) and Hippel-Lindau syndrome (VHL) [3].

As for lifestyle factors like nutrition, overweight, and tobacco use, there is limited research linking them directly to the formation of ependymomas.

Intracranial ependymomas are more commonly observed in childhood with the peak incidence occurring in the first decade of life, while spinal ependymomas are more frequently seen from adolescence through adulthood. The median duration of symptoms prior to presentation is 2-4 years.

Symptoms of myxopapillary ependymomas often result from compression of the nerve roots in the cauda equina region. Common symptoms may include lower back pain, sciatica, radicular or cauda equina syndrome, and bowel or bladder dysfunction [4].

Because of the propensity of these tumors for seeding the craniospinal axis, cerebrospinal fluid (CSF) evaluation and craniospinal magnetic resonance imaging (MRI) are strongly recommended for patients diagnosed with ependymoma.

According to the 2021 WHO Classification of Tumors of the Central Nervous System update, by combining histopathological and molecular features, ependymomas can be more accurately categorized into distinct molecular subgroups within their anatomic locations [5]. The identification of these molecular subgroups has been crucial in understanding the heterogeneity of the disease and may lead to more personalized and targeted therapies in the future. In contrast to previous editions of WHO classifications, the myxopapillary ependymoma has been reclassified as WHO grade 2, reflecting its potential for more aggressive behavior compared to other grade 1 tumors.

Because of their slow growth and limited metastatic potential, sacral ependymomas have a better prognosis compared to more aggressive types of cancer. However, their location within the sacrum can still pose significant treatment challenges. Treatment typically involves surgical removal of the tumor when possible. The success of surgical intervention depends on the tumor's size, location, and the involvement of critical structures. In some cases, additional treatments such as radiation therapy or chemotherapy may be recommended.

Hence, in this paper, we report the excellent outcome of adjuvant radiotherapy for an uncommon location of the myxopapillary ependymoma in the sacrum after an incomplete tumor removal with a review of literature.

Case report

A 68-year-old male patient with no significant medical history presented with a 3-month history of persistent lower back pain, radiating to the legs and fecal dysfunction. The patient did not report any bladder or sexual dysfunction.

The neurological examination revealed the absence of muscle weakness and sensory disturbances. Babinski reflex was present bilaterally and the Hoffmann test was negative. Sphincter control was preserved.

Magnetic resonance imaging (MRI) of the spine revealed an endocanal heterogeneous expansile mass in the terminal lumbosacral region, which was further characterized through contrast-enhanced imaging. The tumor was associated with areas of bone destruction and locoregional infiltration. It exhibited characteristics consistent with myxopapillary ependymoma, including a cystic component with papillary projections (Fig. 1).

Given the patient's symptoms and the radiological findings, surgical excision of the tumor was deemed necessary. Because of the tumor's location and its proximity to critical neural structures, a sacral laminectomy and subtotal excision of the tumor were performed. Intraoperative neurophysiological monitoring was employed to minimize the risk of neurological damage.

The surgery was a complete success with no intraoperative or immediate postoperative complications, and there were no new neurological deficits observed.

The excised tumor tissue underwent rigorous histopathological assessment. The microscopic examination revealed papillary formations. Epithelioid to cuboidal cells were arranged around blood vessels with perivascular myxoid change (Fig. 2). Immunohistochemical study revealed diffuse positive staining for GFAP and S100 protein (Fig. 3). The lesion was immunonegative for CK7, CK20, RCC, CD10, and TTF1. Ki67 labeling index was 30%. The diagnosis of myxopapillary ependymoma, WHO grade 2, was made.

Postoperative imaging indicated that a portion of the tumor was not successfully removed, likely due to its challenging location and potential risk to neurological structures, and the patient was subsequently referred for adjuvant radiotherapy. A personalized treatment plan was developed, targeting the remaining tumor cells while sparing the adjacent healthy tissues (Fig. 4).

The treatment was delivered using a 6 MV photon beam generated by the Truebeam linear accelerator (Varian, CA) utilizing VMAT (volumetric modulated arc therapy) technique with daily imaging guidance (IGRT) using cone-beam computed tomography (CBCT). The total prescribed dose was 59.4 Gy, administered over the course of the treatment. The radiotherapy sessions were scheduled 5 days per week, with a daily dose per fraction of 1.8 Gy.

The gross tumor volume (GTV) encompassed the tumor size visible on CT scans along with the initial tumor volume based on the preoperative MRI. The clinical target volume (CTV) was defined by adding a uniform 0.5 cm margin to the GTV, and subsequently, the planning target volume (PTV) was established by extending the CTV with an additional 0.5 cm margin.

Throughout the course of radiotherapy, the patient's progress was closely monitored. The acute side effect observed was grade 1 radiation dermatitis based on RTOG and common terminology criteria for adverse-events version 5 in the gluteal fold. This was managed using emollients and a

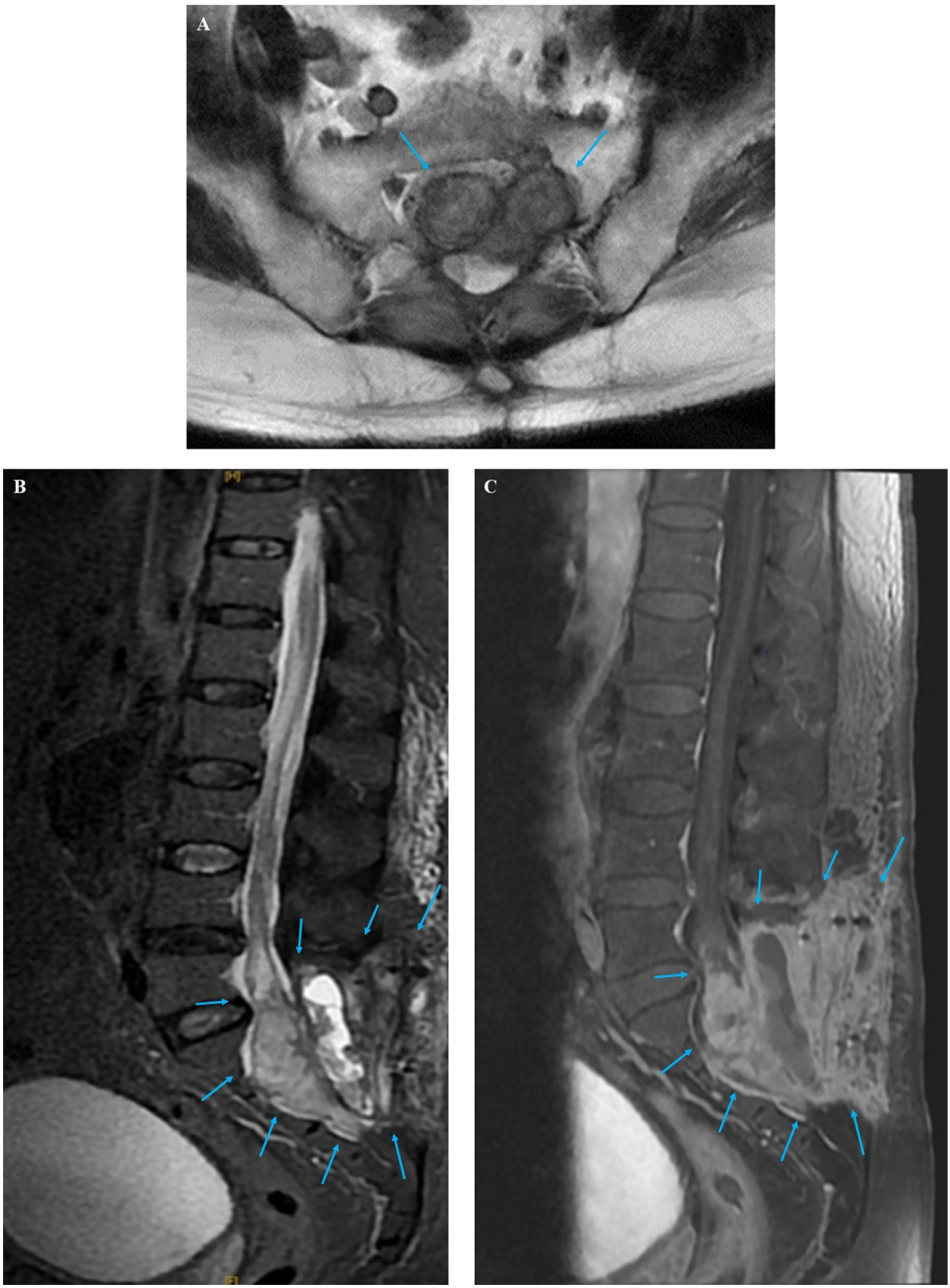

Fig. 1 – Magnetic Resonance Images showing a heterogeneous expansile endocanal mass in the terminal lumbosacral region with hyperintense cystic component and isointense patches on axial T2-weighted sequence (A), sagittal T2-STIR sequence (B) and intense heterogeneous enhancement on sagittal postcontrast T1-weighted image (C) [blue arrows], associated to areas of bone destruction and locoregional infiltration.

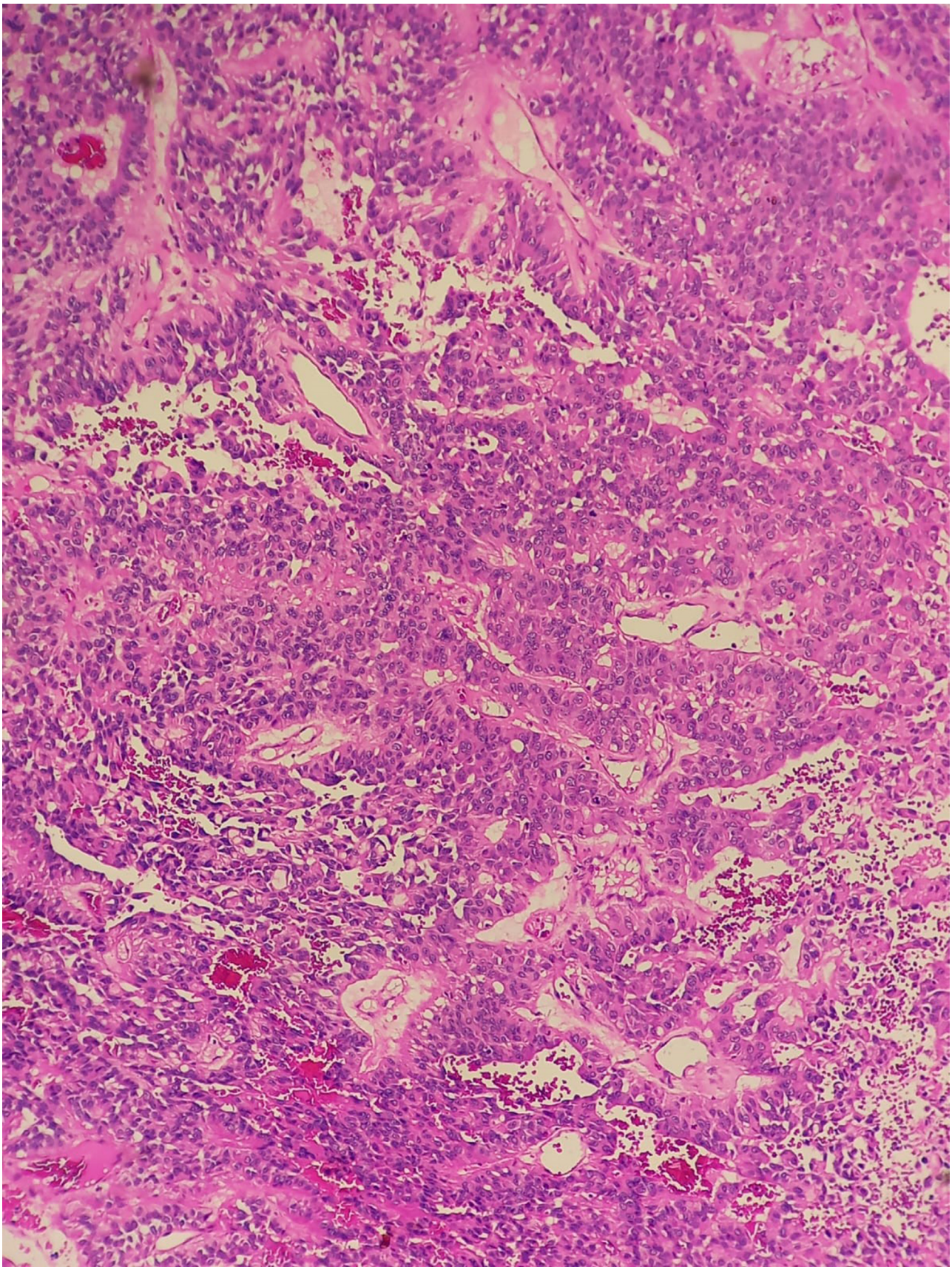

Fig. 2 – Representative micrograph of the tumor. There are papillary formations. Cuboidal to epithelioid tumor cells are arranged around hyalinized fibrovascular cores. Hematoxylin-eosin; 1 x 100, 2 x 200.

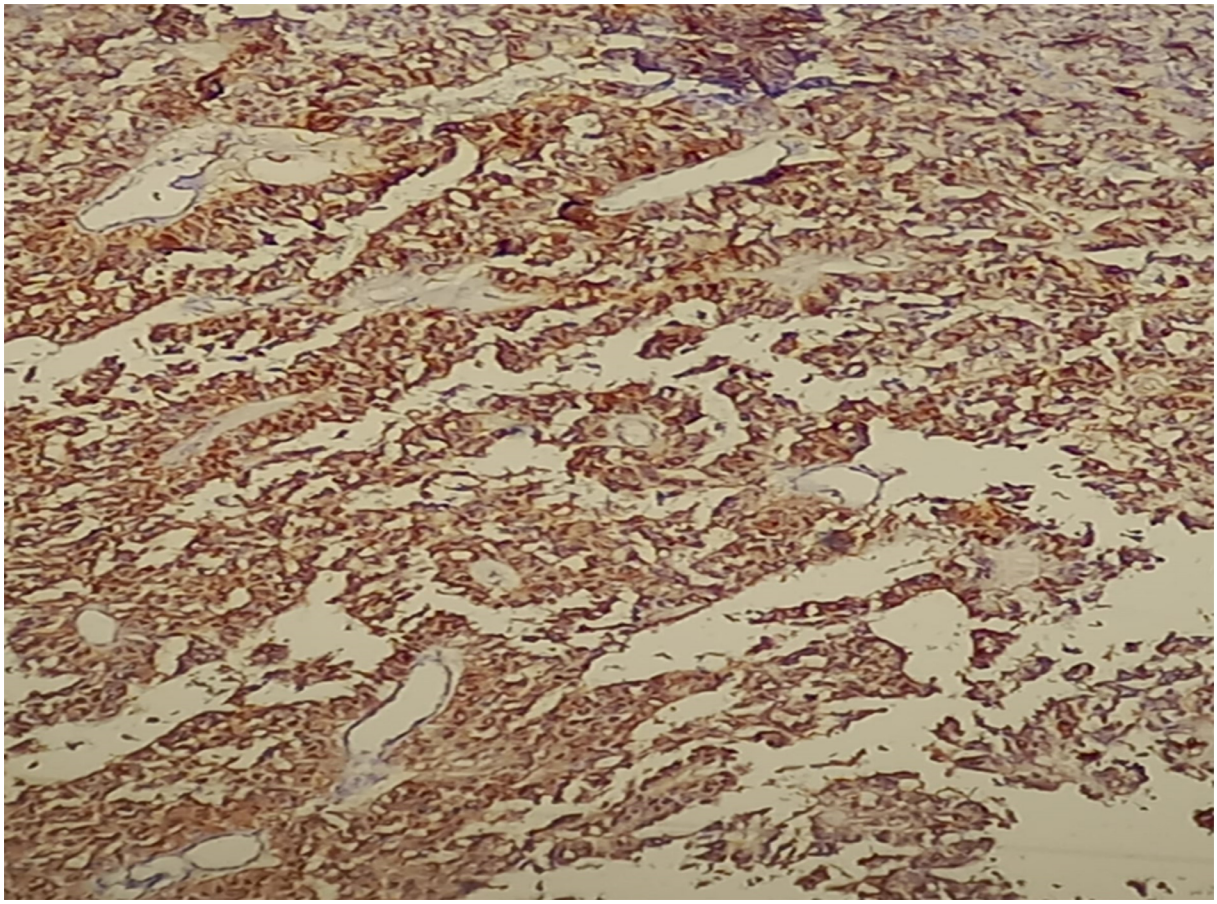

Fig. 3 – Immunohistochemical profile of the tumor: The tumor cells express S100 protein.

therapeutic cream, resulting in favorable recovery progress. The patient was educated about proper skincare practices to minimize the impact of radiation dermatitis. Following adjuvant radiotherapy, the patient's symptoms showed improvement.

During the follow-up period, the patient underwent regular clinical evaluations, radiological assessments such as MRI scans, and periodic neurological examination assessments aimed to evaluate the efficacy of the salvage radiotherapy and monitor any potential recurrence of the tumor or neurological deficits. The 18-month follow-up revealed a successful outcome. There were no clinical signs of residual tumor in the sacral region. Additionally, the patient did not exhibit any neurological deficits attributed to the treatment or the tumor.

Discussion

Ependymomas are considered one of the most common intramedullary spinal cord tumors in adults, but they are still relatively rare overall. The prevalence of ependymomas in the general population is quite low, with only about 2%-4% of all central nervous system tumors being ependymomas.

These tumors almost exclusively occur near the conus medullaris, cauda equina, and filum terminale of the spinal cord, but rarely affect the sacrum [6].

The rarity of these tumors can make their diagnosis and treatment challenging.

Due to their slow growth and nonspecific early symptoms, the diagnosis is often delayed with an average elapsed time of 2.3 years between symptom onset and diagnosis [7].

MRI is considered the gold standard for imaging spinal tumors, including myxopapillary ependymomas of the sacrum, as it provides more detailed and accurate images of soft tissues, such as the spinal cord and surrounding structures. On MRI, the lesion typically appears as a well-defined, lobulated, T1-isointense, and T2-hyperintense solid lesion within the spinal canal, with or without neural foraminal extension, osseous infiltration, or compression of the cauda equina nerve roots [8,9].

The main differential diagnoses for sacral ependymoma are astrocytomas, schwannomas, meningiomas, neurofibroma, and hemangioblastomas.

It's typically present as soft, vascular masses during gross examination. They are well-defined and often encapsulated

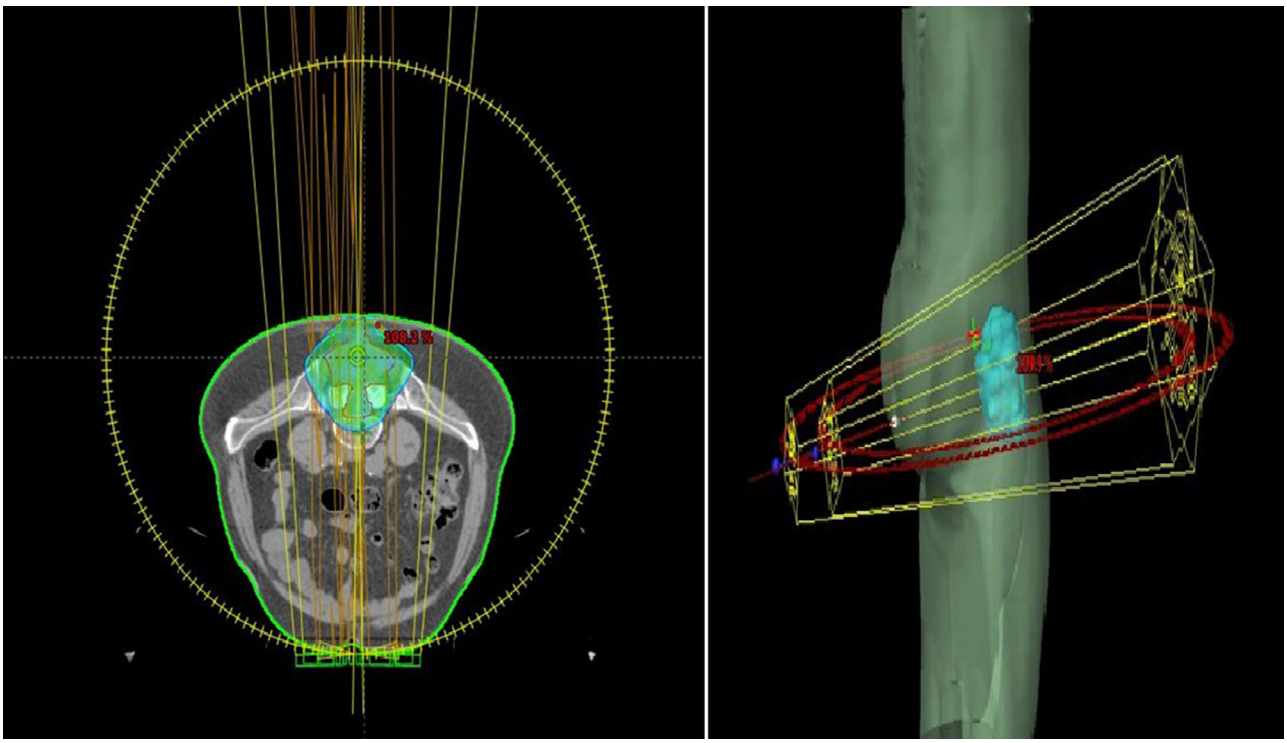

Fig. 4 – Graphical representation of treatment planning using VMAT radiotherapy.

and may show signs of hemorrhagic or mucinous degeneration. The tumors often have a lobular or sausage-like shape.

Histologically, myxopapillary ependymomas are characterized by 2 main features: papillary regions with vascular cores and extensive mucoid matrix. Immunohistochemically, the tumor cells usually exhibit positive staining for GFAP (glial fibrillary acidic protein) and S100 [10].

Myxopapillary ependymoma was first described as a distinct variant of ependymoma by Harvey Cushing and Louise Eisenhardt in 1929. In 1932, Percival Bailey and Harvey Cushing introduced a classification system for ependymal tumors, which later became known as the Bailey and Cushing classification. According to this classification, ependymal tumors were categorized into 4 types: subependymoma, myxopapillary ependymoma, ependymoma (cellular ependymoma), and ependymoblastoma.

Based on the 2021 WHO Classification of Tumors of the Central Nervous System update, ependymomas are now classified based on a combination of histopathological and molecular features, along with the anatomical site (supratentorial, posterior fossa, or spinal) [5]. Currently, supra tentoriel ependymomas are divided into different molecular groups based on their genetic features, including supratentorial ependymomas with ZFTA fusion (new designation for C11orf95) and those with YAP1 fusion.

Myxopapillary ependymoma, which was previously classified as a CNS WHO grade 1 tumor, is now considered a grade 2 tumor. This change is likely due to an improved understanding of its likelihood of recurrence, which is now recognized to be similar to conventional spinal ependymomas.

It's important to note that treatment decisions for sacral ependymoma should be made on an individual basis, taking into account the specific characteristics of the tumor, the patient's overall health, and other factors that may influence the treatment approach.

The treatment of choice is gross total resection [11]. Complete surgical removal of the myxopapillary ependymoma can often alleviate symptoms related to compression of the spinal cord or nerves and provide significant relief to the patient. However, the extent of resection depends on factors such as the tumor size, location, and involvement of nearby structures. For sacral ependymomas, specialized surgical techniques may be required to access the tumor safely and achieve complete resection. In some instances, the tumor may be inoperable due to its location or involvement of critical structures.

Radiotherapy is an essential component of the treatment for spinal ependymoma, especially when complete surgical resection is not feasible or when there is a risk of tumor recurrence. The primary goal of radiotherapy for spinal ependymoma is to target and destroy any remaining tumor cells, reduce the risk of tumor progression or recurrence, and improve local tumor control.

Typically, the dose given to the tumor bed is 49-56 Gy, whereas the craniospinal axis (if indicated) received 30-36 Gy. Low-grade lesions with a low risk of seeding are typically

treated with limited fields to 50.4-55.8 Gy in 1.8 Gy daily fractions.

In patients with tumors at high risk of seeding, when pretreatment CSF cytologic studies reveal malignant cells, or if the spinal MRI scan shows evidence of leptomeningeal disease, the craniospinal axis should be treated to 36 Gy in 1.5-1.8 Gy daily fractions [12]. Subsequently, the primary tumor site is boosted to a total dose of 50.4-55.8 Gy if the gross leptomeningeal spread is evident, the cranio-spinal axis dose should be 39.6 Gy (1.8 Gy/fractions) or 40.5 Gy (1.5 Gy/fraction), with the same boost dose to the primary tumor as previously discussed.

Ideally, physicians aim to begin postoperative RT within 5 weeks after surgery to maximize its effectiveness. However, in some cases, the recovery process after surgery may take longer, or complications may arise, leading to delays in initiating radiation [13].

In patients undergoing incomplete resection followed by EBRT, OS at 5, 10 and 15 years is 67%-100%, 67%-100%, and 75% respectively.

The role of chemotherapy in the treatment of spinal ependymoma is less well-defined compared to surgery and radiation therapy. Unlike some other types of tumors, ependymomas are generally considered to be less responsive to chemotherapy [14].

Due to the rarity of this disease and the lack of large-scale clinical trials, the evidence supporting the use of chemotherapy in these cases is limited. As a result, decisions regarding chemotherapy as salvage therapy for ependymoma are usually made on a case-by-case basis, considering the patient's overall health, tumor characteristics, and potential benefits versus risks.

In recent years, ongoing research and clinical trials may shed more light on the role of chemotherapy and other targeted therapies in the management of this rare tumor type.

Conclusion

The present case emphasizes the significance of early and accurate diagnosis, the challenges posed by rare tumor locations, and the importance of a multidisciplinary approach to achieve optimal patient outcomes. It contributes to the existing literature by expanding the knowledge base surrounding ependymoma occurrences and encouraging healthcare practitioners to remain vigilant in their diagnostic pursuits, especially when confronted with unexpected tumor locations.

The use of radiotherapy as a salvage approach highlights its effectiveness in managing unconventional tumor locations that are challenging to completely remove. The choice of the Varian Truebeam linear accelerator, known for its advanced capabilities, emphasizes the need for state-of-the-art technology in such cases.

In light of the limited number of reported cases involving myxopapillary ependymomas in the sacrum, further research is warranted. Collaborative efforts to gather additional cases and data could lead to a more comprehensive understanding of the disease's behavior in this unique context.

Patient consent

Written informed consent for the publication of this case report was obtained from the patient.

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