Journal Homepage: -www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI:10.21474/IJAR01/18977
DOI URL: http://dx.doi.org/10.21474/IJAR01/18977

RESEARCH ARTICLE

RADIOTHERAPY OF RECURRENT SPINAL EPENDYMOMA

Asmae Hamdan, Oumaima Eddarif, Salma El Baz, Karima Nouni, Amine Lachgar, Hanan El Kacemi, Tayeb Kebdani and Khalid Hassouni
Department of Radiotherapy Oncology, National Institute of Oncology, Mohamed V University, Rabat, Morocco.

Manuscript Info

Manuscript History
Received: 25 April 2024
Final Accepted: 28 May 2024
Published: June 2024

Key words:-
Tanycytic Ependymoma, Spinal Ependymoma, Recurrent Ependymoma, Str, Radiotherapy

Abstract

Spinal ependymoma is a rare tumor for which there is no consensus on optimal treatment and prognosis. However, complete resection is generally recommended when possible, offering a high rate of local control and favorable long-term survival. In cases where complete resection is not feasible, adjuvant radiotherapy may be considered to reduce the risk of recurrence. A 36-year-old patient, with no prior medical history, was diagnosed with a grade II spinal ependymoma according to the 2021 WHO classification. He underwent total resection in 2021. Twenty-one months later, he experienced a local recurrence and a spinal metastasis, for which he underwent partial resection urgently due to a sudden onset of spinal cord compression symptoms. The patient then received adjuvant radiotherapy, with a total dose of 39.6 Gy and a boost of 14.4 Gy. His pain improved starting from the second week of radiotherapy. One year later, his clinical and radiological condition remains stable.

Introduction:-

Primary spinal cord tumors are uncommon, accounting for 4%-10% of all CNS tumors; however, ependymomas remain the most common primary intramedullary spinal cord tumors, representing 30%-45% of such lesions [1,2]. In adults, spinal ependymoma most commonly occurs in the cervical spine alone, accounting for 44%, with an additional 23% extending into the upper thoracic spine. Although less common, the thoracolumbar localization represents a few cases [3], among which our case falls. The median age at diagnosis of patients with spinal ependymoma ranges from 25 to 45 years [2].

Rare variants of spinal ependymomas have been described, including cellular, papillary, clear cell, and tanycytic variants. The tanycytic variant, initially described by Fiede and Pollak in 1978, is a malignancy with low to moderate cellularity. It is characterized by streams of elongated cells with modest nuclear pleomorphism and an absence of mitotic figures [4]. Tanycytic cells can mimic other tumor cells with similar features under light microscopy, often making the diagnosis difficult [4].

To date, only a small number of tanycytic variant ependymomas have been described in the spinal cord. The tanycytic variant was included in the World Health Organization (WHO) classification of 2016 but was removed from the new classification of 2021 due to its lack of clinical relevance to date [5,6].

Corresponding Author:- Asmae Hamdan
Address:- Department of Radiotherapy Oncology, National Institute of Oncology, Mohamed V University, Rabat, Morocco.

The management of this tumor consists of surgery followed by radiotherapy in cases of incomplete resection. Although radiotherapy is a controversial subject in terms of improvement and benefit in progression-free survival and overall survival, we seek to discuss therapeutic recommendations focusing on the role of radiotherapy through the case of a young man with recurrent spinal ependymoma.

Case Presentation:

A 36-year-old patient with no significant medical history experienced episodes of back pain in 2021. Despite symptomatic treatment, the symptoms worsened with the onset of paresthesia in the lower limbs 11 months after the onset of pain. A dorso-lumbar MRI showed a tumor measuring 54x15x14 mm in the dorsal spinal cord from D10 to D12. The patient underwent a total resection of the tumor. The pathological examination of the surgical specimen showed a glial proliferation of ependymal origin with moderate cell density. The cells were regularly rounded or elongated, with hyperchromatic nuclei and rare eosinophilic cytoplasm. The diagnosis of grade II tanycytic ependymoma according to the 2016 WHO classification was made (**Figure 1**).

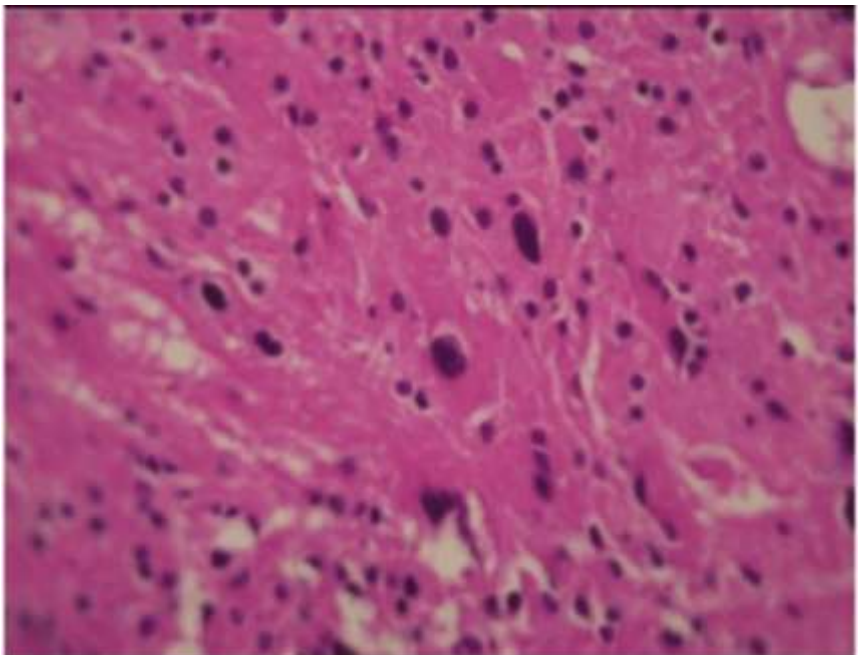

Figure 1:- Histological section showing regularly rounded or elongated cells with hyperchromatic nuclei and rare eosinophilic cytoplasm (HES x40).

Twenty-one months later, the patient presented to the neurosurgical emergency department with a rapidly developing spinal cord compression syndrome that developed in less than 72 hours. On clinical examination, the patient was alert, with a Glasgow Coma Scale score of 15, hemodynamically stable, but unable to walk or stand. He had normal muscle strength in the upper limbs but weakness in the lower limbs, absent reflexes, hypoesthesia at the level of D12, and genitourinary dysfunction. Examination revealed intense pain on palpation of the spinous processes at D8, D9, and D10, radiating to the ribs in a half-belt distribution. The rest of the physical examination was unremarkable. The examination concluded the presence of a slow spinal cord compression syndrome at D8, D9, and D10 (a D8, D9, and D10 spinal cord syndrome, a radicular syndrome with a sensory level at D12, and a sublesional syndrome). A spinal cord MRI showed a tumor mass at the level of D9 and L1 measuring 86x17x13 mm.

The patient underwent a partial resection this time. The pathological examination revealed the same histological type, a grade II spinal ependymoma according to the 2021 WHO classification (corresponding to the tanycytic variant according to the 2016 WHO classification). A postoperative spinal MRI showed a tumor mass at the level of D10, D11 and D12, measuring 46x12x10 mm, and the appearance of a new posterior epidural lesion at the level of D4 measuring 10x5 mm (**Figure 2**). The case was presented at the multidisciplinary meeting, and adjuvant radiotherapy was decided upon.

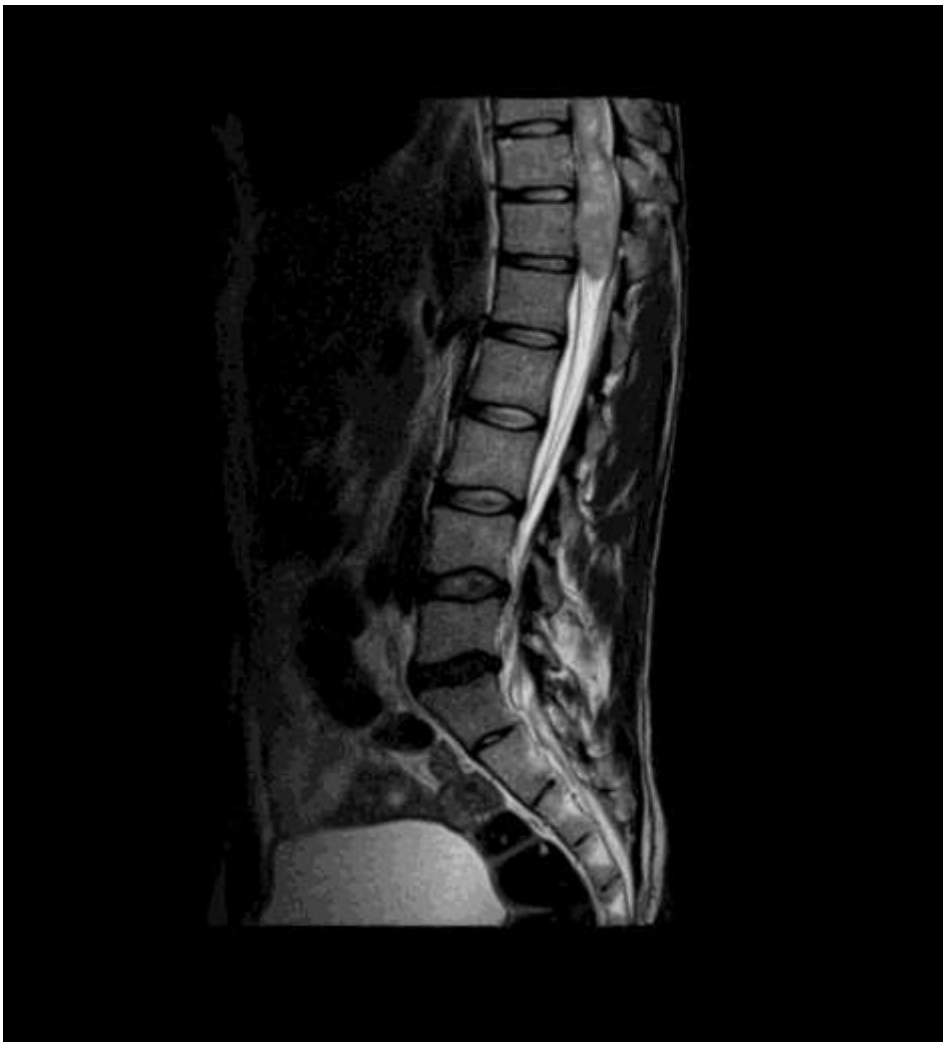

Figure 2:- Sagittal T2-weighted image of the cervical spine showing an isointense lesion between D10 and D12.

The treatment plan was established using intensity-modulated radiotherapy (IMRT). The simulation was performed using a CT simulator. The patient was immobilized in a supine position with a 3-point thermoplastic head and neck mask. Planning CT images were acquired with intravenous iodine contrast and a slice thickness of 3 mm. The DICOM CT images were transferred to the treatment planning system for target delineation. The acquired images were then co-registered with those from diagnostic MRIs to define the pre-surgical, post-surgical, and metastatic gross tumor volume (GTV) to better delineate the clinical target volume (CTV).

The postoperative Gross Tumor Volume (GTV) included the tumor cavity and the residual tumor after surgical resection, as well as the metastatic site at the level of the 4th dorsal vertebra. Clinical Target Volume 1 (CTV-1) included the skull and the entire spinal canal, and also encompassed the entirety of Clinical Target Volume 2 (CTV-2). Clinical Target Volume 2 (CTV-2) was defined by a 1 cm expansion from the GTV, extended to include bony surfaces and connective tissues included in the preoperative GTV. It included nerve roots exiting the cord or tail in the tumor and/or tumor bed region. Planning Target Volume 1 and 2 (PTV-1 and PTV-2) were constructed with a 3 mm expansion from CTV-1 and CTV-2 without cropping or other modification.

Organs at risk (OAR) were contoured according to the Radiation Therapy Oncology Group (RTOG) atlas for normal tissue contouring. They included the spinal cord, brainstem, caudal nerve roots, lungs, heart, liver, kidneys, stomach, esophagus, intestines, bladder, and rectum. A prescription dose of 39.6 Gy in 22 fractions was given to PTV-1 and 54 Gy in 30 fractions to PTV-2. Volumetric modulated arc therapy (VMAT) with a simultaneous integrated boost

(SIB) technique was generated using 6 MV photon beams (**Figure 3**). PTV coverage and dose to OARs were acceptable. Dose constraints to OARs were defined according to the RECORD. Patient setup was verified daily with cone-beam CT imaging before treatment.

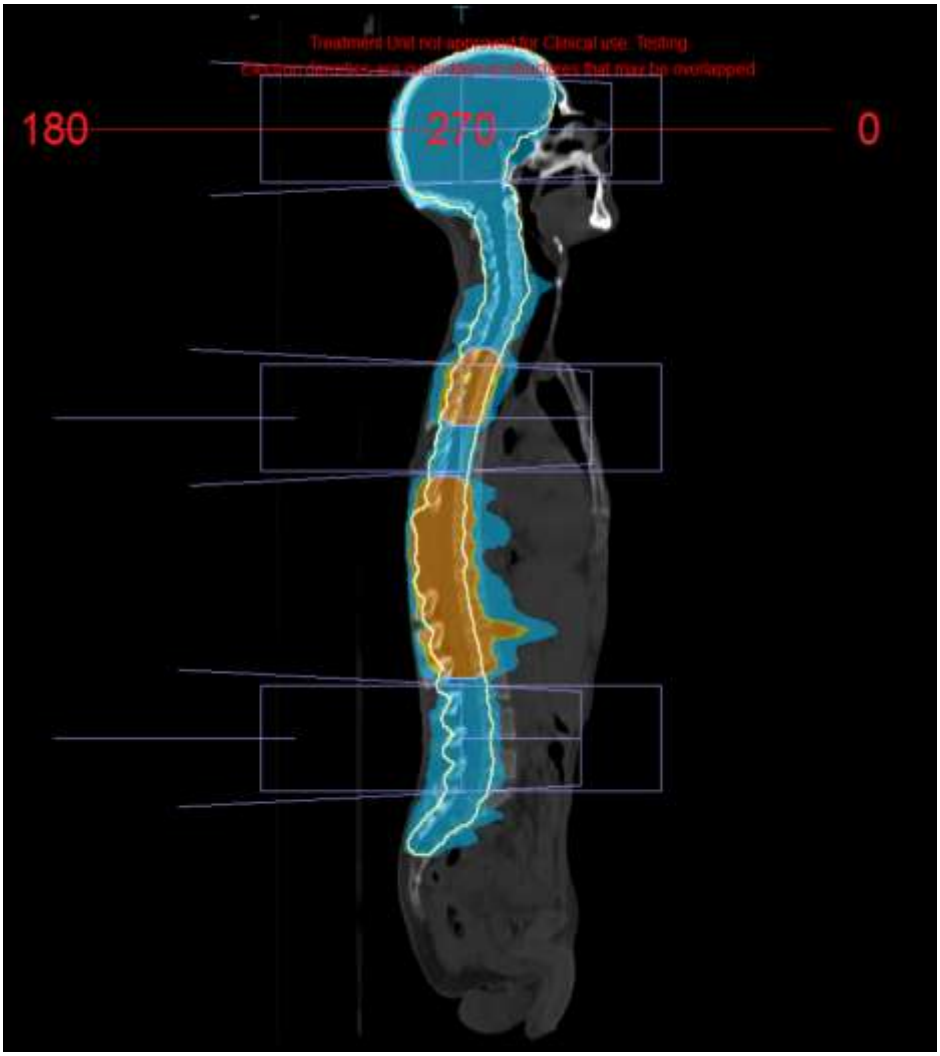

Figure 3:- The planning CT scan with 39.6 Gy (in blue) and 54 Gy (in orange) isodose lines.

The patient tolerated the radiotherapy well and did not experience any toxicity. Additionally, there was an improvement in pain starting from the second week of radiotherapy. At the end of treatment, the patient's clinical condition improved, with less pain and resolution of genitourinary symptoms. However, weakness in both lower limbs persisted, with the ability to walk with assistance. He was followed up at one month, three months, six months, nine months, and one year after irradiation for follow-up assessment, with a stable clinical and radiological condition.

Discussion:-

Intramedullary ependymomas are well-circumscribed tumors, which facilitates surgical resection. In a retrospective analysis conducted by Rodriguez et al. [7], patients who underwent surgery had better outcomes than those who did not. Complete resection (GTR) can provide definitive cure in most cases [8]. That is why GTR is the goal of any spinal cord ependymoma surgery, offering the best prognosis if significant neurological morbidity can be avoided [9,10]. However, when surgery cannot be complete for various reasons, spinal cord ependymomas tend to recur at rates of up to 50% to 70% without adjuvant treatment [11].

Although adjuvant radiotherapy is recommended after subtotal resection of grade II spinal cord ependymomas and in all cases of grade III ependymomas [12], the benefit in terms of prolonging progression-free survival (PFS) and overall survival (OS) is controversial. Some series have not shown a significant impact of radiotherapy on recurrence or progression in patients undergoing subtotal resection, compared to total gross resection alone. Sgouros et al. concluded that in patients treated with postoperative radiotherapy, the 10-year survival rate was 48%, compared to 96% in those who did not receive postoperative radiotherapy [13].

However, Michael C. Oh et al., in a literature review of 348 patients with WHO grade 2 and 3 spinal ependymomas, showed a significantly prolonged progression-free survival (PFS) with adjuvant radiotherapy after subtotal resection (STR). The median PFS was 48 months in patients treated with STR alone and 96 months for patients treated with STR followed by radiotherapy [8]. Rodriguez et al. examined over 2400 cases of ependymomas from the entire central nervous system including those from the spinal cord, in the SEER database and reported that patients with partially resected tumors who do not receive radiotherapy have a poorer prognosis than those treated with radiotherapy. The short-term and 10-year survival rates after radiotherapy reached over 70% and 50% respectively [7].

The optimal radiation dose for subtotally resected spinal cord ependymomas remains to be determined. No correlation between the doses of radiotherapy used (≤ 50 Gy vs. > 50 Gy) and progression-free survival (PFS) or overall survival (OS) has been recorded [8]. In the literature, the dose administered to the tumor bed varies from 45 to 60 Gy, while on the craniospinal axis, it varies from 30 to 45 Gy in cases of evident radiographically or pathologically confirmed spinal column seeding [14-20].

Conclusion:-

In summary, current guidelines recommend maximal resection followed by adjuvant radiotherapy in cases of grade II spinal ependymomas with subtotal resections (STR) and all grade III spinal ependymomas. However, radiotherapy is not discussed after total resection in grade II ependymomas, raising several questions regarding the need for immediate adjuvant radiotherapy or waiting for recurrence before intervening. The rarity of these tumors limits additional studies to reassess the indications for adjuvant radiotherapy and the appropriate dose. Overall, complete resection is generally recommended when possible, offering a high rate of local control and favorable long-term survival. For cases where complete resection is not feasible, adjuvant radiotherapy should be considered to reduce the risk of recurrence.

References:-

1. Sung Mo Ryu, Sun-Ho Lee, Eun-Sang Kim, Whan Eoh: predicting survival of patients with spinal ependymoma using machine learning algorithms with the SEER database. World neurosurgery. 2019, 124:e331-e339. 10.1016/j.wneu.2018.12.091
2. Luca Bertero, Alessia Andrea Ricci, Cristian Tampieri, Paola Cassoni, Piergiorgio Modena: Ependymomas. Pathologica. 2022, 114:436-446. 10.32074/1591-951X-817
3. Eliezer Villanueva-Castro, Juan Marcos Meraz-Soto, Itzel Ariadna Hernández-Dehesa, et al.: Spinal ependymomas: an updated WHO classification and a narrative review. Cureus. 2023, 15:e49086. 10.7759/cureus.49086
4. Krisht KM, Schmidt MH: Tanycytic ependymoma: a challenging histological diagnosis. Case reports in neurology medicine. 2013, 2013:170791. 10.1155/2013/170791
5. David W. Ellison, Kenneth D. Aldape, David Capper, et al.: cIMPACT-NOW update 7: advancing the molecular classification of ependymal tumors. Brain pathology. 2020, 30:863-866. 10.1111/bpa.12866
6. David N Louis, Arie Perry, Pieter Wesseling, et al.: The 2021 WHO classification of tumors of the central nervous system: a summary. Neuro-oncology. 2021, 23:1231-1251. 10.1093/neuonc/noab106
7. Dayron Rodríguez, Michael C Cheung, Nadine Housri, Alfredo Quinones-Hinojosa, Kevin Camphausen, Leonidas G Koniaris: Outcomes of malignant CNS ependymomas: an examination of 2408 cases through the surveillance, epidemiology, and end results (SEER) database (1973-2005). The journal of surgical research. 2009, 156:340-351. 10.1016/j.jss.2009.04.024
8. Michael C Oh, Michael E. Ivan, Matthieu Z Sun, et al.: Adjuvant radiotherapy delays recurrence following subtotal resection of spinal cord ependymomas. Neuro-oncology. 2013, 15:208-215. 10.1093/neuonc/nos286
9. Yong Deng, Haifeng Chen, Chenghong Wang, Yukang Zhang: Risk factors for the recurrence of World Health Organization grade II ependymomas of spinal cord in adults after microsurgical resections: a retrospective study

of 118 patients in a single center. Clinical neurology and neurosurgery. 2020, 195:105856. 10.1016/j.clineuro.2020.105856
10. Daniel T. nagasawa, Z achary a. smiTh, nicolecremer, chrisTina Fong, Daniel c. lu, isaac yang: Complications associated with the treatment for spinal ependymomas. Neurosurgical focus. 2011, 31:E13. 10.3171/2011.7.FOCUS11158
11. Cooper P. R.: Outcome after operative treatment of intramedullary spinal cord tumors in adults: intermediate and long-term results in 51 patients. Neurosurgery. 1989, 25:855-859. 10.1097/00006123-198912000-00001
12. Desmond A. Brown, Anshit Goyal, Hirokazu Takami, Christopher S. Graffeo, Anita Mahajan, William E. Krauss, Mohamad Bydon : Radiotherapy in addition to surgical resection may not improve overall survival in WHO grade II spinal ependymomas. Clinical neurology and neurosurgery. 2020, 189:105632. 10.1016/j.clineuro.2019.105632
13. Sgouros, S., Malluci, C. L., & Jackowski, A.: Spinal ependymomas-the value of postoperative radiotherapy for residual disease control. British journal of neurosurgery. 1996, 10:559-566. 10.1080/02688699646862
14. Mark P McLaughlin, Robert B Marcus Jr., John M Buatti, et al.: Ependymoma: results, prognostic factors and treatment recommendations. International journal of radiation oncology, biology, physics. 1998, 40:845-850. 10.1016/s0360-3016(97)00893-6
15. Jenna Kahn, Jay Steven Loeffler, Andrzej Niemierko, E Antonio Chiocca, Tracy Batchelor, Arnab Chakravarti: Long-term outcomes of patients with spinal cord gliomas treated by modern conformal radiation techniques. International journal of radiation oncology, biology, physics. 2011, 81:232-238. 10.1016/j.ijrobp.2010.05.009
16. M Nakamura, K Ishii, K Watanabe, et al.: Surgical treatment of intramedullary spinal cord tumors: prognosis and complications. Spinal cord. 2008, 46:282-286. 10.1038/sj.sc.3102130
17. J N Waldron, N J Laperriere, L Jaakkimainen, W J Simpson, D Payne, M Milosevic, C S Wong: Spinal cord ependymomas: a retrospective analysis of 59 cases. International journal of radiation oncology, biology, physics. 1993, 27:223-229. 10.1016/0360-3016(93)90231-j
18. T T Lee, E B Gromelski, B A Green: Surgical treatment of spinal ependymoma and post-operative radiotherapy. Acta neurochirurgica. 1998, 140:309-313. 10.1007/s007010050103
19. Mark J Amsbaugh 1, David R Grosshans, Mary Frances McAleer, et al.: Proton therapy for spinal ependymomas: planning, acute toxicities, and preliminary outcomes. International journal of radiation oncology, biology, physics. 2012, 83:1419-1424. 10.1016/j.ijrobp.2011.10.034
20. Daniel R Gomez, Brian T. Missett, William M Wara, et al.: High failure rate in spinal ependymomas with long-term follow-up. Neuro-oncology. 2005, 7:254-259. 10.1215/S1152851704001231.