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# Subependymoma of the Cervicothoracic Spinal Cord

**Yvan Maque-Acosta[1], Carol K Petito[1], Michael E Ivan[2], Charif Sidani[3] and Macarena I de la Fuente[4,5]***

[1]*Departments of Pathology, University of Miami, Florida, USA*
[2]*Department of Neurosurgery, University of Miami, Florida, USA*
[3]*Department of Radiology, University of Miami, Florida, USA*
[4]*Department of Neurology, University of Miami, Florida, USA*
[5]*Sylvester Comprehensive Cancer Center, University of Miami, Florida, USA*

***Corresponding author:** Macarena I. de la Fuente, Department of Neurology and Sylvester Comprehensive Cancer Center, University of Miami, FL 33136, USA, **E-mail:** mdelafuente@med.miami.edu

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## Background

Subependymomas are rare, World Health Organization (WHO) grade I tumors [1,2]. They typically arise in the ventricles and represent less than 1% of intracranial tumors [3]. Spinal subependymomas are even less frequent, comprising approximately 2% of all symptomatic spinal cord tumors [4]. They are usually intramedullary and located in the cervical region, however thoracic and lumbar lesions have also been reported [2,5,6].

Radiologically, intracranial subependymomas present as well defined intraventricular lesions that are classically T2-weighted images (WI) hyper intense and T1WI hypo or isointense to white matter in MRI [5,7]. Heterogeneity on T2WI is often reported and is related to cystic changes, blood products or calcifications, particularly in larger lesions [5]. Calcifications and blood products can manifest as low signal intensity on T2WI gradient echo sequence. Subependymomas typically do not enhance or only mildly enhance. Avid enhancement has been reported particularly in lesions located in the fourth ventricle. The tumor size typically ranges from 1 to 2 cm, however lesions greater than 5 cm have also been reported [2,5]. Spinal subependymomas usually present as eccentric, well-defined lesions with mild to moderate enhancement. Lesions of the spine have significant associated edema [2,6].

Histologically, subependymomas are characterized by the presence of nuclear clustering and a densely fibrillar and paucicellular background [1]. Microcysts can be present, particularly in lesions located closer to the foramen of Monro. Subtle pseudorosettes can also be seen [1,8]. In tumors located far from the foramen of Monro, the nuclear clustering is more prominent. Occasionally, an ependymoma component can be identified, although this is more common in fourth ventricle tumors. By immunohistochemistry, subependymoma are diffusely positive for glial fibrillary acidic protein (GFAP) which demonstrate its glial origin and positive for epithelial membrane antigen (EMA) (showing a dot-like pattern) which is consistent with an ependymal origin. They usually have a low Ki-67 proliferative index, although it can be variable [1,8].

We describe a case of spinal subependymoma and discuss the clinical, radiographic and histological characteristics.

## Clinical Case

A 37-year-old-man initially presented with a 10-year-history of left foot weakness and bilateral lower extremity pain. His symptoms worsened over the following years including left lower extremity weakness, left hand weakness and urinary urgency. Eighteen months before coming to our institution, the patient had a cervical magnetic resonance imaging (MRI) without contrast done, which showed diffuse spinal cord edema and expansion from C2-3 to T3 level (Figure 1A). One month later, the patient underwent C6-T1 laminectomy with tumor biopsy followed by focal radiation therapy from C3 to T3. Pathology was read as WHO grade II astrocytoma. He has not received any further therapy.

One year later, he moved to Miami and established care at Sylvester Comprehensive Cancer Center/University of Miami. He did not report any new symptoms. His physical exam revealed left upper extremity weakness (3/5), left lower extremity weakness (4/5), generalized hyper reflexia, positive Babinski sign bilaterally and paretic gait. Sensation was normal. A MRI with contrast of the total spine was done and compared to pre-operative and post-operative MRIs, revealing persistence of the diffuse T2 hyper intensity and cord expansion extending from C4 to T3. There was a 7 mm × 7 mm well defined intramedullary enhancing lesion within the dorsal aspect of the cord at C7-T1. The lesion was isointense on T2WI (Figures 1B and 1C). There was also a focus of low signal on T2WI gradient echo sequence that likely represented blood or calcification and a smaller lesion with similar signal within the ventral aspect of the cord at the same level. It was difficult to compare the degree of enhancement as there were no post-contrast sequences on the prior outside imaging. Overall, the craniocaudal extent of the lesion did not change significantly. These findings were consistent with a combination of residual tumor/post treatment changes, particularly in the areas of intramedullary enhancement, with associated post treatment changes, edema and/or myelomalacia. There was no evidence for drop metastasis in the thoracic and lumbar spine, and neither brain metastasis.

The biopsy sample was reviewed at our institution (Figure 2). The tumor showed nuclear clustering and a fibrillar, paucicellular background. It was diffusely positive for GFAP immunostaining, positive for EMA immunostaining in a dot-like pattern, and it was negative for Ki-67 immunostaining. All these finding were consistent with a subependymoma (WHO grade I).

Twenty five months after his biopsy, the patient remains clinically and radiologically stable off treatment.

## Discussion

We describe a case of a young adult male with a cervicothoracic spinal cord lesion. He presented with a 10-year history of slowly progressive lower extremity pain, motor and urinary dysfunction. Differential

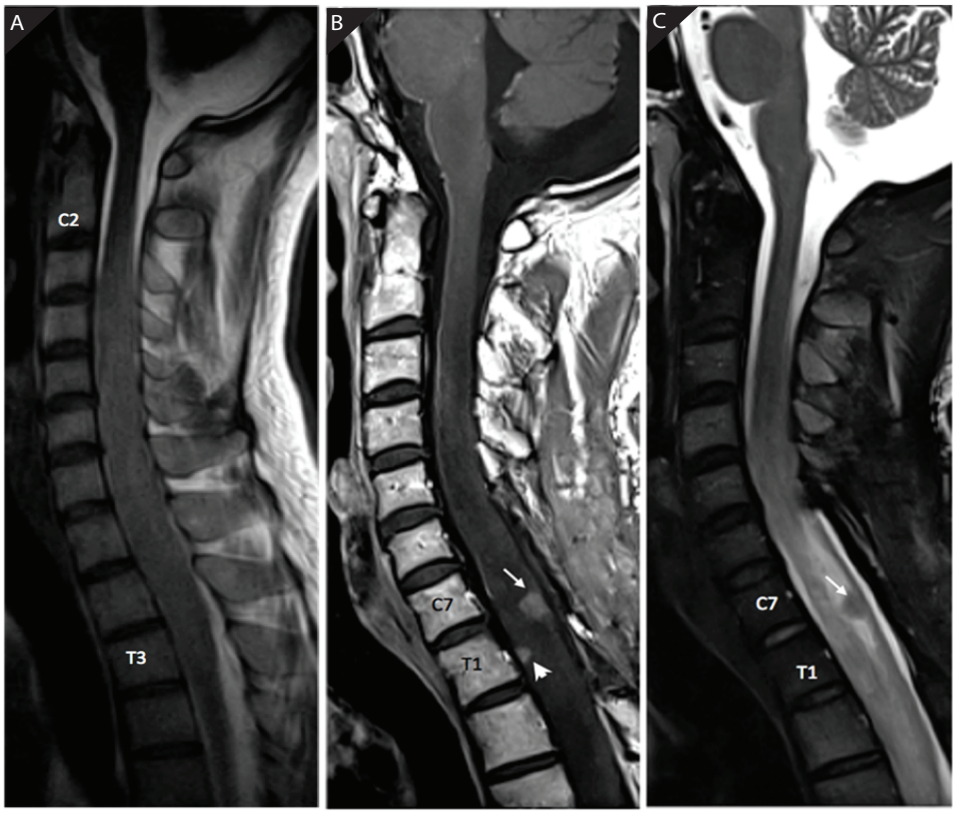


**Figure 1**: Radiological features.
A. Preoperative scan. Sagittal T2-weighted images (WI) MRI. There is cord edema and expansion between C2-C3 to T3 levels.B-C. Postoperative scan. B. Sagittal T2WI fat saturated MRI. C. Sagittal T1WI Post contrast. There is a 7 mm × 7 mm T2 isointense solid enhancing lesion within the dorsal aspect of the cord at C7-T1 level (arrow). A smaller lesion is seen within the ventral aspect of the cord at mid T1 level (arrow head). Laminectomy changes are also noted.

diagnosis for this lesion includes spinal cord astrocytoma, ependymoma and subpendymoma.

## Radiological features

The primary radiologic consideration in this setting was a spinal ependymoma. These lesions represent 60% of primary intramedullary spine lesions, are common in this age group and typically present as well defined solid enhancing lesions [9]. Cystic component, which is commonly seen with ependymomas, and syrinx which is associated with 50-90 % of spinal ependymomas, were both absent. Subependymomas have been described with features identical to this case, however, since these commonly present as non-enhancing intraventricular lesions [5,7], it was felt to be a less likely etiology. This case serves as a reminder to include subependymoma in the differential of a well-defined solid enhancing intramedullary spinal lesion, particularly when low signal foci are seen on T2WI [10].

## Histological features

In spinal cord tumors located far from the foramen of Monro, the differential diagnosis includes ependymoma, infiltrating astrocytoma, and subependymoma. Subependymomas located in this area usually present with a more prominent nuclear clustering and few microcysts, if any; and these were features of our case. Even though our patient's tumor showed areas with increased cellularity (Figure 2B) which is a feature of ependymoma, clustering was still noted and others features including uniform medium to high cellularity and true rosettes were not identified. An infiltrating astrocytoma was also ruled out due to the lack of an infiltrating pattern, presence of nuclear clustering, and EMA positivity [8]. Additionally, several hyalinized vessels were present in the specimen (Figure 2C), which is a common and unspecific finding among CNS tumors [11].

## Neurosurgical approach

Surgical intervention for spinal cord ependymomas remains the mainstay treatment option. Due to spinal cord compression from these tumors, patients usually present with neurological deficits such as paresis, dysesthesias, or incontinence. The goals of surgery are to obtain tissue for diagnosis, decompression to provide symptomatic relief, and to provide long term tumor control [2]. These tumors are usually amenable to a gross total resection and considering their slow and benign growth, outcomes are favorable [12,13]. Surgery entails a laminectomy with intramedullary tumor resection. Fusion is indicated only if instability results from the extent of bony removal during exposure. Perioperative steroids and prophylactic antibiotics are administered before incision and steroids are typically continued after surgery as well. Somato sensory and motor evoked potentials are electrophysiologically monitored during the entire tumor resection. Microsurgical technique is used to obtain a safe maximal resection. The tumor is often, 74% of the time, in an eccentric location with a sharp demarcation between tumor and cord, however occasionally there can be areas where tumor can infiltrate the surround tissue making it difficult for a gross total resection [14]. The tumor is often soft and greyish with minimal to no vascularization. In one review series of 30 patients with subependymomas in the spinal cord immediate postoperative deficits were noted in 60% of patients, however, 75% of these deficits

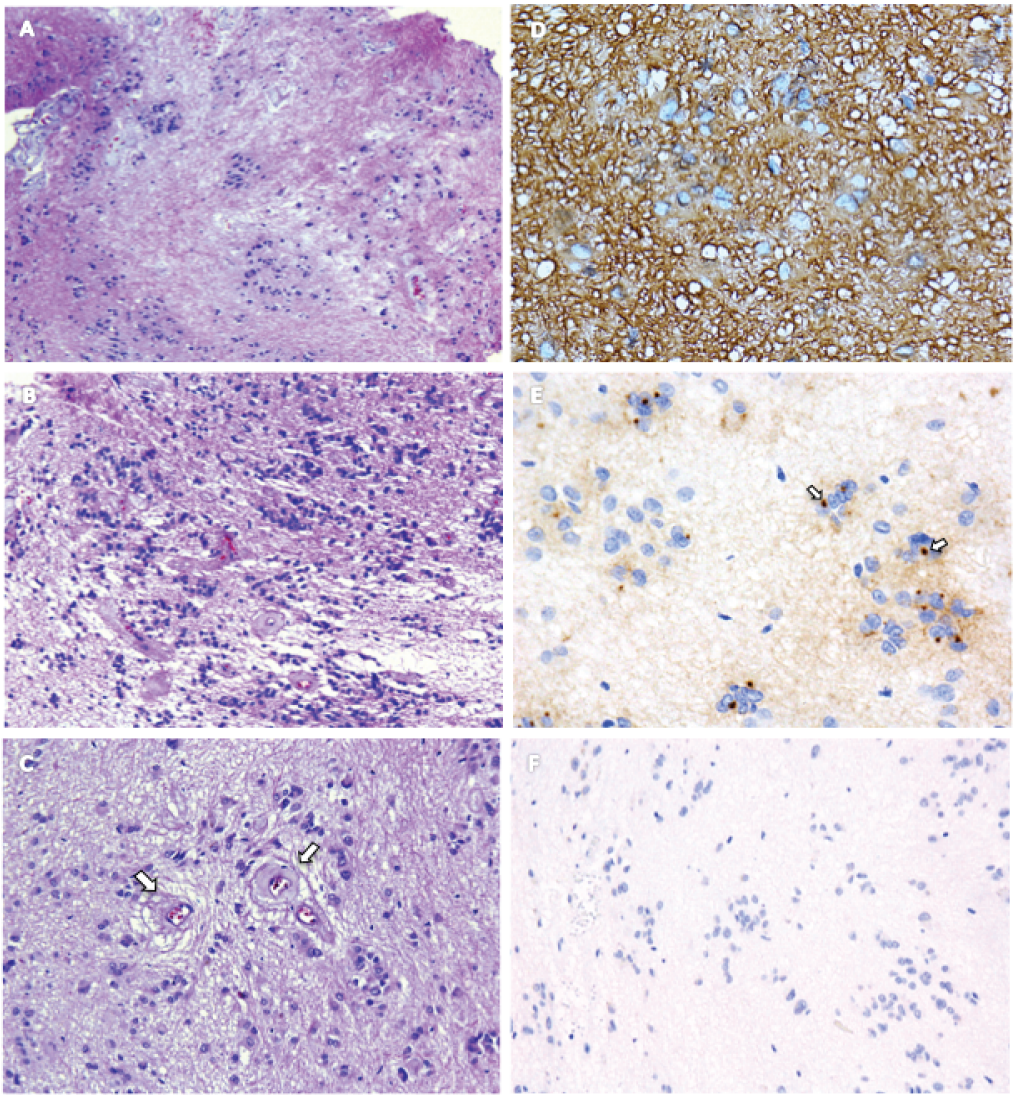


**Figure 2:** Histological features.
A. Microscopic image of the tumor demonstrating the classic features of subependymoma, including nuclear clustering and a fibrillar, paucicellular background; Microcysts are not evident in this case (magnification 10x). B. The tumor shows areas with medium cellularity, however cell clustering is still present (20x). C. Hyalinized vessels are observed in the specimen (arrows, 20x). D. The tumor is diffusely positive for GFAP immunostain (40x). E. It shows dot-like EMA positivity (arrows, 40x). F. It is negative for Ki-67 immunostain (20x).

improved on long term follow-up [14]. In a more recent series, four of five patients had resolution of their preoperative symptoms on long term follow-up [2]. Long term follow up after gross total resection or maximal safe resection has shown no tumor recurrence or progression for greater than 3 years in multiple series [2,15-17]. Therefore surgical resection is usually curative and no adjuvant therapy recommended during initial treatment [18].

### Other therapeutical options

The role of further therapy as radiation therapy and/ or chemotherapy remains unclear. Radiation therapy may be consider for the management of recurrent or symptomatic residual disease [2].

## Consent

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

## Conflict of Interests

The authors declare that they have no conflict of interests.

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