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# *MYCN*-amplified spinal ependymomas: a rare aggressive subtype. Illustrative cases

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**BACKGROUND** Spinal ependymomas are typically slow-growing tumors with a favorable prognosis. Recently, a new aggressive subtype has emerged with its own distinct histopathological and molecular features characterized by *MYCN* amplification. However, this subtype of spinal ependymoma is rare, and studies on its imaging characteristics are limited. In this case series, the authors present the imaging findings of three patients with *MYCN*-amplified spinal ependymoma from their institution.

**OBSERVATIONS** Unlike typical spinal ependymomas, the *MYCN*-amplified spinal ependymomas were intradural extramedullary in location in the thoracic and lumbar spine. Imaging revealed T1 isointensity and T2 hyperintensity with avid enhancement and peritumoral edema. The tumor masses were adherent to the spinal cord with filling of the canal and resultant cord compression. There were focal areas without a clear tissue plane between the mass and the cord, which was concerning for cord infiltration. Thus, complete resection was difficult to achieve, and all patients demonstrated residual tumor in the resection bed. Their clinical course was also characterized by early central nervous system (CNS) dissemination, including one case with intracranial involvement.

**LESSONS** This case series highlights three instances of *MYCN*-amplified spinal ependymoma, a rare and aggressive subtype with distinctive imaging features, including an intradural extramedullary location and CNS dissemination at recurrence.

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**KEYWORDS** spinal neoplasms; spinal ependymoma; *MYCN*-amplified spinal ependymoma; case series; case report

Ependymomas are classified according to anatomical site and histopathological and molecular features, divided into the supratentorial, posterior fossa, and spinal compartments. Spinal ependymomas are most commonly grade 2 tumors, rarely grade 3, and are typically slow growing with a favorable prognosis. Recently, a new histopathological and molecular subtype of spinal ependymomas has been identified through DNA methylation profiling, characterized by *MYCN* amplification.[1–4] This subtype is notable for its aggressive clinical course and intradural extramedullary location and was recognized as a separate entity in the 2021 World Health Organization (WHO) classification of central nervous system (CNS) tumors.[5] While spinal ependymomas are the most common intramedullary tumors in adults, primary spinal intradural extramedullary tumors are exceedingly rare, with intramedullary lesions being even less common.[6] Because of the rarity and recent recognition of *MYCN*-amplified spinal ependymomas, there are limited studies on their radiological features. In this case series, we present imaging features of three patients with *MYCN*-amplified spinal ependymoma from our institution.

## Illustrative Cases

### Case 1

A 36-year-old male initially presented to the emergency department with back and bilateral lower-extremity numbness after a fall 2 weeks earlier. Computed tomography was unrevealing, and he was discharged with pain control. He returned 2 weeks later with worsening back pain, bilateral leg weakness, and urinary retention and was no longer able to ambulate. Magnetic resonance imaging (MRI) of the thoracic spine revealed multifocal intradural extramedullary, T1-isointense, and T2-hyperintense enhancing masses throughout the spine, with a dominant mass at T7–9 causing cord compression (Fig. 1).

He underwent a T7–8 bilateral transpedicular approach for resection of the intradural tumor and T5–10 posterior spinal fusion. The histopathology was initially reported as WHO grade II ependymoma, and later sequencing demonstrated *MYCN* amplification. Postoperative MRI revealed residual disease in the resection bed and scattered metastatic lesions (Figs. 2 and 3). The radiation oncology

**ABBREVIATIONS** CNS = central nervous system; MRI = magnetic resonance imaging; WHO = World Health Organization.
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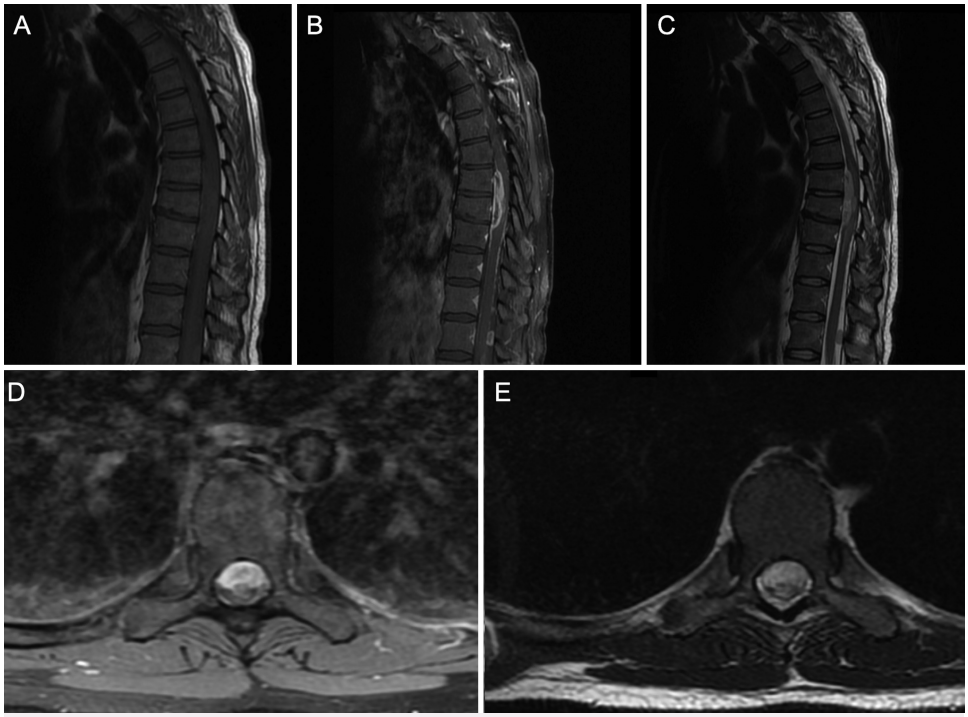


**FIG. 1.** Case 1. Sagittal T1-weighted (**A**), T1-weighted postcontrast with fat saturation (**B**), and T2-weighted (**C**) MRI demonstrating T1 isointensity, T2 hyperintensity, and enhancement of the mass spanning two vertebral body levels and filling the canal. Heterogeneous enhancement could represent areas of necrosis. There is a T2-hyperintense signal abnormality of the adjacent cord. Axial T1-weighted postcontrast with fat saturation (**D**) and T2-weighted (**E**) MRI demonstrating the mass filling the canal and resulting cord compression. There is a focal area without a clear plane between the cord and mass with associated cord signal abnormality suspicious for infiltration.

team recommended total spine radiation of 45 Gy over 5–6 weeks, with a focal boost to gross nodules for a total of 50.4 Gy. The patient completed radiation at another institution and reported improved symptoms.

One year later, the patient had progression with cord compression in the resection bed on follow-up imaging and underwent repeat resection. A multidisciplinary discussion decided against repeat radiation due to the risk of paralysis. Follow-up imaging demonstrated

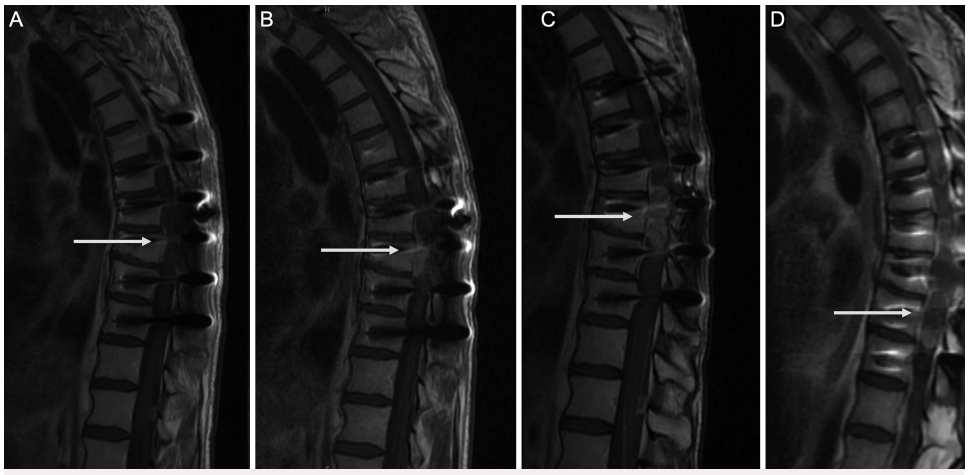


**FIG. 2.** Case 1. Sagittal T1-weighted postcontrast sequences with initial postoperative imaging (**A**) demonstrating a small amount of residual disease (*arrows*) and subsequent follow-up imaging demonstrating progression at 9 months (**B**), 1 year (**C**), and 2 years (**D**) despite interval repeat resection at 1 year.

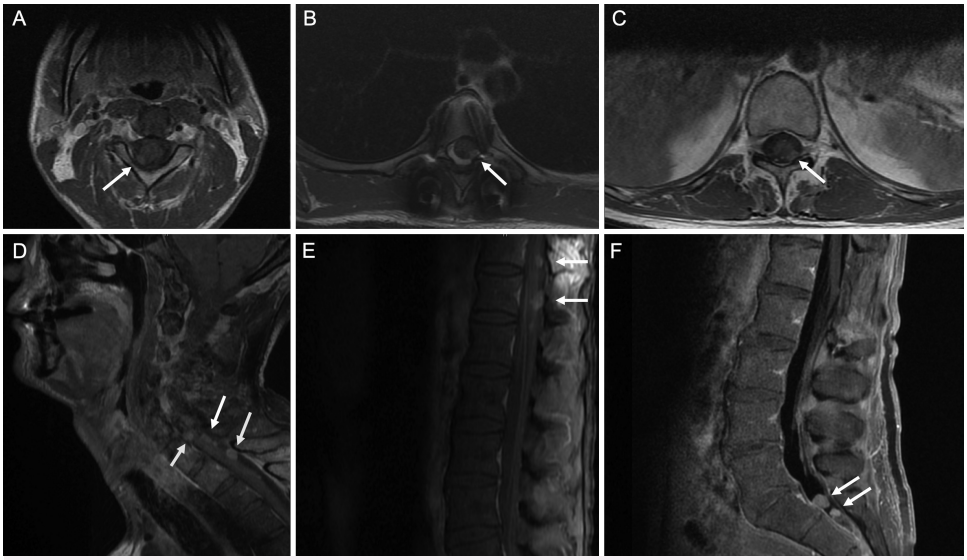


**FIG. 3.** Case 1. Axial (**A–C**) and sagittal (**D–F**) T1-weighted postcontrast images at different levels demonstrating the diffuse extent of small enhancing metastatic nodules along the cord surface, as indicated by the *arrows*.

continued progression of the disease with severe canal narrowing, cord compression, and worsening cord edema (Fig. 2). The patient reported loss of sensation below T10 and worsening balance and coordination. He was treated with temozolomide and lapatinib for 2 months but stopped because of the side effects of worsening leg weakness, fatigue, and bowel dysfunction.

In 2022, 1 year later, he had progression in the cervical spine with resulting quadriplegia. Multidisciplinary consensus was not to pursue further radiation therapy. His lesions continued to progress on subsequent imaging, and the patient had multiple hospitalizations during this time related to urinary tract infections and ulcers. The decision was made not to pursue further treatment, and a year later, he was transferred to hospice, where he died.

## Case 2

A 56-year-old male presented in 2019 with progressive intractable low-back pain for 2 months. He was originally treated with a steroid taper, with some symptomatic improvement; however, at the time of presentation, he was barely able to ambulate due to pain. MRI revealed a dominant, T1-isointense, T2-hyperintense, enhancing mass at L1–2 with multiple additional small enhancing nodules throughout the spine, consistent with diffuse leptomeningeal disease.

He underwent L1–2 laminectomy and tumor resection with symptomatic improvement. Histopathology was initially reported as a WHO grade III anaplastic ependymoma, and sequencing subsequently demonstrated focal high-level *MYCN* amplification and a truncating frameshift mutation of *PTEN*. Postoperative imaging demonstrated interval resection and extensive metastatic disease throughout the spine. The patient completed total spine radiation therapy to 45 Gy with a lumbar spine boost to 50.4 Gy in 1.8-Gy daily fractions with concurrent temozolomide. His course was complicated by grade 2 thrombocytopenia.

The next year, follow-up imaging demonstrated disease progression in the lumbar spine and new involvement of the right Meckel's cave. He underwent Gamma Knife radiosurgery to the right Meckel's cave at another institution and was treated for 8 months with temozolomide and lapatinib. Treatment was stopped due to pancytopenia, and he was ultimately diagnosed with concurrent T-cell large granular lymphocytic leukemia and treated with methotrexate.

The patient continued to demonstrate progressive intracranial and spinal disease on subsequent follow-up imaging over the past 4 years with clinical progression including vision and hearing changes (Figs. 4 and 5). He received multiple courses of radiation therapy, including 30 Gy in 5 fractions to L3, stereotactic radiosurgery to 18 Gy to left trigeminal involvement, and 30 Gy in 10 fractions to progressive left trigeminal and L1–3 disease. The most recent follow-up imaging demonstrated continued progressive intracranial and spinal disease. Radiation oncology did not recommend additional radiation therapy due to the risk of irradiation injury including tissue necrosis. The patient is currently on everolimus and carboplatin.

## Case 3

A 12-year-old female presented with 2 weeks of back pain and lower-extremity weakness and numbness. She had difficulty walking, was no longer attending school, and had multiple falls in the past month. MRI of the spine revealed an intradural extramedullary, T1-isointense, T2-hyperintense, enhancing mass at T1–4 with associated cord edema. She underwent T1–3 laminectomy and tumor debulking with some symptomatic improvement. Histopathology was initially thought to be primary spinal round cell sarcoma, with molecular testing revealing the final diagnosis to be *MYCN*-amplified spinal ependymoma.

Follow-up imaging demonstrated residual disease in the resection bed due to cord infiltration and an additional metastatic focus in the lumbar spine. She received full craniospinal radiation of 36 Gy in 20 fractions following a thoracic spine boost of 14.4 Gy in 8 fractions for a total of 50.4 Gy. She is currently 11 months post–radiation completion, with stable disease on imaging, and is able to ambulate with a walker. Her clinical course has been complicated by radiation-induced hypothyroidism.

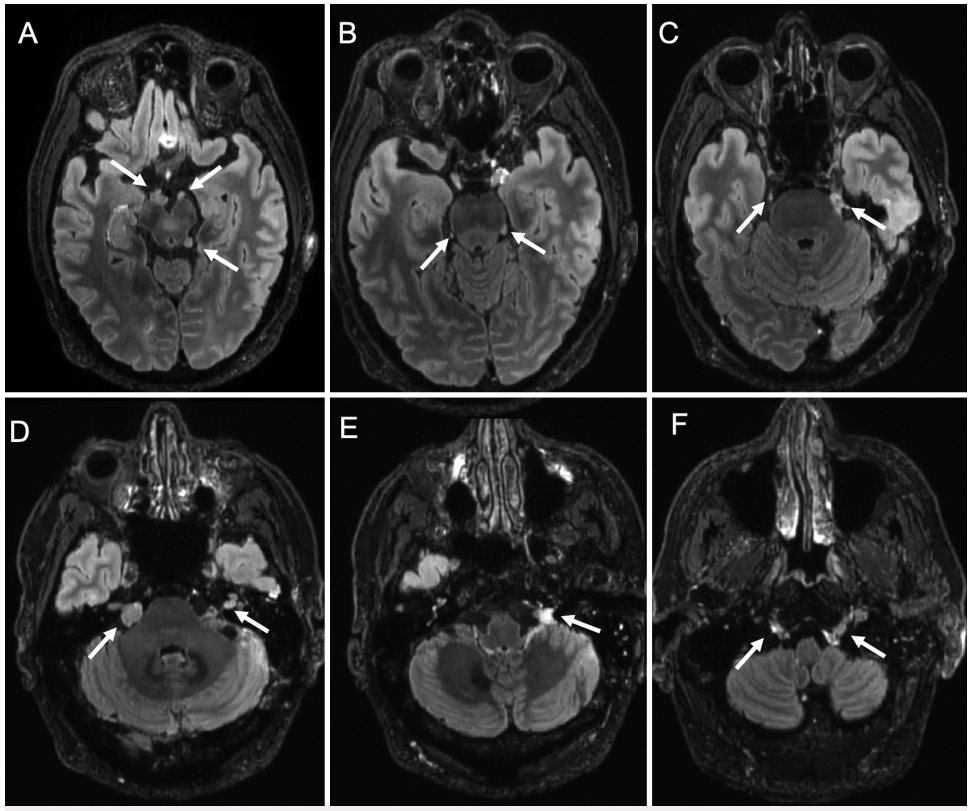


**FIG. 4.** Case 2. Axial fluid-attenuated inversion recovery images demonstrating extensive metastatic nodules involving the cranial nerves and along the brainstem including right greater than left oculomotor nerves, left ambient cistern (**A**), along the midbrain (**B**), left greater than right trigeminal nerves (**C**), right greater than left internal auditory canals with extension into the cerebellopontine angle cistern (**D**), left jugular foramen (**E**), and bilateral hypoglossal canals (**F**), as indicated by the *arrows*.

### Informed Consent

The necessary informed consent was obtained in this study.

## Discussion

### Observations

*MYCN*-amplified spinal ependymomas are a recently defined, aggressive subtype of spinal ependymoma. Their pathological features have been previously described and are characterized by focal high *MYCN* amplification on sequencing.[1–4] These tumors exhibit other histological signs of ependymal differentiation, including perivascular pseudo-rosettes, perivascular GFAP expression, and dot-like EMA positivity.[7] They often retain H3K27Me3, which is frequently lost in posterior fossa ependymomas.[8] *MYCN*-amplified ependymomas do not have a designated WHO grade.[5]

They are intradural extramedullary tumors that exhibit imaging characteristics similar to classic spinal ependymomas, including T1 isointensity, T2 hyperintensity, and heterogeneous to homogeneous enhancement. The patients in cases 1 and 3 had dominant masses in the thoracic spine, whereas the patient in case 2 had dominant disease in the lumbar spine, spanning 1–3 vertebral body levels. The dominant mass was adherent to the cord and filled the canal with resultant cord compression. There was associated segmental T2 hyperintensity of the cord, suggestive of peritumoral cord edema.

Their distinguishing feature is their aggressive appearance, characterized by adherence to the spinal cord, lack of a distinguishing cleavage plane, and filling of the canal. The absence of a clear tissue plane raises concern for cord infiltration with associated cord signal abnormalities (Fig. 1). The intimate association with the cord and potential for infiltration likely contribute to the high rate of local recurrence, as evidenced by all three patients in our series, who showed residual or recurrent disease in the resection bed. The patients in cases 1 and 3 demonstrated frank residual disease on postoperative follow-up imaging. The patient in case 2 did not have definite residual disease on immediate follow-up but did eventually develop recurrence in the region of the resection bed. When present, residual disease had the tendency to progress, owing to the aggressive nature of the tumor (Fig. 2). Postoperative studies should therefore pay special attention to the resection bed due to this elevated likelihood.

Early CNS dissemination was observed in all three patients, with metastatic nodules often small and occasionally poorly characterized on initial imaging. The patients in cases 1 and 2 had diffuse metastatic involvement at presentation. The patient in case 3 demonstrated a metastatic lesion at the 2-week follow-up, which might suggest that it existed at presentation but was not perceptible by imaging. Metastatic lesions initially appeared as small enhancing nodules, often multiple, in the dural space along the surface of the cord (Fig. 3). Over time, these small nodules can grow into larger masses with the potential

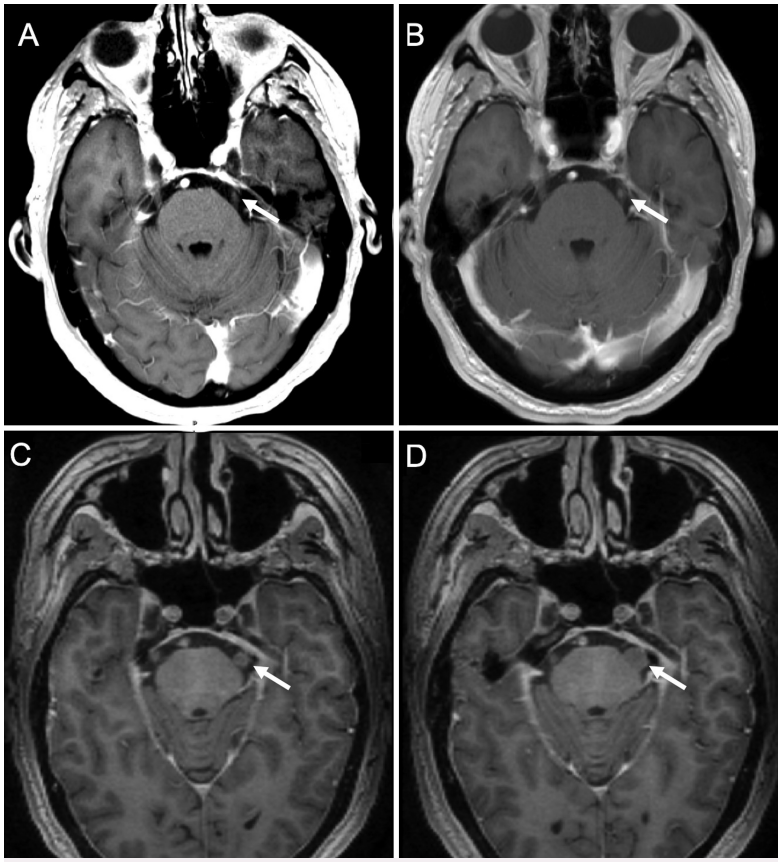


**FIG. 5.** Case 2. Axial T1-weighted postcontrast images demonstrating subtle asymmetric enhancement of the left trigeminal nerve (**A**), which becomes more prominent on 3-month follow-up imaging (**B**) and continues to progress to a discrete, minimally to nonenhancing nodule on the 6-month (**C**) and 9-month (**D**) follow-up, as indicated by the *arrows*.

for cord compression. Therefore, it is crucial to identify these nodules early and maintain vigilance when *MYCN*-amplified spinal ependymoma is suspected. Imaging of the entire spine is essential, with protocols optimized for detecting leptomeningeal disease, including steady-state free precession sequences.

The patient in case 2 notably exhibited intracranial involvement with disseminated leptomeningeal disease involving the brainstem and cranial nerves. These intracranial lesions were T1 isointense, T2 hyperintense, and mildly to nonenhancing (Figs. 4 and 5). Although these lesions were not directly biopsied, they are presumed to be metastatic *MYCN*-amplified spinal ependymoma. The patient in this case was unique in that their pathology was reported as a grade III ependymoma with *MYCN* amplification and a *PTEN* mutation. *PTEN* mutations are linked to various hamartomatous syndromes, including Lhermitte-Duclos disease, and are associated with high-grade glial tumors when part of a 10q deletion.[9,10] A case study has similarly reported the concomitant loss of *PTEN* in an anaplastic grade III ependymoma with *MYCN* amplification; however, that patient did not have intracranial involvement.[11] In prostate cancer, *MYCN* amplification combined with *PTEN* disruption has been shown to contribute to more aggressive disease and poor clinical outcomes.[12] Larger studies exploring the interaction between *MYCN* amplification and *PTEN* loss are warranted. Regardless, the potential for intracranial involvement in *MYCN*-amplified spinal ependymoma should be considered in surveillance strategies.

Given the aggressive nature of *MYCN*-amplified spinal ependymomas, it is crucial to differentiate them from other types of spinal ependymomas. Non–*MYCN*-amplified classic spinal ependymomas are the most common intramedullary neoplasm in adults.[13] Most are grade 2 lesions, with grade 3 being rare. These lesions are unencapsulated but well-circumscribed tumors with associated cord expansion that favor the cervical cord and span an average of four vertebral body levels. They are T1 iso- to hypointense with enhancement and T2 hyperintense with associated cord edema. Hemorrhage can result in the "cap sign" with a T2 hypointense hemosiderin rim, though this is not a specific finding. Associated cysts and syringohydromyelia can occur, but calcification is uncommon.[14–16] These tumors compress rather than infiltrate the cord tissue, preserving a cleavage plane between the tumor and spinal cord.[17] Recurrence is rare following complete resection.

Myxopapillary ependymomas are a variant of ependymomas found almost exclusively in the conus or cauda equina. Although historically classified as grade 1 lesions, they have been upgraded to grade 2 in the fifth edition of the WHO classification of CNS tumors because their recurrence rate is similar to that of other spinal ependymomas.[5] These lesions are intradural extramedullary in location and appear lobulated,

encapsulated, and sausage-shaped. They are T2 hyperintense with homogeneous enhancement. Associated features can include hemorrhage, calcification, or cystic degeneration.[13–15] Myxopapillary ependymomas are generally slow growing with a good prognosis.

### Lessons

The major limitation of our study is the small size of this case series; however, given the scarcity of research on the imaging features of *MYCN*-amplified spinal ependymomas, even limited case series can be valuable for informing differential diagnoses. These observations can also aid in developing clinical and imaging follow-up protocols and guiding discussions on management and prognosis once the diagnosis is confirmed. As awareness of this entity grows, our case series can serve as a foundation for further exploration of findings and associations related to this tumor subtype. We have presented three cases of *MYCN*-amplified spinal ependymoma, a rare, aggressive subgroup of spinal ependymomas with unique imaging features including an intradural extramedullary location and a disseminated recurrence pattern.

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### Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

### Author Contributions

Conception and design: both authors. Acquisition of data: Zhou. Analysis and interpretation of data: both authors. Drafting the article: Zhou. Critically revising the article: Zhou. Reviewed submitted version of manuscript: both authors. Approved the final version of the manuscript on behalf of both authors: Zhou. Administrative/technical/material support: Zhou. Study supervision: Cha.

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