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Surgical treatment of a clival-C2 atypical teratoid/rhabdoid tumor

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Abstract

The authors present the case of en bloc resection of a clival-C2 atypical teratoid/rhabdoid tumor. These aggressive lesions of early childhood generally occur in the cerebellum or cerebral hemispheres. This 7-year-old boy presented with pain on turning his head and was found to have a clival-C2 mass. A metastatic workup was negative for disseminated disease. A transoral biopsy procedure revealed an atypical teratoid/rhabdoid tumor on histological examination. The tumor was resected via a transoral approach, and the patient's spine was stabilized with posterior instrumented fusion from the occiput to C-5. Postoperatively, the patient underwent 16 months of chemotherapy along with 6 weeks of overlapping radiation therapy. Twenty-seven months after the initial surgery he presented with leg pain and was found to have a solitary metastatic lesion at the conus medullaris. There was no local recurrence at the clivus. The conus tumor was resected and found to be consistent with the primary tumor. Several months later the patient presented with disseminated intrathecal disease and ultimately died 42 months after the initial resection.

Keywords

medulloblastoma; transoral approach; clivus; atypical teratoid/rhabdoid tumor

A typical teratoid/rhabdoid tumors are aggressive lesions that most often occur in early childhood.[4,8,16,18] In the past these lesions have been misdiagnosed as primitive

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neuroectodermal tumors, but pathological and molecular genetic analyses have defined this tumor as a distinct entity.[3,18]

More than one-half of AT/RTs occur as lesions of the posterior fossa, although they have been described in other intracranial locations as well as extramedullary sites.[16] Spinal locations are extremely rare, and there has been only 1 report of a patient presenting with this tumor type in the clivus.[12] In that report the tumor was diagnosed using a biopsy procedure, but the patient did not undergo radical surgical treatment and the patient's family refused adjuvant therapy. The patient died 6 months after presentation. The case presented here is the first instance of managing a clival region AT/RT with en bloc resection followed by aggressive chemotherapy and radiation therapy.

Case Report

History and Examination

This 7-year-old boy presented with an 11-month history of neck pain on turning his head and a 4-month history of photophobia. He presented to our institution after plain radiographs had shown a widened atlantodens interval, and subsequent MR imaging revealed an enhancing mass compressing the brainstem and upper spinal cord from the clivus to C-2 (Fig. 1A and B). Computed tomography scanning showed that the mass had partially eroded the clivus and C-2 (Fig. 1D). A metastatic workup was negative. The patient was admitted to the Children's Hospital of Philadelphia for a transoral needle biopsy procedure. The pathology results indicated numerous rhabdoid cells with a mixture of neuroepithelial and mesenchymal components (Fig. 2A–C) and the loss of *INI1* expression (Fig. 2D), consistent with an AT/RT.[11] Molecular genetic studies using an Illumina 550K single nucleotide polymorphism–based genotyping array platform subsequently demonstrated a homozygous loss of the 22q11.2 region that contains the *INI1* gene.

Even though AT/RTs are aggressive tumors that do not respond well to chemotherapy or radiation therapy, older children who undergo complete resections can live for several years thereafter.[6,9,20,22] Thus, the family was given the options of nonsurgical management, a low-morbidity debulking procedure, or an aggressive 2-stage anterior/posterior procedure to remove the tumor en bloc. The family chose complete resection, and given the patient's older age and atypical tumor location, all of the treating physicians agreed that this procedure was the best treatment option. The goal of the posterior approach was stabilization, whereas the goal of the anterior approach was en bloc resection.

Treatment

The patient underwent instrumented fusion from the occiput to C-5 with Synthes Axon occipital screws, lateral mass screws, and rods. Given the extent of the tumor and the amount of bone that had to be removed from C-1 and -2 to achieve complete resection via the anterior approach, the C-1 and -2 levels were skipped. For the first time in 11 months, the patient's axial neck pain was gone and he was no longer photophobic. Two days later he returned to the operating room for an anterior resection. To assure adequate exposure a tracheostomy tube was placed, the patient's mandible was split, and his tongue was pushed inferiorly (Fig. 3A and B).[2,7,15,17] Following removal of the anterior arch of C-1 a high-speed bur was used to remove bone from the clivus and the body of C-2 until virgin dura was exposed. The tumor was completely extradural and removed en bloc with complete preservation of neurological function and without CSF leakage (Fig. 3C and D). The patient was placed in a halo after the anterior procedure (Fig. 3E).

Posttreatment Course

Postoperative imaging demonstrated GTR (Fig. 1C and E). Ten days after surgery the tracheostomy tube was decannulated. Six months after surgery the patient's midline incision was barely noticeable (Fig. 3F).

Treatment for AT/RT includes radiation and chemotherapy after a surgical biopsy procedure or resection. Despite intensive therapies a local recurrence, a metastatic lesion, or both will eventually develop in most children. Our patient began on the Boston AT/RT CNS clinical trial guidelines and received vincristine, doxorubicin, cyclophosphamide, cisplatinum, etoposide, and intrathecal methotrexate, hydrocortisone, and ARA-C prior to the initiation of radiation. Two months after surgery he received 5400 cGy of involved-field radiation over a 6-week period. During radiation treatment, he also received vincristine, cisplatin, etoposide, and cyclophosphamide but no further doxorubicin until after the completion of radiation. Treatment was completed with intrathecal chemotherapy as well as systemic courses of vincristine/doxorubicin and ultimately actinomycin/cyclophosphamide and additional courses of temozolomide and actinomycin. The patient had the expected complications of mucositis, radiodermatitis, and myelosuppression but overall tolerated this therapy well. A gastrostomy tube was placed for nutrition because of the morbidity related to the chemotherapy and radiation therapy. Chemotherapy was completed 16 months after the resection.

The patient returned 27 months after the initial surgery with left posterolateral thigh pain and slightly decreased strength in his left lower extremity. An MR image demonstrated no tumor at the site of the primary resection; however, an MR image of the lumbar spine revealed a 2-cm extramedullary mass filling the thecal sac at the L-1 level (Fig. 4A and B). The patient underwent a laminectomy from T-12 to L-1, and the tumor was removed (Fig. 4C). The pathology of this lesion was consistent with the previously resected tumor. The boy underwent high-dose chemotherapy and a stem cell rescue clinical trial following resection. Unfortunately, he subsequently relapsed with disseminated disease and died of progressive disease 42 months after the original resection.

Discussion

This patient presented the senior authors with the following management issues. The first was obtaining a diagnosis before recommending an intervention. Tumors in this location in patients of this age group are rare. The considered pathological entities based on the patient's preoperative plain radiography, CT, and MR imaging included chordoma, neuroblastoma, Ewing sarcoma, Langerhans cell histiocytosis, lymphoma, and rhabdoid tumor. The treatment regimen for these different diagnoses varies, ranging from upfront chemotherapy or radiation or both to upfront aggressive resection followed by adjuvant therapy. We elected to perform a transoral biopsy procedure to rule out lesions that should be treated by the oncology service either entirely or prior to attempting a complete resection. The histological diagnosis of AT/RT was confirmed on biopsy based on the deletion of *INI1*. The second management issue was the surgical approach. The treatment for AT/RT is upfront GTR followed by intensive chemotherapy and radiation therapy.[6] After detailed discussions with the neurooncology service, general oncology service, and the family, the decision was made to proceed with upfront surgery with the goal of complete resection.

Our institution has extensive experience with open and endoscopic skull base surgeries. Even though we used a large open anterior approach to the tumor in this case, lesions of the clivus can be effectively approached via an endoscopic endonasal approach, even in children.[1,5,10,13,19] However, given the extent of bony erosion of the clivus and the odontoid process as well as the presence of tumor anterior and posterior to C-2, we believed that fusion was required for stabilization after the resection. We determined that the best chance of safely achieving a

complete resection was through maximum exposure via a mandible-splitting, tongue-sparing approach. Our approach provided outstanding exposure and allowed the mass to be safely removed en bloc. This approach has been extensively used by other authors for similarly aggressive tumors in this location. [14,21] The patient tolerated the procedure extremely well and suffered no long-term surgical morbidity from the anterior approach. He required a gastrostomy tube for nutrition, but that was caused by the chemotherapy and radiation therapy. After completing the chemotherapy regimen, the patient returned to school fulltime and resumed all of his normal activities.

Despite the complete resection, aggressive chemotherapy and radiation therapy, and no local recurrence, the patient presented with a metastasis to his lumbar spine 27 months after the resection. Since he had only 1 lesion, he underwent resection and again fared well. Unfortunately, 13 months after this resection another recurrence developed, and this time it was disseminated. The patient died 42 months after the original resection.

This case is only the second reported instance of an AT/RT appearing as a clival mass and the first report of treating it with an en bloc resection. In the previous report by Kazan et al.,[12] the authors performed a posterior open biopsy procedure to confirm the diagnosis, but the patient did not undergo a radical resection or receive additional treatment and died within 6 months of the diagnosis. Our patient underwent both GTR and aggressive chemotherapy and radiation therapy and had a significant improvement in survival. Unfortunately, as is common with the aggressive nature of AT/RTs, the tumor recurred and was fatal. Given the rarity of AT/RTs in general and their occurrence at the clivus in particular, it is difficult to make firm recommendations for their management; however, there are data showing that patients with atypical presentations of AT/RTs can have a prolonged survival compared with patients with typical presentations.[6,9,20,22]

Conclusions

The AT/RT is a rare and aggressive tumor of early childhood and can occur in unusual locations. Although these lesions are associated with a poor outcome, the overall prognosis for AT/RTs located outside the posterior fossa in older patients is unclear given their rarity. Based on reports showing prolonged survival with this subset of AT/RTs that are treated with complete resection and based on our own experience, we advocate GTR followed by aggressive chemotherapy and radiation.

Abbreviations used in this paper

AT/RT	atypical teratoid/rhabdoid tumor
GTR	gross-total resection

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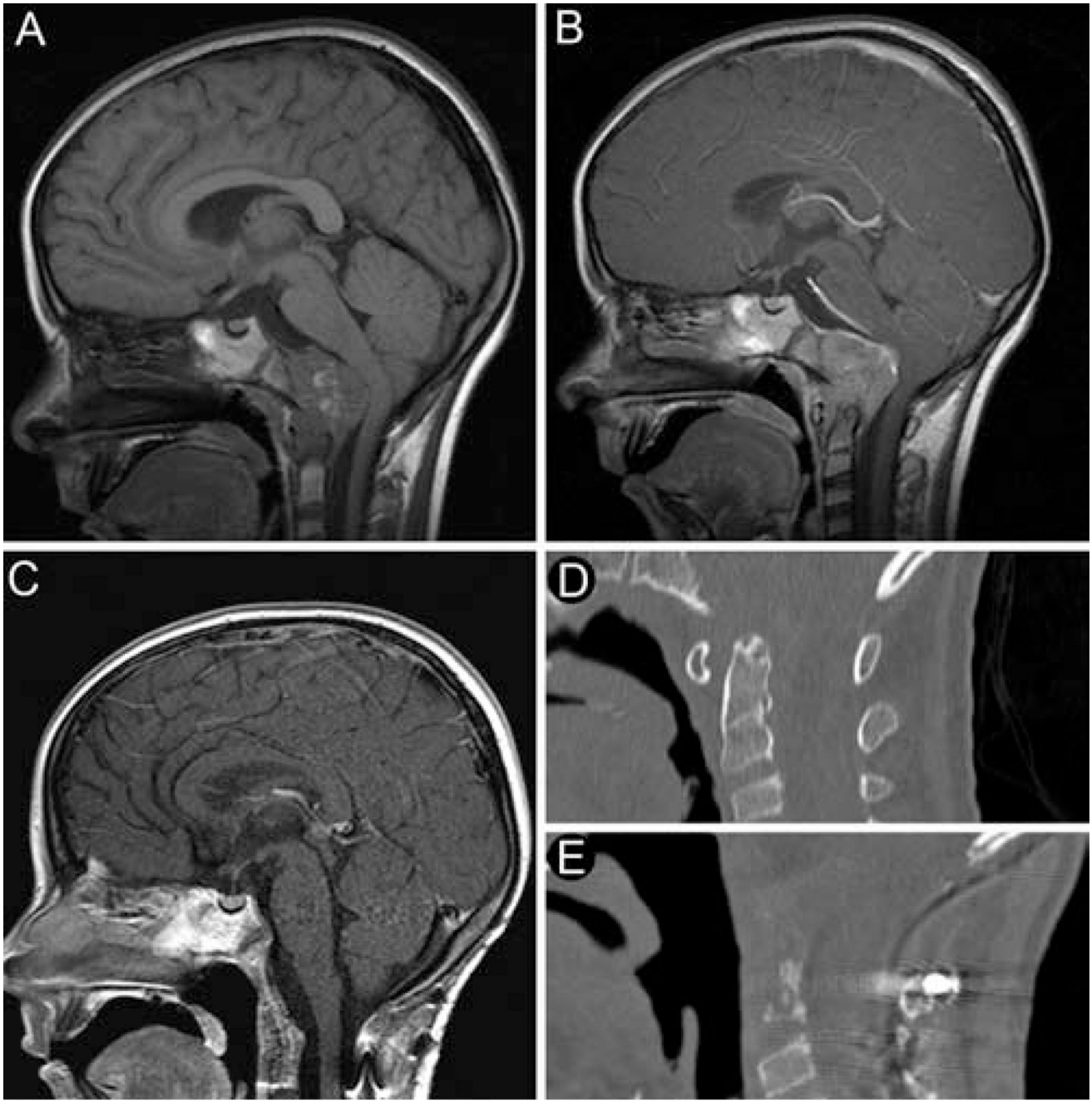

FIG. 1.

Preoperative sagittal precontrast **(A)** and postcontrast **(B)** MR images demonstrating an enhancing clival-based tumor with mass effect on the brainstem. Postoperative sagittal MR image **(C)** revealing resection of the mass. Preoperative CT scan **(D)** demonstrating tumor and bony erosion of the clivus and dens, and postoperative CT scan **(E)** showing removal of the tumor, dens, most of the body of C-2 and the inferior half of the clivus.

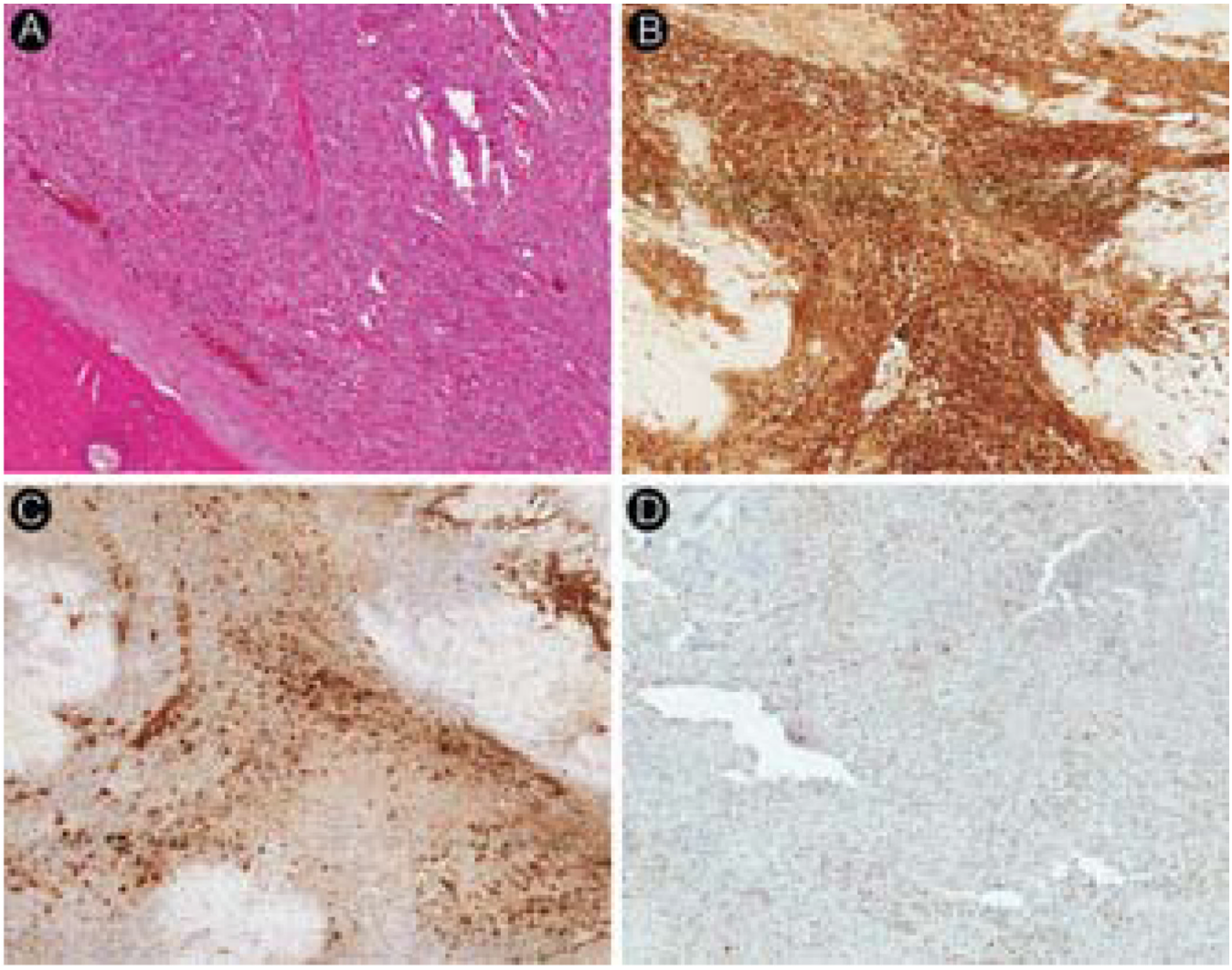

FIG. 2.

Photomicrographs showing spindle and epithelioid tumor cells adjacent to bone **(A)**, tumor cells with strong expression of cytokeratins (AE1.3, **B**), epithelial membrane antigen focally **(C)**, and diffuse loss of nuclear *INI1* expression in large neoplastic cells but retained expression in intratumor vasculature and lymphocytes **(D)**. H & E **(A)**, original magnification × 100.

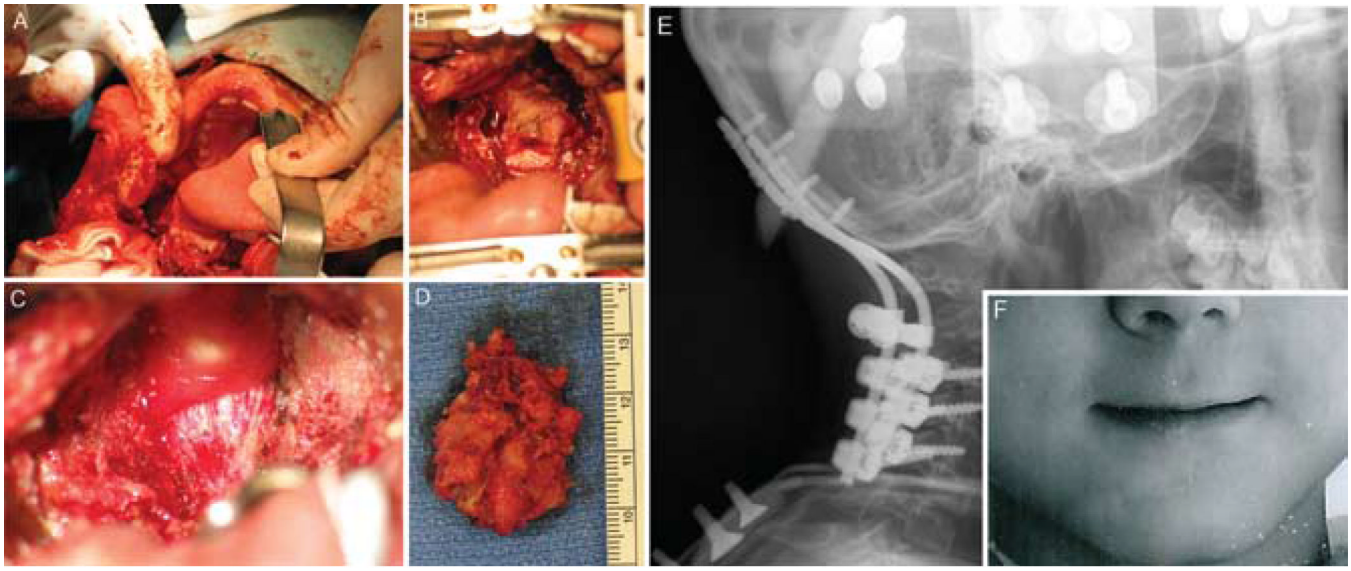

FIG. 3.

Intraoperative and postoperative images showing the transoral approach to the clival mass **(A)**, the mass itself **(B)**, the anterior dura and ligaments **(C)**, the resected tumor specimen **(D)**, post–posterior fusion and alignment in the halo **(E)**, and the anterior surgical incision 6 months after surgery **(F)**.

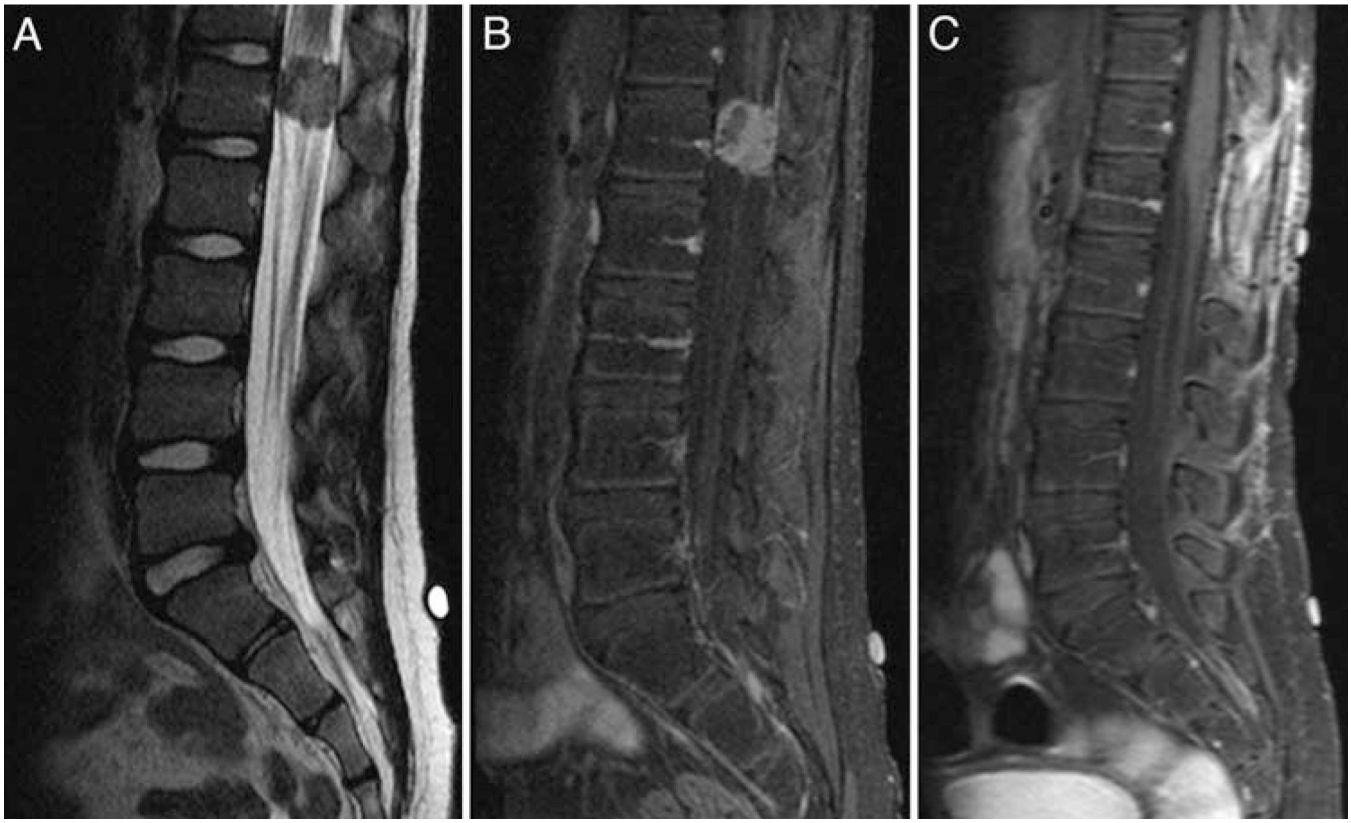

FIG. 4.
Preoperative sagittal MR images, precontrast **(A)** and postcontrast **(B)**, demonstrating an enhancing mass at L-1. Postoperative sagittal MR image **(C)** confirming resection of the mass.