Paraparesis caused by intradural thoracic spinal granuloma secondary to organizing hematoma: illustrative case

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BACKGROUND Spinal granulomas form from infectious or noninfectious inflammatory processes and are rarely present intradurally. Intradural granulomas secondary to hematoma are unreported in the literature and present diagnostic and management challenges.

OBSERVATIONS A 70-year-old man receiving aspirin presented with encephalopathy, subacute malaise, and right lower extremity weakness and was diagnosed with polysubstance withdrawal and refractory hypertension requiring extended treatment. Seven days after admission, he reported increased bilateral lower extremity (BLE) weakness. Magnetic resonance imaging showed T2–3 and T7–8 masses abutting the pia, with spinal cord compression at T2–3. He was transferred to the authors' institution, and work-up showed no vascular shunting or malignancy. He underwent T2–3 laminectomies for biopsy/resection. A firm, xanthochromic mass was resected en bloc. Pathology showed organizing hematoma without infection, vascular malformation, or malignancy. Subsequent coagulopathy work-up was unremarkable. His BLE strength significantly improved, and he declined resection of the inferior mass. He completed physical therapy and was cleared for placement in a skilled nursing facility.

LESSONS Spinal granulomas can mimic vascular lesions and malignancy. The authors present the first report of paraparesis caused by intradural granuloma secondary to organizing hematoma, preceded by severe refractory hypertension. Tissue diagnosis is critical, and resection is curative. These findings can inform the vigilant clinician for expeditious treatment.

https://thejns.org/doi/abs/10.3171/CASE22432

KEYWORDS inflammation; intradural hematoma; neurocritical care; spinal cord injury; spinal granuloma; spine surgery

Spinal granulomas are subacute to chronic inflammatory masses commonly caused by infectious (e.g., pyogenic abscess, tuberculosis) or noninfectious (e.g., autoimmune, foreign body in extra-axial space) processes.[1,2] Tuberculous and fungal granulomas are formed from compact aggregates of activated macrophages (histiocytes) and lymphocytes with characteristic central caseous necrosis, whereas pyogenic granulomas are suppurative with liquefactive necrosis from neutrophils.[3,4] In contrast, noninfectious granulomas are composed of epithelioid macrophages and few lymphocytes, without caseous necrosis.[3] Diagnosis and management of spinal granulomas are challenging due to differences in systemic and neurological clinical presentation, because formal diagnosis requires tissue.[5] In intradural cases, a thoughtful and expeditious approach to the possible etiologies and the delicate surrounding anatomy is required to inform medical decision making.

Although spinal hematomas are commonly associated with vascular malformations, anticoagulation, malignancy, and trauma, granuloma formation from a spinal hematoma is exceedingly rare. In a review of 613 patients with spinal hematomas, the frequency of epidural, subdural, subarachnoid, and intramedullary locations was 75%, 4%, 16%, and 1%, respectively.[6] Common etiologies of intradural hemorrhage include

vascular malformation rupture (arteriovenous malformation [AVM], spinal angioma/cavernous malformation) and rupture of dural, radicular, and/or subarachnoid vessels during microtrauma (e.g., lumbar puncture) or hemodynamic instability (e.g., increase in intrathoracic or intra-abdominal pressure); the latter becomes symptomatic usually only in the setting of coagulopathy or related comorbidities.[7–9] From an intraspinal perspective, Fukao et al.[10] described a single case of an epidural granuloma at T10 causing paraplegia 2 weeks after trauma in an 84-year-old male with chronic inflammation. To date, no report exists regarding intradural granuloma formation from hematoma unrelated to vascular malformation.

Herein we present a rare case of a 70-year-old male with multiple comorbidities presenting with subacute weakness found to have an intradural dorsal T2–3 mass causing spinal cord compression. After operative resection, the pathological diagnosis was granuloma secondary to organizing hematoma, without signs of infection. Specific diagnostic and management strategies are discussed.

Illustrative Case

Presentation to Outside Institution and Initial Evaluation

A 70-year-old male presented to an outside regional medical center with malaise and worsening right lower extremity (RLE) weakness over several days. His medical history was significant for bilateral carotid artery stenosis on aspirin, hypertension, prostatomegaly, polysubstance abuse, and remote C5–7 anterior fusion and L4–5 laminectomies for stenosis. He had mild chronic baseline RLE weakness (motor strength 4+/5), which progressed to inability to ambulate without assistance before presentation. The patient did not recall recent trauma and did not have urinary incontinence.

The patient was diagnosed with hypertensive urgency, alcohol and methamphetamine withdrawal, and encephalopathy, prompting admission to the intensive care unit (ICU). Over 7 days, he required uptitration to 4 antihypertensive agents for refractory hypertension (systolic blood pressure 180–200 mm Hg, diastolic blood pressure 80–100 mm Hg) and developed posterior reversible encephalopathy syndrome (PRES). He was treated with benzodiazepines per Clinical Institute Withdrawal Assessment for Alcohol protocol and dexmedetomidine for agitation. After medical stabilization and emergence from encephalopathy, the neurological examination findings were RLE 3/5 and left lower extremity (LLE) 4/5 motor strength and numbness below the upper thoracic spine. Noncontrast lumbar spine magnetic resonance imaging (MRI) on hospital day (HD) 7 showed layering intrathecal blood without a compressive lesion. A comprehensive infectious work-up (systemic cultures, lumbar puncture with cerebrospinal fluid [CSF] analysis, infectious disease consultation) showed no systemic or intrathecal infection. Thoracic spine MRI with and without contrast on HD 11 showed dorsal extra-axial masses at T2–3 (3.5 × 1.2 × 0.6 cm) and T7–8 (0.7 × 0.6 × 0.5 cm) with intrinsic T1 hyperintensity, cystic T2 hypointensity, and peripheral contrast enhancement. The T2–3 mass was eccentric to the right, causing spinal cord compression and leftward deviation with central T2 cord signal change. The T7–8 mass was eccentric to the left and did not cause cord compression. There was myelomalacia distal to T11. Due to concern for spinal vascular malformations, the patient was transferred to our facility on HD 16 for a higher level of care.

Transfer to Our Institution and Interval Evaluation

Upon admission to our hospital, the patient was afebrile and reported unchanged bilateral lower extremity (BLE) weakness. The findings of his

neurological examination were as follows: alert and oriented × 3, right upper extremity motor: deltoid, biceps, and triceps 4+/5, grip and interossei 4/5; left upper extremity motor: 4+/5 throughout; RLE motor: iliopsoas and quadriceps 4−/5, tibialis anterior, external hallucis longus, and gastrocnemius 3/5; LLE motor: iliopsoas and quadriceps 4/5; tibialis anterior, external hallucis longus, and gastrocnemius 4−/5; incomplete T1 sensory level with worsening distal numbness, 3+ patellar reflexes, negative Babinski and clonus, positive rectal tone and sensation. He had subacute bilateral T2–3 radiculopathy with focal point tenderness in the upper thoracic region. His upper extremity weakness was chronic and unchanged, secondary to prior cervical fusion.

The patient was admitted to the hospital ward with standard neurological checks. He was restarted on his 4 oral antihypertensive agents, comanaged with our hospital medicine service. Aspirin was held in the setting of urgent diagnostic work-up. Given the presence of intradural masses, on HD 2 at our institution, computed tomography (CT) scans of the head, chest, abdomen, and pelvis with and without contrast were obtained to evaluate for primary malignancy, which was negative. On HD 3, he underwent MRI with and without contrast of the full neuraxis. The brain MRI showed a prior right lacunar infarct and resolved PRES without central nervous system (CNS) malignancy. The spine MRI confirmed two discrete dorsal intradural masses at T2–3 and T7–8 contiguous with the pia with characteristics similar to those in the outside hospital report (Fig. 1A–G). There was evidence of arachnoiditis of the lumbosacral nerve roots. The finding of spinal angiogram on HD 4 was negative for a shunting lesion.

BLE ultrasound was obtained due to prolonged immobility pretransfer, and a focal nonocclusive thrombus of the left tibioperoneal trunk was found. Although the patient did not report any symptoms of deep venous thrombosis (DVT), his reliability was limited due to BLE numbness. Because he could not be safely anticoagulated in the perioperative setting, an inferior vena cava (IVC) filter was placed on HD 4.

The patient was medically optimized for T2–3 laminectomies for biopsy and resection of the superior intradural mass. The leading preoperative diagnoses were cavernous malformation and less likely atypical hemorrhagic tumor or indolent infection.

Novel Approach for Localization in the Thoracic Spine

Localization in the thoracic spine presents challenges for identification of the correct operative level. Fiducial screw placement in the bony spine was not available at our institution. Preoperatively, the patient underwent low-dose CT of the cervical and thoracic spine. A large adhesive sheet with radiopaque gridlines was applied to the lower cervical and thoracic spine before acquiring the localization image. Using the radiopaque gridlines, the T2 (Fig. 2A and B) and T7 (Fig. 2D and E) spinous process tips were identified on imaging and physically marked on the patient. Although not part of the planned surgery, the T7 spinous process tip was identified to further aid intraoperative localization. The adhesive sheet was then removed, and a 1-mm spherical radiopaque marker attached to an adhesive was applied to the skin overlying the T2 and T7 spinous process tips (Fig. 2C). A final CT image was acquired to confirm correct anatomical placement of the markers. The markers were then covered with gauze and adhesive to maintain their placement while maximizing patient comfort (so as not to lie supine on the firm markers) before surgery (Fig. 2F).

Surgical Approach for Biopsy and Resection

The patient was positioned prone, and localizing fluoroscopy confirmed the T2 spinous process marked by the external fiducial marker.
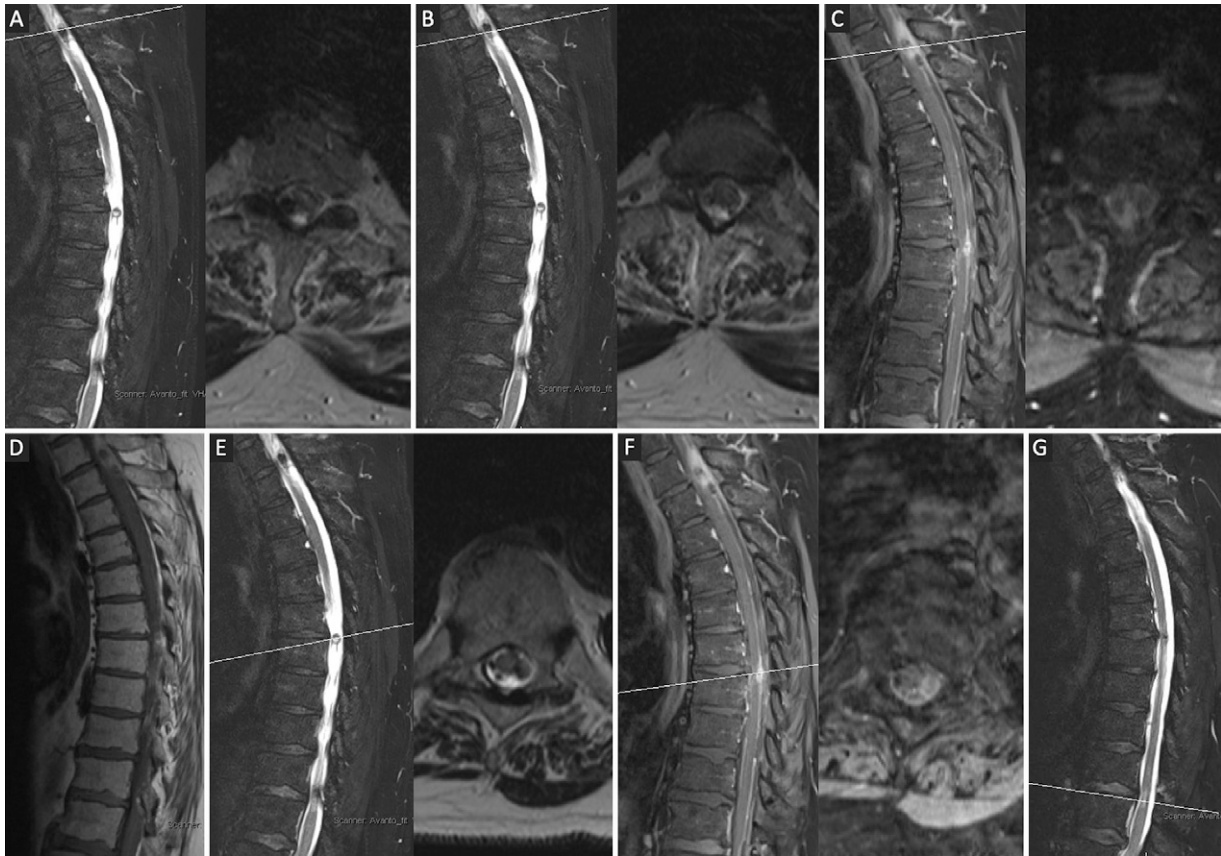
FIG. 1. Preoperative thoracic MRI with and without contrast showing two intradural masses at T2–3 and T7–8. **A:** T2-weighted sagittal and axial sequence at superior 50% of the superior mass, showing a right-eccentric hypointense mass that deviates the spinal cord to the left and T2 signal change within the spinal cord. **B:** T2-weighted imaging at inferior 50% of mass. **C:** T1-weighted contrast-enhanced sequence showing peripheral enhancement of the superior mass. **D:** T1-weighted sagittal image without contrast (axial image unavailable) showing intrinsic hyperintensity in the center. **E:** T2-weighted imaging of the inferior hypointense mass, which is left-eccentric, abutting the pia, without mass effect on the spinal cord. **F:** T1-weighted contrast-enhanced sequence of the inferior mass, showing peripheral enhancement (similar to panel C). **G:** T2-weighted midsagittal image showing myelomalacia at T11–12, consistent with remote injury.

The microscope was used for intradural work, and intraoperative images are provided in Fig. 3. Thickened arachnoid was found eccentric to the right, congruent with the preoperative MRI, and was opened sharply. Xanthochromic, membranous adhesions were found and removed using suction and blunt dissection. A firm, reddish-colored, nonpulsatile mass emerged, with superficial fibrinous deposits and a discrete plane that abutted the spinal cord pia. There was some mass effect; however, the spinal cord did not appear under severe pressure. Small blood vessels feeding and draining the mass in the subarachnoid space were cauterized and disconnected carefully to minimize risks of hemorrhage in the setting of thickened adhesions. The plane between the mass and the surrounding tissue was defined, and small pieces of the mass were removed for biopsy. There was no hemorrhage from the mass. Intraoperative pathology revealed rare foamy cells and fibrous tissue. The mass was circumferentially resected with visual gross total resection and sent for permanent pathology (final dimensions 10 × 5 × 5 mm). Intraoperative motor and somatosensory signals were stable.

Final Pathologic Diagnosis

Diagnostic pathology consisted of several features: (1) organizing granulation tissue with reactive fibroblasts and endothelial cells and (2) hemosiderin and hematoidin suggestive of old hemorrhage, layered fibrin suggestive of organizing hematoma, scattered foamy histiocytes, and reactive meningothelial cells with psammomatous calcifications. Pathology did not find evidence for AVM, cavernous malformation, hemangioblastoma, solitary fibrous tumor, metastatic carcinoma or melanoma, Langerhans cell histiocytosis, other malignancy, or infection. The final pathological diagnosis was most consistent with organizing hematoma (Table 1).

Treatment Course

The patient was admitted postoperatively to the ICU for close neurological monitoring with 24-hour lie-flat precautions followed by gradual mobilization. The findings of the patient's neurological examination on postoperative day (POD) 1 improved to RLE 4−/5 and LLE 4/5 strength. Postoperative MRI showed gross total resection of the T2–3 intradural mass (Fig. 4). He was transferred to the ward on POD 2 and improved with daily physical and occupational therapy to RLE strength 4/5 proximally, 4+/5 distally, LLE 4+/5 throughout, and decreased BLE numbness. He was cleared for discharge to a skilled nursing facility (SNF) on POD 8 for rehabilitation. Given interval neurological recovery, the patient declined surgical intervention for the T7–8 mass.
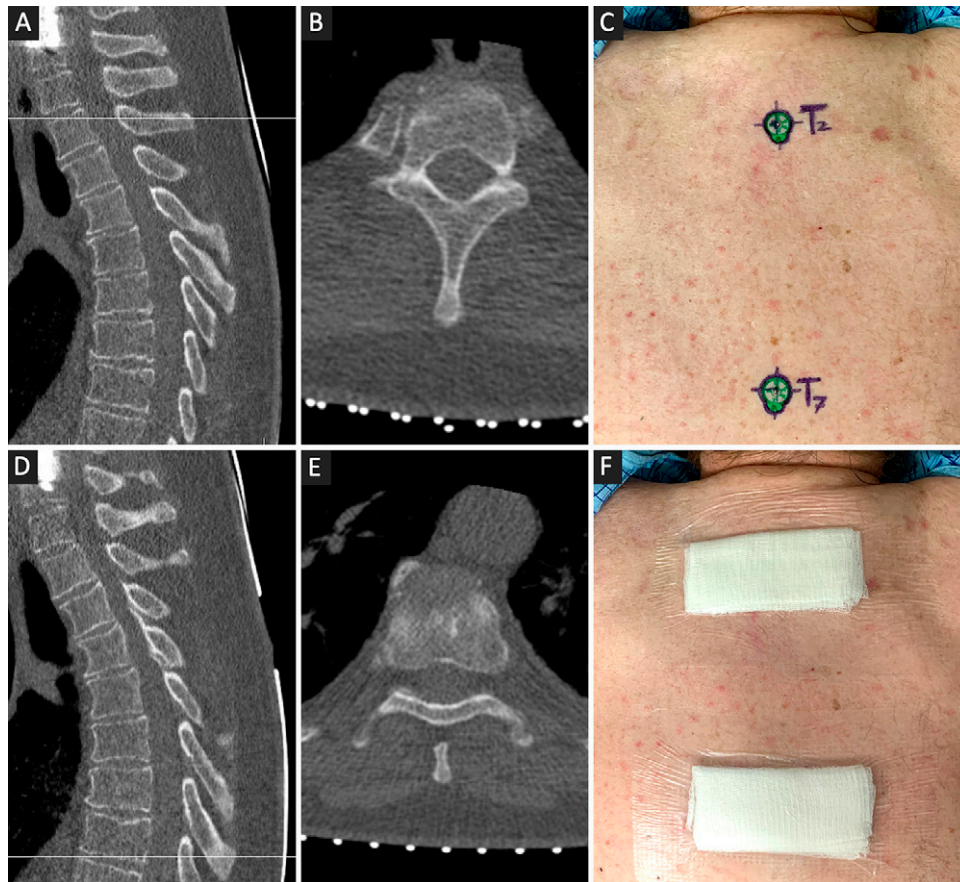
FIG. 2. Technique for noninvasive localization in thoracic spine. Fiducial screw placement was not available at our institution. Preoperatively, a large adhesive sheet with radiopaque gridlines was applied to the cervical and thoracic spine. **A:** Sagittal CT scan showing the T2 spinous process tip, and the radiopaque gridlines are seen immediately posterior to the soft tissue. Prior C5–7 construct is partially visualized at the *left superior corner* of the panel. **B:** Axial image showing the T2 spinous process tip and radiopaque markers to aid in identification. **C:** Circular radiopaque markers measuring 1 mm with adhesive placed at T2 and T7 spinous process tips after localization. **D and E:** Sagittal and axial images showing the T7 spinous process tip and radiopaque gridlines (similar to panels A and B). **F:** External fiducial markers carefully covered with gauze and transparent adhesive to maintain their position while maximizing patient comfort.

The preoperative DVT and final pathologic diagnosis of organizing hematoma raised concern for an underlying disorder, and the hematology service was consulted for evaluation and anticoagulation initiation. Hematology did not recommend further work-up, because the patient's complete blood count and coagulation factors remained within normal limits, and he had no history of excessive bleeding or clotting apart from the nonocclusive LLE DVT. Anticoagulation was to be initiated on POD 14, with elective removal of the IVC filter. Home aspirin was restarted on POD 10.

The patient was transferred back to the referring hospital on POD 10 to expedite referrals to local SNFs. There were no medical, surgical, or 30-day complications.

Discussion
Observations
Granulomas can form from infectious and noninfectious inflammatory processes. The incidence of spinal intradural granulomas is unknown due to their rarity. We present the first report of BLE paraparesis caused by a thoracic intradural granuloma secondary to organizing hematoma in the absence of infection, foreign body, or other previously reported etiology.

To date, literature on intradural granulomas is limited to 30–40 case reports, and primary etiologies consist of infection (most commonly tuberculous, followed by fungal, parasitic, or bacterial) or inflammation secondary to intrathecal catheter or foreign body, and rarely sarcoidosis or other causes. On MRI, granulomas show heterogeneous T1 and T2 signal and variable contrast enhancement (none, peripheral, or nodular) and can resemble vascular lesions, tumors, or cysts.[11] Understanding the mechanism of their formation and presentation is fundamental to developing appropriate surgical approaches and management guidelines.

Intradural hemorrhage in the spine has been attributed to sudden changes in intra-abdominal, intrathoracic, or intravascular pressure exceeding the extravascular CSF pressure, causing vessel rupture into the subdural and subarachnoid space (particularly from radiculomedullary veins);[12,13] rupture of inner dural surface vessels
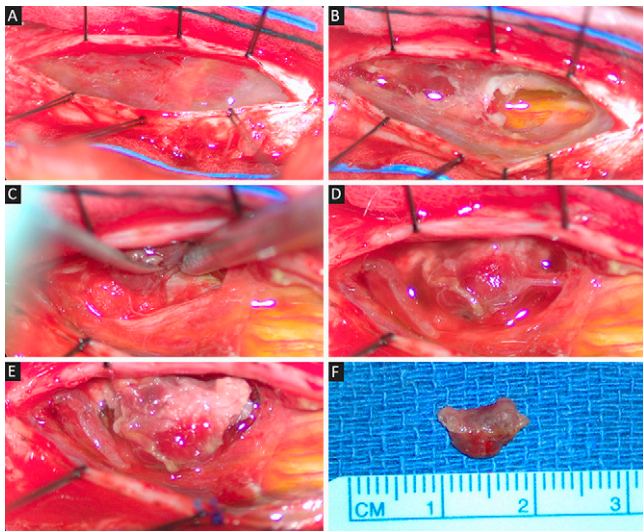
FIG. 3. Resection of T2–3 mass. The *left* side of each panel is cranial, and the *right* side of the panel is caudal. **A:** Dural opening with tack-up sutures and thickened arachnoid observed. **B:** Thickened arachnoid partially opened, with underlying xanthochromic fluid. **C:** Careful dissection of the plane between the right-eccentric intradural fibrinous mass and the spinal cord pia. **D:** Partial dissection of the fibrinous mass, with adhesions and small vessels emerging from its surface. **E:** Further dissection of the fibrinous mass from the surrounding planes. **F:** Fibrinous mass resected en bloc, measuring 1 cm in maximal dimension.

and subarachnoid hemorrhage (SAH) traversing the subdural space are alternative etiologies.[14] Regardless of the vascular origin, under normal physiological conditions, small SAHs are diluted in circulating CSF, which prevents clot formation. Profuse hemorrhage and/or underlying coagulopathy can alter normal CSF flow, causing stasis and hematoma organization,[15,16] and can lead to a chronic inflammatory

state that promotes granuloma formation. To date, a single 2009 report discussed the formation of an epidural granuloma from subacute epidural hematoma,[10] providing support for the intradural pathogenesis in our case.

The intradural granuloma in our patient presumably formed from subarachnoid and subdural hemorrhage. The mass was contiguous with the pia and showed evidence of xanthochromia upon dural opening. Given the characteristic T1/T2 signals on MRI, our leading hypothesis for its formation is hemorrhage from small radicular vessels and/or subdural veins in the setting of severe, prolonged refractory hypertension over the course of days to more than 1 week before his transfer. As a result, varying ages of small hemorrhages continued to activate inflammatory cascades and precipitated the granuloma. The progression from initial RLE weakness on admission to worsened BLE weakness after stabilization supports our hypothesis. The patient was receiving aspirin for his carotid stenosis, which can exacerbate the risk of occult hemorrhage. Arachnoiditis seen on his lumbar MRI is another contributor, because adhesions between the clumped nerve roots and subarachnoid space can impair CSF circulation and further induce inflammation.[17]

However, the timing of arachnoiditis is variable,[18] and in our patient, it could have resulted from prior trauma, chronic systemic inflammation, or remote history of lumbar decompression. Although the patient does not recall specific trauma immediately before his hospitalization and had no obvious fractures on CT, occult trauma is possible because the presenting history is unclear due to initial encephalopathy, and point tenderness was found in the upper thoracic spine on examination. It is unlikely that the granuloma resulted from the lumbar puncture at the outside institution, which was performed to evaluate existing intrathecal blood seen on lumbar MRI.

Lessons

We present the first report of paraparesis caused by a spinal intradural granuloma formed from organizing subdural/subarachnoid

TABLE 1. Comprehensive pathology results

	Result	Pathology Comment
Stain type		
CD1a	Negative	Against Langerhans cell histiocytosis
CD34	Negative	Against solitary fibrous tumor
Cytokeratin 8/18	Negative	Against metastatic carcinoma
HMB-45	Negative	Against metastatic melanoma
Melan A	Negative	Against metastatic melanoma
S100	Negative	Against hemangioblastoma
Inhibin	Negative	Against hemangioblastoma
GMS	Negative	Argues against infection
PASD	Negative	Argues against fungal infection
AFB	Negative	Against mycobacterial organisms
Characteristic		
Vascular spaces	Not observed	No cavernous malformation
Thick-walled arteries or veins	Not observed	No arteriovenous malformation

AFB = acid-fast bacteria; GMS = Grocott's methenamine silver; PASD = periodic acid-Schiff-diastase.
Comprehensive staining results and cellular characteristics observed in the operative specimen sent for final pathological diagnosis. CD1a, CD34, HMB-45, and S100 are the full names of their respective stain type.
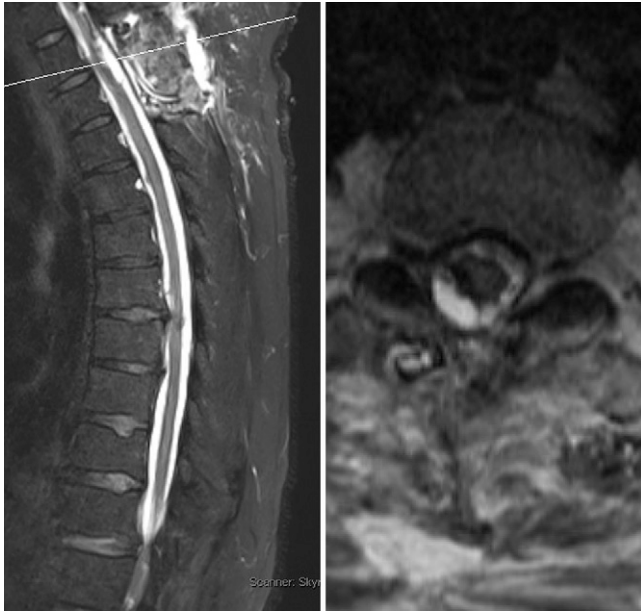
FIG. 4. Postoperative thoracic MRI with and without contrast obtained on POD 2 showed gross total resection of the T2–3 mass. The previously seen T1-hyperintense, T2-hyperintense mass is no longer present, and the space it previously occupied is replaced by CSF. The spinal cord has migrated back to midline.

hematoma after a period of refractory hypertension. Tissue diagnosis is critical because intradural granulomas can mimic vascular lesions and malignancy. Surgical resection is nuanced due to the differential diagnosis. The patient's BLE strength and sensation improved after resection due to removal of the mass effect on the spinal cord, which was curative.

Our report suggests that severe hemodynamic changes may be associated with spinal hematomas that present insidiously and/or evolve over time. The relationship between waxing and waning hypertensive episodes and progressive damage of delicate radicular arteries and subdural veins underscores the need for expeditious treatment of refractory hypertension to minimize risk of unexpected morbidity. Importantly, after pathologic diagnosis of organizing hematoma, we consulted hematology to address the concern for occult coagulopathy, which was ruled out in our patient.

Although no local or systemic signs/symptoms of infection were found, we cannot exclude the possibility of remote infection, because no imaging before this admission was available. We were also limited by the relative scarcity of documentation of serial neurological examinations before transfer to our institution. The importance of clinical history, serial neurological examinations, and acquisition of full neuraxis imaging in any patient presenting with neurological deficits for the goal of establishing a timeline for CNS pathology cannot be overstated, especially if neurological examinations are confounded by intubation and encephalopathy. Notably, we describe our facile and noninvasive technique for CT-guided placement of external fiducial markers to aid intraoperative localization in the thoracic spine as an option when bony fiducial screw placement is unavailable.

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Author Contributions

Conception and design: Yue, Lee, Huang. Acquisition of data: Yue, Lee, Huang. Analysis and interpretation of data: Yue, Lee, Quintana, Krishnan, Wozny, Andrews, Huang. Drafting the article: Yue, Lee, Quintana, Krishnan, Wozny, Andrews, Huang. Critically revising the article: all authors. Reviewed submitted version of manuscript: Yue, Lee, Quintana, Krishnan, Wozny, Andrews, Huang. Approved the final version of the manuscript on behalf of all authors: Yue. Statistical analysis: Yue. Administrative/technical/material support: Yue. Study supervision: Yue, Huang.

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