Primary extradural paraganglioma of the thoracic spine: A case report

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ABSTRACT

Paragangliomas are rare, mostly benign neuroendocrine tumors arising from autonomic paraganglia. Spinal paragangliomas are uncommon, and among these, paragangliomas of the thoracic spine are distinctly unusual. We present the case of a primary paraganglioma of the extradural thoracic spine in a 34-year-old woman.

CASE REPORT

CASE REPORT

A 34-year-old woman was admitted to the hospital after acute loss of motor and sensory function in lower extremities as well as urine and bowel incontinence. On admission, the patient was normotensive and was not diaphoretic, tachycardic, tremulous or pale. The patient denied recent trauma, chest pain, palpitations, dysphagia, vision changes or headaches. Thoracic MRI revealed a 5.7 x 4.8 x 1.6 cm extradural, mildly enhancing mass spanning from T6 to T8 with spinal canal stenosis and dorsal cord compression at T6-T7 level as well as extension into the left T7-T8 neural foramen and left paraspinal soft tissues (Fig 1). The lesion was relatively iso-intense to spinal cord on T1 weighted imaging (T1WI) and T2 weighted imaging (T2WI). Spinal cord in affected region showed increased T2 signal intensity with no enhancement of the cord or myelomalacia. Differential considerations included lymphoma, metastasis and meningioma, though lymphoma was considered most likely given appearance on imaging, patient's age and absence of known primary malignancy. Emergent T6-T8 decompressive laminectomy and tumor resection was performed. Pathological examination of the mass demonstrated positivity for synaptophysin, elevated chromogranin A, and indiscernible mitotic activity, confirming the diagnosis of a neuroendocrine tumor.

Nine days post-operatively, an octreotide scan revealed residual neuroendocrine tumor with increased somatostatin receptors at the left T7 paravertebral region and midline T8-T9 level (Fig 2) with no other masses suggestive of a separate primary origin. Subsequent radiation therapy was performed and the patient followed up with physical rehabilitation. An MRI performed four months post-operatively showed no recurrence at resection site and stable left paravertebral region residual lesion (Fig 1).

DISCUSSION

Pathology Overview:

Paraganglia are clusters of non-neuronal cells originating from the neural crest that are located throughout the body in association with sympathetic and parasympathetic nervous systems [1]. Rarely, paraganglia can undergo neoplastic transformation to become paragangliomas. Paragangliomas are vascular, neuroendocrine tumors of the autonomic nervous system comprised of paraganglion cells [1]. All paragangliomas contain neurosecretory granules, but few actually secrete catecholamines [1]. Most paragangliomas are relatively slow growing, non-functional and benign; however, some may be malignant or functional, potentially causing symptoms such as hypertension, tachycardia, and diaphoresis [2].

Paragangliomas can be derived from either parasympathetic or sympathetic nervous system ganglia. Parasympathetic paragangliomas are mostly non-functional and most commonly arise in the carotid body or jugular foramen [3]. Sympathetic paragangliomas are mostly catecholamine-secreting with approximately 80-90% located in the adrenal medulla (termed "pheochromocytomas") and 10-20% located outside of the adrenal medulla along the sympathetic chain anywhere from the neck to the urinary bladder, particularly in the organ of Zuckerkandl [1]. The exact incidence of paragangliomas is not known; the estimated prevalence is 0.2-1/100,000 [1]. Spinal paragangliomas are uncommon and usually present as intradural tumors of the filum terminale and cauda equina. Thoracic spinal paragangliomas are rare, with only 15 reported cases [1].

Etiology & Demographics:

Paragangliomas are most commonly spontaneous; however, approximately 40% of paragangliomas arise as part of a hereditary syndrome, often involving Multiple Endocrine Neoplasia type 2A/2B (MEN2A/2B), Von Hippel-Lindau syndrome (VHL) or Neurofibromatosis type 1 (NF1) [1]. Spontaneous paragangliomas usually present between the third and fifth decade of life while hereditary paragangliomas usually present earlier in life [1]. The spontaneous form occurs more commonly in women (71%) than men (29%) while the hereditary form occurs equally in men and women [4].

Clinical & Imaging Findings:

Spinal paragangliomas are often asymptomatic, with back pain being the most common symptom [5]. In the uncommon case of a functional paraganglioma, the patient can present with the features of a pheochromocytoma such as hypertension, episodic headaches, diaphoresis, and tachycardia [2]. Depending on the size and location of the paraganglioma, the patient may also present with mass effect findings. In the case of spinal lesions, mass effect can include local or radicular pain, radiculopathy, and, if they involve the spinal cord, myelopathy like the paraplegia seen in our patient.

The diagnosis of thoracic paragangliomas is usually made postoperatively via MRI with subsequent histopathological evaluation. On MRI, thoracic spinal paragangliomas are nonspecific and display low to intermediate signal on T1 and intermediate to high signal on T2 with variable enhancement (Fig 1) [3]. The classic radiographic characteristics of head and neck paragangliomas (a "salt and pepper" appearance on T2WI due to hypervascularity of paragangliomas, serpiginous flow voids, and a peripherally T2-hypointense rim around the mass relating to presence of hemosiderin) are usually not present.

In our case, Octreotide scan was used for post-operative monitoring for residual tumor. Octreotide is a somatostatin analogue that binds to tumor cells that have somatostatin receptors. It is useful in detection of neuroendocrine and endocrine tumors. To our knowledge, utilization of octreotide scintigraphy for confirmation of spinal paragangliomas has not been documented outside of rare occasions for the detection of neck paragangliomas. Octreotide scintigraphy is useful in the evaluation of patients with spinal neuroendocrine tumors post-operatively for residual, recurrent, or metastatic lesions.

Other Diagnostic Evaluations:

Histologically, paragangliomas have a typical "Zellballen" pattern, which describes nests of uniform cells surrounded by vascular tissue [5,6]. Immunohistochemical analysis is routinely positive for chromogranin A and synaptophysin [3,6,7,8]. A 24-hr urine metanephrine and plasma metanephrine analysis can be used to evaluate the functionality of sympathetic paragangliomas.

Differential Diagnosis:

The differential diagnosis for an extradural thoracic spinal mass includes but is not limited to paraganglioma, hematoma, meningioma, neurofibroma, abscess-phlegmon, metastasis, multiple myeloma, lymphoma, and angiolipoma.

Epidural Hematoma

On MRI, epidural hematomas vary in presentation based on the timing of evolution and are usually heterogeneous in signal. For instance, early subacute hematomas are hyper-intense on T1WI and hypo-intense on T2WI. Late-subacute hematomas are hyper-intense on T1 and T2WI while chronic hematomas are hypo-intense on T1WI and T2WI. On CT, lesion is hyper- or iso-dense to soft tissues. Subacute and chronic hematomas may enhance peripherally. Epidural hematomas usually occur in patients who have had spinal dural puncture or trauma. These patients also usually have some form of bleeding diathesis.

Meningioma

Spinal meningiomas typically present as iso-intense to the cord on T1WI and T2WI, though presentation on T2WI can vary based on presence of calcifications or cystic degeneration. On CT, lesions are iso-dense to spinal cord, occasionally with calcifications. On contrast imaging, lesions are well circumscribed and homogeneously enhancing, often with visible dural tails. SPECT/PET shows increased tracer uptake and is used primarily to evaluate for recurrence or residual tumor after resection.

Neurofibroma

Neurofibromas are usually iso-intense to cord on T1WI and iso- or hyper-intense to cord on T2WI with variable enhancement. On CT, neurofibromas are iso-dense to spinal cord with mild homogeneous enhancement. PET is not commonly used in diagnosis of these tumors; however, metabolically active tumors are FDG avid. Lesions vary in size, but commonly involve multiple nerve roots. Patients usually also present with other stigmata of Neurofibromatosis type 1 such as Café-au-lait spots, Lisch nodules (pigmented hamartomas of the iris), cutaneous neurofibromas and optic gliomas.

Epidural Abscess

Epidural abscesses show restricted diffusion, seen as hyper-intensity on diffusion-weighted imaging (DWI) and

hypo-intensity on apparent diffusion coefficient (ADC). They are iso- or hypo-intense to the cord on T1WI and hyper-intense on T2WI with peripheral enhancement. On CT, lesions show heterogeneous enhancement of involved soft tissues. Additionally, gallium scan, though not commonly used, will show increased uptake within abscess. Patients also usually have constitutional symptoms reflective of an infectious process (fever and sometimes hypotension).

Metastasis

Metastatic bone lesions present as focal or diffuse low to intermediate signal intensity on T1WI compared to the bone marrow. Lesions are usually iso- or hyper-intense on T2WI, and hyper-intense on STIR with homogeneous enhancement. On CT, diffuse or multifocal trabecular bone destruction can be seen, sometimes with an extra-osseous, enhancing soft tissue component extending into the epidural space. PET/CT and bone scan reveal increased tracer uptake. Patients often have a known primary malignancy prior to vertebral metastasis.

Multiple Myeloma

Bone involvement in Multiple Myeloma presents as focal or diffuse lytic lesions with low to intermediate signal on T1WI compared to bone marrow and with hyper-intense appearance on T2WI and STIR. Active lesions most commonly show diffuse enhancement. CT imaging similarly shows multifocal lytic lesions and may reveal enhancing extra-osseous soft tissue infiltration. Bone scan is usually negative, though PET/CT is useful for identifying metabolically active disease. Patients commonly present with back pain and have other findings associated with multiple myeloma including anemia, hypercalcemia, and renal dysfunction.

Lymphoma

Lymphoma of the spine has variable appearance on imaging depending on which structures it involves. Epidural lymphoma presents as iso-intense to the cord on T1WI and iso- or hyper-intense on T2 and STIR with intense, homogeneous enhancement. CT imaging shows mass that is iso- or hyper-dense to muscle. PET, gallium and bone scans show increased tracer uptake. Patients commonly present with back pain, though cord compression can occur.

Epidural Angiolipoma

Epidural angiolipomas are heterogeneous, as they contain adipose and vascular elements, and characteristically are hyper-intense on unenhanced T1WI (from the fat component) and iso-intense to the cord on T2WI. They show heterogeneous enhancement of the vascular component on fat-suppressed T1WI [9]. On CT imaging, the mass is hypo-dense to spinal cord with mild, irregular enhancement. PET scan shows mild tracer uptake.

Treatment & Prognosis:

Management of paragangliomas is usually accomplished by gross total resection followed by adjunctive radiotherapy for long-term stabilization and prevention of tumor growth [2,5,6]. Preoperative alpha blockade is often used to prevent hypertensive crisis from catecholamine release [6]. In some cases, due to hypervascularity often associated with paragangliomas (especially those in the jugular foramen), pre-operative embolization has been used to decrease blood loss during resection, though the effectiveness of this therapy is under debate [5].

Paragangliomas are most commonly benign and slow growing. Malignant transformation rarely occurs. One study of 86 cases of head and neck paragangliomas found no difference in life expectancy from the general population with excellent five and ten year survival rates [10]. Unexpected deaths that arose in patients with paragangliomas were usually secondary to operative complications, which account for an approximate 2% mortality rate in carotid body tumor surgery [10].

TEACHING POINT

Spinal paragangliomas are uncommon neuroendocrine tumors, usually arising in the cauda equina, which can cause mass effect with myelopathy and radicular pain. Thoracic spine epidural paragangliomas are particularly rare, but should be considered in the differential for well-circumscribed, enhancing epidural mass with or without extra-spinal paravertebral involvement.

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FIGURES

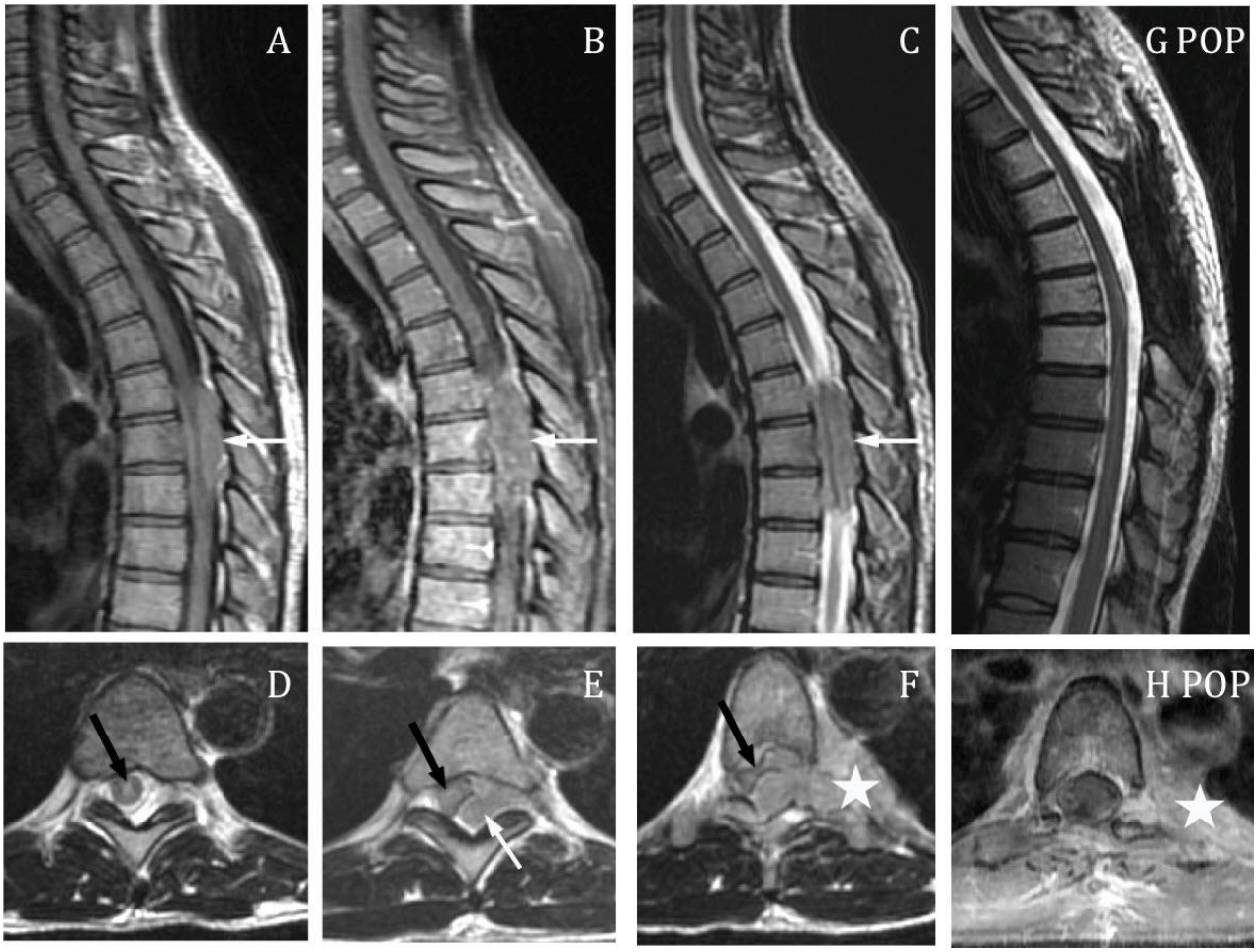

Figure 1: 34-year-old female with epidural and extradural neuroendocrine tumor of the thoracic spine.
Findings: Preoperative MRI sagittal T1WI pre (A) and post-contrast (B), sagittal T2WI (C), axial T2 (D, E), axial T1WI post contrast (F) images show an almost isointense to the cord epidural mass (white arrows) extending outside the spinal canal through the left T7-T8 foramen into the left paravertebral region (white star). There is increase T2WI signal within the cord which is compressed to the right (black arrows) by the left extradural mass (white arrows). Postoperative sagittal T2WI (G POP) shows decompressive laminectomy, epidural tumor removal and residual left paravertebral lesion seen on axial T1 post-contrast (H POP) images (white star).
Technique: 1.5 tesla General Electric (GE) Healthcare Genesis Signa HDxt scanner, scanner, software version 15 (GE Healthcare, Milwaukee, WI); sagittal T2 (TR 4016 ms, TE 105 ms, slice thickness 3 mm skip 1 mm), sagittal T1 (TR 500 ms, TE 13 ms, slice thickness 3 mm skip 1 mm), sagittal T1 post (TR 566 ms, TE 11 ms, slice thickness 3 mm skip 1 mm), axial T2 (TR 3666 ms, TE 106 ms, slice thickness 5 mm skip 1mm), axial T1 post (TR 616 ms, TE 19 ms, slice thickness 4 mm skip 0 mm)

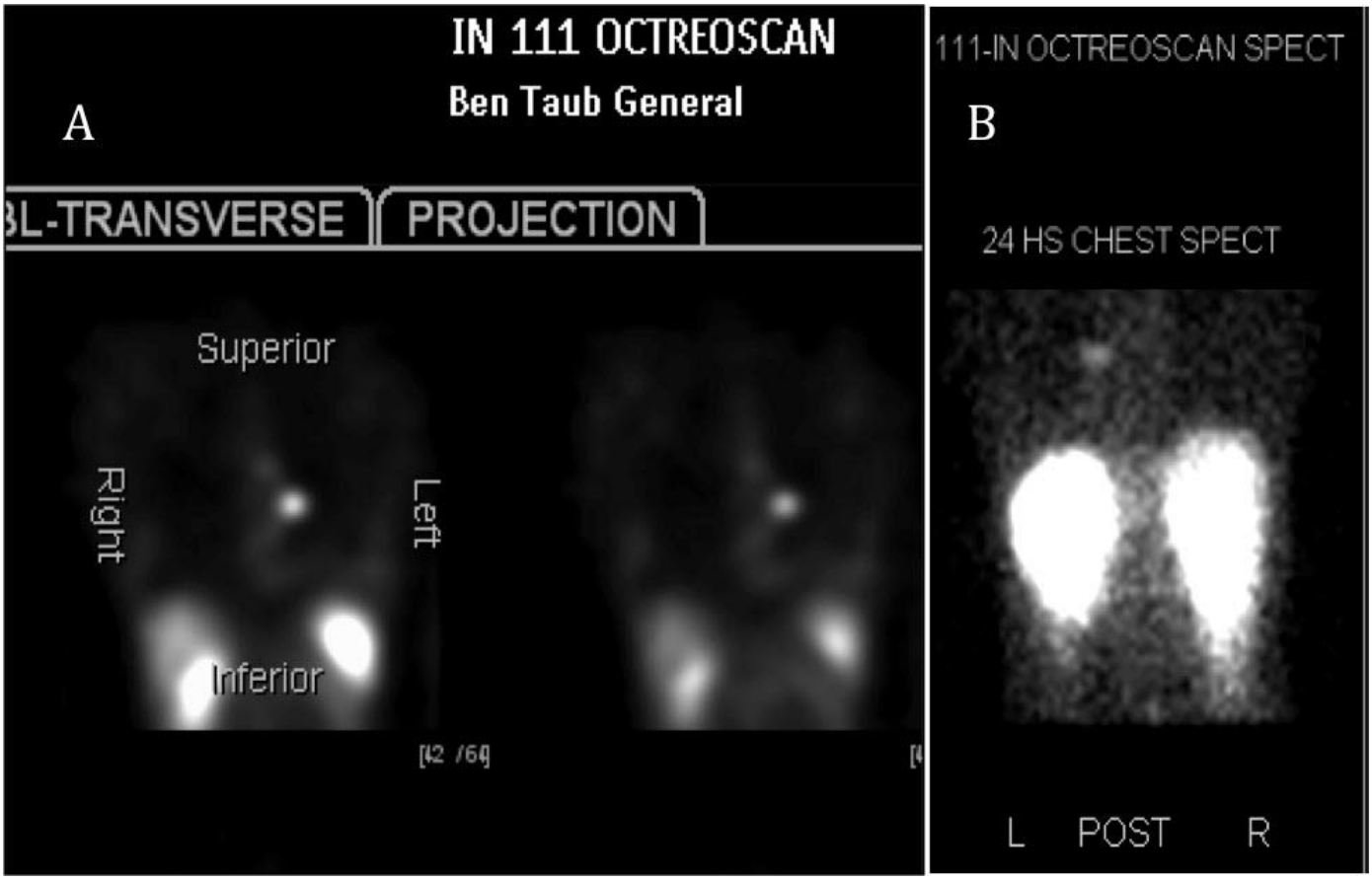

Figure 2: 34-year-old female with epidural and extradural neuroendocrine tumor of the thoracic spine.
Findings: Postoperative 111-IN Octreoscan anterior and posterior images (A) after the surgery demonstrates radiotracer uptake in the left T7 paravertebral region and at midline T8-T9; persistent left paravertebral radiotracer uptake on delayed SPECT image (B) obtained 24 hours later; consistent with residual tumor. No other sites of uptake were identified

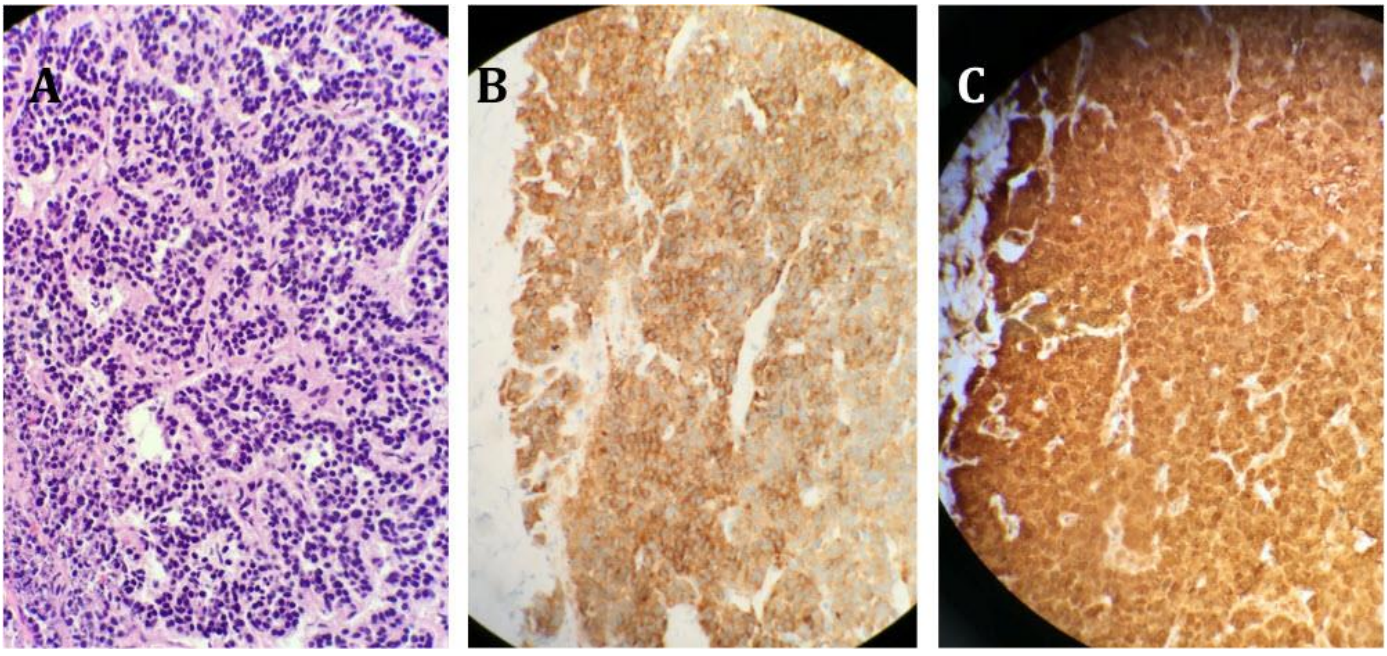

Figure 3: 34-year-old female with epidural and extradural neuroendocrine tumor of the thoracic spine
Findings: Hematoxylin and eosin 400x (A). Pseudorosettes pattern; round aggregates of cells with small uniform nuclei surrounded by vascular tissue or "Zellballen" pattern.
Immunohistochemical staining 400x was positive for Synaptophysin (B) and Chromogranin A(C).

Disease	MRI Findings	CT Findings	Nuclear Medicine Findings
Paraganglioma	Thoracic epidural findings are non-specific. These tumors usually have low to intermediate signal on T1 and intermediate to high signal on T2 with variable enhancement.	Thoracic epidural findings are non-specific, usually has soft tissue density and variable enhancement.	Octreotide scintigraphy for confirmation of thoracic spinal paragangliomas has not been documented.
Epidural Hematoma	Early subacute: T1WI hyper-intense and T2WI hypo-intense. Late subacute: Hyper-intense on T1 and T2WI. Chronic: Hypo-intense on T1 and T2WI may enhance peripherally in the subacute and chronic phases.	NECT: Hyper- or iso-dense to soft tissues. Extradural fluid collection. CECT: Rim enhancement in subacute phase.	NA
Meningioma	Iso-intense to the cord on T1WI. Iso-intense on T2WI, though appearance can vary based on presence of calcifications or cystic degeneration. Lesions are well circumscribed and homogeneously enhancing. Lesions often show dural tails.	NECT: Iso-dense to spinal cord. Calcifications are occasionally present. CECT: Strong, homogeneous enhancement	SPECT/PET: Shows increased tracer uptake. Useful for evaluating response to treatment and metabolic status of tumor.
Neurofibroma	Usually iso-intense to spinal cord on T1WI. Iso- to hyper-intense on T2WI. Hyper-intense on STIR. Variable enhancement on T1WI.	NECT: Soft tissue mass. Iso-dense to spinal cord. CECT: Mild enhancement, relatively homogeneous.	PET: Malignant, metabolically active tumor will have elevated FDG uptake.
Abscess	Restricted diffusion on DWI, iso- or hypo-intense on T1WI and hyper-intense on T2WI. Peripheral enhancement.	NECT: NA CECT: Heterogeneous enhancing epidural phlegmon or peripheral fluid collection.	Gallium scan: shows increased uptake in the epidural area.
Metastasis	Usually bone disease that may present with epidural extension. Presents as focal or diffuse low to intermediate signal intensity on T1WI compared to the bone marrow. Usually iso- or hyper-intense on T2WI, and hyper-intense on STIR with homogeneous enhancement.	NECT: Multifocal or diffuse bone trabecular destruction with extra-osseous soft tissue component extending into the epidural space. CECT: Enhancement of the paravertebral and epidural soft tissue component.	Bone scan: Multifocal increased tracer uptake. PET: FDG uptake in the osseous and soft tissue components.
Multiple Myeloma	Bone disease that may extend to the epidural space with focal low to intermediate signal on T1WI compared to the bone marrow. Hyper-intense on T2W1-STIR. Diffuse marrow involvement and patchy pattern ("salt and pepper") can also be present. The enhancement can be heterogeneous or diffuse.	NECT: Multifocal bone lytic lesions with extra-osseous soft tissue component extending into the epidural space. CECT: The soft tissue component may enhance.	Bone scan: Characteristically negative, positive in 10%, shows photopenic foci. PET/CT: Identifies active MM, useful in monitoring treatment response.
Lymphoma	Iso-intense to the cord on T1WI, iso- or hyper-intense on T2 and STIR with homogeneous enhancement. May present with bone involvement.	NECT: Iso- or hyper-dense to muscle soft tissue epidural mass with/without bone involvement. CECT: Homogeneous enhancement of the epidural soft tissue and the bone if involved.	Bone scan: Increased uptake. PET: Increased uptake, useful for diagnosis and treatment response. Gallium Scan: Increased uptake.
Angiolipoma	Hyper-intense to the cord on unenhanced T1WI and iso-intense to heterogeneous on T2WI, with heterogeneous enhancement of the vascular component on fat-suppressed T1WI.	NECT: Epidural mass of density -20 to -60 HU intermixed with foci of soft tissue. CECT: Irregular enhancement of the soft tissue component.	PET: Can present intermediate increased uptake.

Table 1: Differential diagnosis table for paraganglioma.

	Non-spinal (extra-spinal)	Spinal
Etiology	Neuroendocrine tumor of the autonomic nervous system	Neuroendocrine tumor of the autonomic nervous system
Incidence	Exact incidence is not known, estimated prevalence 0.2 to 1/100.000	Exact prevalence is not known Lumbar: About 9% of all paragangliomas Thoracic extradural: 15 cases reported
Gender ratio (M:F)	M=F	M>F = 1.7:1
Age predilection	Third and fifth decades	Third and fifth decades
Location	Most are adrenal (80 to 90%) (ref 1) Extra-adrenal: correspond to 10 to 20%. Most extra-adrenal (80 to 90%) are in the carotid body and jugular bulb	Lumbar: Filum terminale and cauda equina. Thoracic extradural: 15 cases reported
Risk factors	Unknown	Unknown
Treatment	Surgical excision +/- preoperative embolization	Surgical excision
Prognosis	Excellent	Excellent
Findings on imaging	Head and neck paragangliomas: "salt and pepper" appearance on T2WI MRI due to hypervascularity with serpiginous flow voids, and a peripherally T2-hypointense rim around the mass related to the presence of hemosiderin.	Lumbar: Hypervascular enhancing mass, prominent flow voids, hemosiderin from prior hemorrhage. Bone remodeling. Thoracic: Non-specific; low to intermediate signal on T1WI and intermediate to high signal on T2 with variable enhancement

Table 2: Summary table for paraganglioma.

ABBREVIATIONS

ADC = Apparent Diffusion Coefficient
CECT = Contrast enhanced CT
CT = Computed tomography
DWI = Diffusion Weighted Imaging
FDG PET-CT = Fluorodeoxiglucose Positron Emission Tomography-Computed Tomography
HU = Hounsfield units
MEN2A = Multiple Endocrine Neoplasia type 2A
MEN2B = Multiple Endocrine Neoplasia type 2B
MM = Multiple Myeloma
MRI = Magnetic Resonance Imaging
NA = Not applicable
NECT = Non-enhanced CT
NF1 = Neurofibromatosis type 1
PET = Positron emission tomography
SPECT = Single-photon emission computed tomography
STIR = Short-tau inversion recovery
T1WI = T1-weighted imaging
T2WI = T2-weighted imaging
VHL = Von Hippel-Lindau syndrome

KEYWORDS

Spinal paraganglioma; octreotide; primary spine tumor; thoracic spine; neuroendocrine

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