HEALSME: Differential Diagnosis for Intramedullary Spinal Cord Lesions

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ABSTRACT

Our purpose is to illustrate and review the differential diagnosis for intramedullary spinal cord lesions and masses and to discuss their distinguishing MR imaging features and clinical presentations. An approach to these lesions by using location, signal-intensity characteristics, and patient age significantly narrows the differential diagnosis. The mnemonic HEALSME can help recall a location-based differential diagnosis, accounting for most intramedullary spinal cord lesions, which can be further refined on the basis of patient age, presentation, and imaging features. HEALSME encompasses a variety of intramedullary pathologies, including but not limited to hemangioblastoma, ependymoma, astrocytoma, lymphoma, syrinx, metastasis, MS, and edema. Images of representative entities are presented, and distinguishing imaging features, diagnostic imaging pearls, patient demographics, and prognoses are discussed. Additional less common entities will also be reviewed.

INTRODUCTION

Spinal masses and lesions are encountered in clinical practice, but when one is faced with an unknown case, generating a reasonable differential diagnosis can be challenging because of the rarity of each process in the spine. We will review those spinal cord lesions and masses limited to the intramedullary space. In this space, the lesions that involve the cord can arise from numerous pathologic processes, including trauma, infection, metabolic derangements, vascular causes, demyelination, neoplasms, and metastasis.

MR imaging is the primary technique for the intramedullary space. CT has a more limited role because of poor visualization of cord detail. CT complements MR imaging by answering questions regarding the surrounding osseous structures and possible calcifications or blood in a lesion or mass. The routine MR imaging protocols are usually sufficient for accurate pathologic characterization and typically include sagittal and axial T1 and T2-weighted imaging and sagittal STIR images. Two-plane postcontrast T1-weighted imaging is also recommended with at least 1 plane using a fat-saturation technique. Some advanced imaging techniques are also emerging that may be beneficial. These include diffusion-weighted imaging, diffusion tensor imaging, perfusion imaging, and high-resolution T2 imaging. These are not generally part of the routine protocol but may be used after the initial imaging to better characterize a lesion or mass.1-3

We sought a method to help remember the more common lesions and masses seen in the spinal cord and developed the mnemonic HEALSME. In this review, we will highlight the common intramedullary lesions and masses outlined in the HEALSME mnemonic. To more thoroughly review the intramedullary differential, we will expand the scope to include other less common entities not specifically mentioned in the mnemonic.

ABBREVIATION KEY

ADEM = acute disseminated encephalomyelitis
AVF = arteriovenous fistula
AVM = arteriovenous malformation
CNS = central nervous system
dAVF = dural arteriovenous fistula (also dorsal intradural arteriovenous fistula)
DSA = digital subtraction angiography
GRE = gradient-recalled echo
HEALSME = mnemonic for intramedullary spinal cord tumors: Hemangioblastoma, Ependymoma, Astrocytoma, AVM, Lymphoma, Syrinx, Sarcoid, Metabolic, Metastasis, Multiple sclerosis, and Edema
HIV = human immunodeficiency virus
MS = multiple sclerosis
NF = neurofibromatosis
NMO = neuromyelitis optica
STIR = short T1 inversion recovery
VHL = Von Hippel-Lindau disease

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Hemangioblastoma

Spinal cord hemangioblastomas are rare, accounting for 1%–7% of spinal cord tumors. Although they are not the most common intramedullary spinal cord tumors (astrocytoma and ependymoma are), they are mentioned first because $H$ is encountered first in the HEALSME mnemonic. They are low-grade capillary neoplasms that can occur sporadically (two-thirds of cases) or with VHL syndrome (one-third of cases). Hemangioblastomas present with nonspecific sensory/motor symptoms, including radicular pain, motor weakness, or proprioception disturbance. Symptoms are attributable to the tumor and/or its associated syrinx. Hemangioblastomas grow slowly without malignant degeneration and are treated with resection.

Imaging demonstrates an enhancing T1 hypointense T2 hyperintense tumor nodule with occasional flow voids that expands the spinal cord. Flow voids are more frequently seen with increasing tumor size. The enhancement is well-demarcated and intense. A review of 12 patients with hemangioblastomas defined on MR imaging concluded that a small (<10 mm) well-demarcated intensely enhancing intramedullary tumor located at the surface of the cord with a relatively large associated syrinx is likely to be a hemangioblastoma. Also likely to be a hemangioblastoma is a large tumor (>10 mm) with associated syrinx and flow voids (Fig 1).4

While spinal cord hemangioblastomas may also present as intra-/extramedullary or extramedullary tumors, most are intramedullary. Within the cord, they are located either deep or in a superficial and posterior location. Fifty percent of cases are associated with a cyst or syrinx. Hemangioblastomas are more common in the cervical and thoracic spine. The brain and entire spine should be imaged with MR imaging in patients with VHL because they are more likely to have multiple hemangioblastomas. Following resection of the enhancing nodule, associated syringes often shrink or disappear.5-9

Another benign neoplastic vascular lesion is the cavernous malformation or cavernoma. This is the same slow-flow vascular lesion seen in the brain. Only 3%–5% of cavernomas occur in the spinal cord. As an intramedullary spinal cord mass, it occurs most frequently in the fourth decade of life, in women twice as often as men. It may be asymptomatic, incidentally identified, or associated with episodic sensory and motor symptoms with intermittent recovery. Cavernomas may also present with acute neurologic decline secondary to hemorrhage. On imaging, there is heterogeneous T1 and T2 signal intensity due to blood products (the classic “popcorn” appearance) and often a peripheral rim of low signal intensity. GRE sequences may demonstrate intraleisional blood products. Enhancement is minimal and occasionally seen at the periphery. Cord edema is not present unless there has been recent hemorrhage. A familial cavernous malformation syndrome with multiple spinal lesions exists and has a higher risk of hemorrhage (Fig 2).10-12

Key Points for hemangioblastomas are the following:

1) Hemangioblastoma is associated with VHL.
2) Hemangioma is avidly enhancing with extensive surrounding edema and is occasionally seen with flow voids and syrinx.
3) One must image the entire neuroaxis for additional lesions in cases of VHL.
4) Cavernoma in the spinal cord is a “popcorn” lesion.

Ependymoma

Spinal cord ependymomas, the first E in HEALSME, are the most common primary adult neoplasm, most often found in adults 35–45 years of age. Ependymomas are the second most common pediatric neoplasm of the spinal cord and are frequently found in patients with NF2.13 They are neoplasms of the ependymal covering of the spinal cord that present with pain more often than sensory or motor symptoms. The symptoms are frequently mild and may be present for years before diagnosis. Ependymomas are benign slow-growing tumors and are treated with resection, which is curative when complete, but are prone to local recurrences when incomplete. Imaging demonstrates a sharply
A variant form, myxopapillary ependymoma, typically arises in the conus or cauda equina of young men more than women. This subtype accounts for approximately 50% of adult spinal ependymomas or 13% of all spinal ependymomas. Myxopapillary ependymoma presents with lower back pain, leg pain, or sphincter dysfunction. They are also treated with resection. They have similar imaging features, including cysts, conus and possible spinal canal expansion, hemosiderin, and avid enhancement. The distinguishing feature of myxopapillary ependymomas is the characteristic location within the conus, filum terminale, and cauda equina (Fig 5). A key feature for myxopapillary ependymomas is the characteristic location within the conus, filum terminale, and cauda equina.

**Key Points for Ependymomas**

1. They are the most common primary intramedullary adult neoplasm.
2. They are associated with NF2.
3. They are sharply marginated and enhancing.
4. Hemorrhage is characteristic. Cysts are frequent.
5. Myxopapillary ependymomas are characteristically located in the conus, filum terminale, and cauda equina.

**Astrocytoma**

Astrocytoma, the first part of the A in HEALSME, is the most common pediatric and second most common adult intramedullary spinal tumor, though only 3% of CNS astrocytomas are...
spinal. Intramedullary spinal cord astrocytomas are gliomas that commonly present insidiously after 3 or 4 years of myelopathy in an adolescent or young adult. Patients with NF1 have intramedullary spinal cord astrocytomas more frequently than the general population. Symptoms typically include radicular pain at the level of the lesion or sensorimotor disturbances of the upper (for cervical lesions) or lower (for thoracic lesions) extremities, such as clumsiness, proprioception disorders, or sensory deficits. These slow-growing typically low-grade tumors are treated with resection: 80%–90% of intramedullary astrocytomas are low grade, WHO I or II, with 80% having a 5-year survival following treatment. On MR imaging, the astrocytoma is typically a heterogeneously enhancing, fusiform, T1 hypointense, T2 hyperintense, expansile mass over 4 or fewer vertebral body lengths. Between 20% and 30% of astrocytomas do not enhance. Margins are irregular and the tumor is often eccentric within the cord. Commonly seen in the thoracic and cervical spine, astrocytomas can have associated cysts, edema, or syrinx. A holocord presentation can also be seen in children. Astrocytoma can be indistinguishable from ependymoma on MR imaging. There is frequently remodeling of the bony canal (Figs 6 and 7).

Another unusual spinal cord tumor that can have features similar to an astrocytoma is the ganglioglioma. This rare spinal cord tumor is mixed pathologically, with mature
neuronal elements and neoplastic astrocytic glial elements. At presentation, gangliogliomas tend to be much larger tumors, frequently extending over 8 vertebral bodies and are more frequently found in the cervical cord. Gangliogliomas are more frequently associated with cysts and scoliosis (Fig 9).²⁴

Key Points for astrocytomas are the following:
1) They are the most common pediatric intramedullary spinal cord mass.
2) They are most common in the cervical spine.
3) Cysts can be seen with astrocytomas or ependymomas.

**AVM and AVF**

The second part of the A in HEALSME reminds the reviewer to consider AVF and AVM in the differential of intramedullary spinal cord abnormalities encountered with MR imaging.

An intradural AVF is an acquired anomalous vascular connection between the arterial and venous network. The most common type, the dAVF, a type I in the Anson-Spetzler classification, previously called dural AVF, is addressed here. DAVFs are fed by the radiculomeningeal arteries. A
venous thrombosis or obstruction in the normal radicular veins leads to drainage into the normal perimedullary veins of the cord. These attempt to accommodate the arterial pressures, and the resulting venous hypertension leads to hypoxia of the cord and clinical symptoms. Clinically, most patients are men between 55 and 60 years of age. A dAVF presents with a progressive myelopathy (Foix-Alajouanine), and if it is not recognized and treated, symptoms will continue to progress. Lesions are typically treated by using endovascular liquid embolic agents in the feeding radiculomeningeal artery or by surgical occlusion. On imaging, the patient will have high T2 signal intensity centrally in the cord. Most lesions are between T6 and L2. Typically there will be flow voids representing the dilated perimedullary veins on the surface of the cord. If suspected, contrast-enhanced MR angiography with subsequent spinal arteriography should be performed (Fig 10).

Intradural intramedullary spinal cord AVM is a congenital abnormal connection between an artery and vein with a nidus. AVMs present with weakness, motor dysfunction, back pain, and bowel and bladder dysfunction. They frequently come to clinical attention because of hemorrhage. AVMs are diagnosed in children younger than 16 years of age in half of the cases. Syndromes associated with spinal AVMs are Klippel-Trenaunay-Weber, Rendu-Osler-Weber, and Cobb. Treatment is with surgical resection or intravascular embolization, which is often incomplete. On imaging, there may be heterogeneous T1 and T2 signal intensity related to blood products. The adjacent spinal cord has increased T2 signal intensity. Serpentine flow voids and cord surface enhancement, along with variable enhancement of the AVM, are often seen. The nidus may be compact (with densely packed vessels) or diffuse (with vessels scattered in the spinal cord), following the Anson-Spetzler classification. GRE sequences may demonstrate intramedullary or subarachnoid hemorrhage (Fig 11). Key Points for AVM and AVF are the following:

1) Dural arteriovenous fistula will have high T2 signal intensity in the cord and flow voids on the cord surface.
2) Intradural intramedullary AVMs will have flow voids, enhancement, and gradient blooming.

### Lymphoma

Lymphoma, the L in HEALSME, is one of the CNS pathologies that can appear in multiple different spaces and has varied imaging appearances. Intramedullary lymphoma is a
lymphoreticular neoplasm presenting in adults during the fourth-to-seventh decades with myelopathy, weakness, numbness, and progressive gait disturbance. Treatment is with radiation, with or without chemotherapy. Of all the primary CNS lymphomas, representing 1% of lymphomas, only 3.3% are intramedullary spinal lymphoma. CNS disease generally has a poor prognosis. On imaging, lymphoma is a T2 hyperintense variably enhancing mass with surrounding edema. Diffusion imaging may be useful, and lymphoma would be expected to restrict diffusion; however, little research exists on the efficacy of diffusion on intramedullary lesions. This will be an area of future research. Lymphoma will present in the cervical > thoracic >
lumbar cord. Vertebral body and epidural space involvement are often seen (Fig 12).6,12,33

Key points for Lymphomas are the following:

1) Patients are generally older.

2) Lymphoma in the spinal cord has a variable presentation.

Syrinx

Syrinx, the S in HEALSME, encompasses both hydromyelia and syringomyelia, which are not reliably distinguishable by imaging and are often combined into the term “syringo-hydromyelia” or “syrinx.” “Hydromyelia” refers to cystic central canal dilatation. Syringomyelia refers to spinal cord cyst not contiguous with the central canal. An intratumoral cyst, as seen with astrocytoma or ependymoma, is a cyst within the tumor.

Clinically, a syrinx is primary, related to basilar invagination or cranio cervical junction abnormalities (such as Chiari malformation), or secondary, due to trauma, obstructing tumor, or CSF flow disturbances from webs or adhesions. A syrinx presents with progressive pain, which increases with coughing or sneezing. Syringes are progressive and are treated with shunt surgery to arrest neurologic progression. They are also seen with hemangioblastoma, ependymoma, and astrocytoma. On imaging, a syrinx is a longitudinally oriented CSF-filled cavity with surrounding gliosis. It is paramedian, nonenhancing, T1 hypointense, T2 hyperintense, and surrounded by myelomalacia. It may have a beaded or cystic expansile configuration (Fig 13).34

Ventriculus terminalis or a terminal ventricle is similar radiographically to syrinx, appearing as cystic dilatation of the distal central conus, normally in neonates and persisting occasionally in older children. It is typically asymptomatic and incidental, seen in children younger than 5 years of age. Like a syrinx, it is a longitudinal, nonenhancing, T1 hypointense, T2 hyperintense CSF signal-intensity lesion. Unlike a syrinx, it is located in the central cord and is isolated to the conus (Fig 14). The lesions are typically 2–3 cm in length and do not require treatment.35,36

Key Points for syrinx are the following:

1) A syrinx is a nonenhancing longitudinally oriented fluid signal-intensity mass commonly associated with trauma or Chiari malformations.

2) Ventriculus terminalis is an incidental finding in the conus in children younger than 5 years of age.
Metastasis

Metastasis is the first part of the M in HEALSME. Intramedullary spinal cord metastases are rare, seen in 1%–2% of patients with cancer at autopsy. Usually solitary, they are most likely to arise from lung or breast primary cancers, though melanoma, renal cell carcinoma, colorectal carcinoma, and lymphoma can also metastasize to the cord. Unlike the other neoplasms in the HEALSME differential, metastases are rapidly progressive. Metastasis presents with motor weakness or other myelopathy, such as pain, bowel or bladder dysfunction, or paresthesias, for less than a month. On imaging, the focally enhancing lesions will enlarge the cord. T2 hyperintensity usually extends over 2–3 vertebral segments and causes diffuse cord edema out of proportion to the size of the cord lesion (Fig 15). CNS metastases have a poor prognosis and are treated with chemotherapy, steroids, and radiation to stabilize the symptomatic myelopathy.6,37

Key Points for metastasis are the following:
1) It is a rapidly progressive enhancing mass.
2) Edema is out of proportion to the size of the mass.

Metabolic Disorders

Metabolic disorders can also cause intramedullary signal-intensity abnormalities and represent the second part of M in HEALSME. The most common is a B12 deficiency, called “subacute combined degeneration of spinal cord.” The deficiency, or error in B12 metabolism, can be secondary to multiple etiologies, including pernicious anemia, vegetarian diet, nitrous oxide abuse, or malabsorption syndromes. B12 deficiency classically presents with symmetric T2 signal intensity in the posterior columns of the cervical cord (Fig 16). Correction of the B12 abnormality will typically result in return of the normal cord signal intensity.38-41 Some patients with HIV will develop HIV-1-associated vacuolar myelopathy of the cord. This has a similar imaging appearance to B12 deficiency, and some believe that the vacuolar myelopathy is a result of impaired use of B12.42,43

Key Points for B12 deficiency are the following:
1) B12 deficiency has a characteristic symmetric location in the posterior columns.
2) Multiple causes of B12 deficiency are possible and may be suggested when the imaging finding is present.

MS and Other Demyelinating or Inflammatory Disorders

MS and other demyelinating or inflammatory disorders are the third part of M in HEALSME.

MS is a primary autoimmune demyelinating disease of the CNS, with multiple lesions disseminated with time and space. MS occurs as isolated spinal cord disease in 10%–20% of patients. Spinal cord lesions present with paresthesia or other myelopathy in 30- to 40-year-old women >
men. Treatment is medical, with immunomodulatory therapy and symptom management and is determined by the presence of new or enhancing lesions. Most often the MS lesions are found in the dorsolateral cervical cord as T2 and STIR/fluid-attenuated inversion recovery hyperintense lesions, extending over \( \frac{1}{2} \) vertebral bodies, without respect for gray/white boundaries. Acute lesions may enhance for 2–8 weeks. Cord expansion or atrophy may also be present. Most patients will have associated intracranial lesions (Fig 17).

Acute transverse myelitis is an idiopathic demyelinating disorder that progresses during several days with symptoms of back pain, radicular pain, or bowel/bladder dysfunction. The etiology involves focal spinal cord inflammation and neural injury that is theorized to be an autoimmune response to a viral infection. On imaging, lesions are T1 hypointense, T2 hyperintense, and variably enhancing. Cord expansion is typically seen. Lesions extend over 3–4 vertebral bodies, in contrast to MS lesion, which are typically over \( \frac{1}{2} \) vertebral bodies. Prognosis is variable, with only 30%–50% attaining complete recovery after steroid therapy.

NMO, formerly known as Devic’s disease, is a syndrome of transverse myelitis and optic neuritis. Recent discoveries have shown that autoantibodies to aquaporin-4 from peripheral B-cells cause the inflammatory demyelination. A recent test for the specific serum autoantibody marker (NMO-immunoglobulin G) helps differentiate neuromyelitis optica from MS. These antibodies can be detected in >75% of patients. While also a demyelinating disorder, brain lesions are rarely seen, and NMO is considered a distinctly separate entity from MS (Fig 18).

ADEM is a demyelinating disorder of the brain and spinal cord that is associated with viral infections and vaccine administration. Intramedullary spinal cord lesions are similar to MS or transverse myelitis. The typical spinal cord lesion is usually larger than an MS plaque and more resembles the lesions seen with NMO. Spinal cord lesions in ADEM have variable enhancement. Rather than being multiphasic, like MS, ADEM is monophasic, with all lesions of the same age. Lesions usually resolve with treatment and should be followed with serial MR imaging (Fig 19).

Key Points for MS, NMO, and ADEM are the following:

1) MS lesions are more likely multiple and focal and have a peripheral location in the cord.
2) Dissemination of disease in time and space is the diagnostic key in MS.
3) Acute MS lesions may enhance.
4) Transverse myelitis may be seen independently or associated with NMO and usually extends over >3 vertebral body lengths.
5) ADEM may resemble NMO in the cord, but the more common presence of brain lesions in ADEM, and clinical history can help distinguish the entities.

**Edema, Infection, and Infarction**
Edema, the second E in HEALSME, is a trigger to remind the reviewer of other non-neoplastic causes of spinal cord edema not yet addressed by the mnemonic. Lumped together into the edema section are the same generic causes for edema commonly encountered: trauma, infection, and ischemic disease.

**Trauma**
Traumatic spinal cord edema includes acute mechanical injury related to trauma or chronic trauma related to degenerative disease. Treatment may include surgical stabilization of the spine or decompression of the spinal cord. With acute trauma, spinal cord contusion can be seen. On imaging, the contusion will be T2 hyperintense and nonenhancing, if acute. There may be associated cord swelling or GRE blooming if there is also hemorrhage (Fig 20). In addi-

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**Fig 18. NMO.** This patient presented with optic neuritis and multiple lower extremity symptoms. Imaging of the thoracic spine shows a long expansile T2 hyperintense intramedullary lesion (arrowheads, A). After contrast, the central aspect of the lesion enhances (arrow, B).

**Fig 19. ADEM.** This 25-year-old woman presented with multiple neurologic symptoms after a viral illness. Sagittal T2 (A) image of the cervical spine shows longitudinally oriented lesions extending over 4 vertebral bodies (arrowheads), which minimally enhance after contrast (arrow, B). Multiple additional lesions are seen in the brain (arrowheads, C). Lesions and symptoms resolved with steroids, and no lesions were seen on follow-up MR imaging examinations.
dition, the causative agent, such as disk herniation, vertebral fracture, or severe spinal stenosis, will be identified. In children, spinal cord contusion can occur without other radiologic abnormalities.56–58

**Infection**

Isolated spinal cord bacterial infections are rare. Patients with pyogenic spinal cord infections are usually at high risk due to intravenous drug use, immunosuppression, or anatomic anomalies of the spinal cord. Presentation is with fever, leukocytosis, back pain, and motor or sensory deficits. Infections are more likely to present in the distal thoracic cord and conus. These lesions are T2 hyperintense with surrounding edema and demonstrate a sequential progression of marginal enhancement. Initially, the marginal enhancement is poorly defined and subtle, but then with time and treatment, it develops into a well-defined ring-enhancement typical of an abscess. As in the brain, a pyogenic abscess of the spinal cord will demonstrate diffusion restriction. The areas of enhancement will resolve with treatment (Fig 21).59,60

**Infarction**

Spinal cord infarction can result from vascular compromise from embolic or iatrogenic injury to the artery of Adamkiewicz during surgery or endovascular repair. The key diagnostic differentiator in spinal cord infarct is the clinical history of sudden-onset sensorimotor disturbance. Despite collateral circulation, all cord levels are potential infarct levels, with the anterior two-thirds and lower thoracic cord the most likely because these locations are the cord watershed zones. T2 hyperintense nonenhancing “pencil-like” lesions will follow the distribution of the local blood supply and involve the central gray matter of the cord preferentially. Restricted diffusion is present for the week following the insult, but then it pseudonormalizes. (Fig 22).61–63

Key Points for trauma, infection, and ischemic disease are the following:

1) Cord contusions will not enhance acutely.
2) Infections will typically develop ring enhancement of the abscess.
3) Spinal cord infarcts do not enhance acutely, preferentially involve the central gray matter, and will restrict diffusion for the first week.
CONCLUSIONS

There is a broad differential for intramedullary spinal cord lesions. The mnemonic HEALSME can help in recalling an initial location-based differential diagnosis that includes most intramedullary pathologies. Distinguishing these lesions by location, signal intensity characteristics, clinical presentation, associated brain lesions, and patient age significantly narrows the differential diagnosis.

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