The Malignant Spine
From Metastases to Myelopathy

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Disclosures
Nothing!
Nichts!
Nada!
Niente!
Rein!

Objectives
• Understand the pathophysiology of metastases to the spine and spinal cord.
• Localize primary and metastatic disease and identify anatomic structures involved.
• Indentify the various etiologies of myelopathy in the cancer setting.
• Be able to clinically evaluate individuals with spine and spinal cord involvement.
• Understand the features important to predicting spinal stability, future deformity, and progressive neurologic compromise in individuals with spine metastases and primary vertebral body tumors.
• Understand the basis of oncologic management and establishment of a rehabilitation plan in patients with spine and spinal cord involvement.
• Emphasize the importance of a multidisciplinary approach to the care of individuals with spine and spinal cord involvement.
ANATOMY

The Malignant Spine-Anatomy

- Regions of the spine
  - Cervical
  - Thoracic
  - Lumbar
  - Sacral
- Epidural Spinal Cord Compression
  - Renal Cell Carcinoma

- Intradural Extramedullary
  - Leptomeningeal Metastases-Breast Cancer

- Intradural Intramedullary
  - Astrocytoma
Anatomy of the Malignant Spine-Structures Involved

METASTASES

The Malignant Spine-Metastases

Adult
- Prostate
- Breast
- Lung
- Thyroid
- Non-Hodgkin’s Lymphoma
- Multiple Myeloma
- Renal Cell Carcinoma
- Colorectal
- Sarcomas
- Unknown Primary

Pediatrics
- Sarcomas
  - Ewing’s
- Germ Cell Tumors
- Hodgkin’s Disease
The Malignant Spine - Pathophysiology of Metastasis

- Direct extension
- Hematogenous spread
- CSF spread

Pathophysiology of Metastasis - Direct Extension

- Direct spread from the vertebral body, intervertebral foramen, paravertebral soft tissues in epidural metastasis
- Direct extension from a parenchymal or dural metastasis adjacent to the subarachnoid space, or along veins leaving the bone marrow in intradural extramedullary metastasis
- Direct extension along the epineurium and perineurium of spinal nerves in intradural extramedullary and intramedullary metastases

Pathophysiology of Metastasis - Hematogenous & CSF Spread

- Hematogenous spread
  - Both arterial and venous (Batson’s plexus) routes
- CSF spread
  - “Shedding” of tumor cells from cerebral or cerebellar metastatic lesions
  - Often follows surgical manipulation
The Malignant Spine -
Etiologies of Epidural Metastases

- Lung, breast, prostate are most common
- Renal cell carcinoma, thyroid, and colon cancer are relatively common
- Non-Hodgkins lymphoma and Multiple Myeloma are most common hematologic tumors
- In children sarcoma and neuroblastoma are most common

Epidural Metastases -
Location

- 60% thoracic spine
- 25% lumbosacral spine
- 15% cervical spine
- 1/3 of patients have epidural involvement at multiple spinal levels
- Can result in cord compression
  - Most commonly compression anterior and lateral thecal sac

The Malignant Spine -
Epidural Cord Compression

- 3rd most common cause of compressive myelopathy in adults
- 2nd most common neurological complication in the cancer population
- 2-5% of patients develop clinical manifestations of ESCC during the course of their disease
  - 20% ESCC is the 1st manifestation
    - Lung cancer, Lymphoma, Myeloma
The Malignant Spine-Intradural Extramedullary Metastases (Leptomeningeal Disease)

- 1-8% of cancer patients in autopsy studies
- Female predominance
- 70% have a concurrent or prior diagnosis of brain parenchymal metastasis

Leptomeningeal Disease

Histology & Location

- Most common histologies: leukemia, lymphoma, lung and breast carcinoma, and melanoma
- Most common site of involvement is the dorsal aspect of the spinal cord, particularly in the cauda equina

The Malignant Spine-Primary Intradural Intramedullary Tumors and Metastases

- Diagnosed in <1% of cancer patients
  - Of these approximately 5% are identified before death secondary to systemic disease
  - Detected in approximately 2% of autopsies
- Usually occur in the setting of extensive metastatic disease
- Typically a solitary cord lesion
- 57% of patients have prior or concomitant brain parenchymal metastases
- Concomitant leptomeningeal tumors are common
Intradural Intramedullary Metastases-

**Histology**

- Small cell lung cancer is most common associated primary
- Breast and colon cancer, renal cell carcinoma, lymphoma, and melanoma are also common

Intradural Intramedullary Metastases-

**Location**

- Lesions are equally distributed between the cervical, thoracic, and lumbar segments of the cord
- Usually start in the dorsolateral aspect of the spinal cord

**MYELOPATHY**
The Malignant Spine-Myelopathy

- Spinal cord injury secondary to neoplastic spinal cord compression accounts for 26-45% of nontraumatic SCI admissions to inpatient rehabilitation, and 10-14% of all SCI admissions.

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- External beam radiation therapy
- Chemotherapy Induced Myelopathy
- Paraneoplastic Myelopathy
- Myelopathies Not Directly Related to Malignancy

The Malignant Spine-Etiologies of Myelopathy

- Epidural Spinal Cord Compression
- Leptomeningeal Metastases
- Primary Intramedullary Tumors and Metastases
- Radiation Induced Myelopathy
  - External beam radiation therapy
- Chemotherapy Induced Myelopathy
- Paraneoplastic Myelopathy
- Myelopathies Not Directly Related to Malignancy

The Malignant Spine-Spinal Cord Injury Cascade

- Mechanical injury to myelin and axons
- Vascular compromise resulting in venous congestion and cord infarction
  - Patient with rapidly progressing symptoms are more likely to have cord infarction
The Malignant Spine-Radiation Myelopathy

- Treatment of primary and metastatic spine/spinal cord tumors
- Prophylactic radiation to prevent metastases
- Included in field of treatment
  - Primary colorectal cancer

Radiation Myelopathy-Tissue Tolerance to Radiation

- Total doses received
- Number of fractions over which it is delivered
- Number of treatment days
- Length of the cord irradiated
- Dose is restricted to figures with a ≤5% risk
  - Estimated to be 4200-4500 cGy in 25 fractions

Radiation Myelopathy-2 Phases of Adverse Effects

- Early Myelopathy
- Late Myelopathy
Radiation Myelopathies - Early Myelopathies

- Acute Complete Radiation Myelopathy
- Lower Motor Neuron Disease
- Acute Transient Radiation Myelopathy

Early Myelopathies - Acute Complete Radiation Myelopathy

- Rare!
- Progression to complete tetra/paraplegia over the course of hours to days
- Presumed to be the result of spinal cord infarction secondary to radiation induced vascular damage

Early Myelopathies - Lower Motor Neuron Disease

- Rare!!
- Presumed to be related to anterior horn cell damage
Early Myelopathies-
Acute Transient Radiation Myelopathy

- Most common form of radiation induced myelopathy
- Occurs from 1-29 months after completion of radiation therapy
  - Median 4 months post completion
- Hypothesized to result from mild radiation induced demyelination of the posterior columns

Acute Transient Radiation Myelopathy

- Generally associated with cervical spine irradiation
  - Can occasionally be found in association with radiation to other cord segments
- Common after radiation for head and neck cancers and Hodgkin’s disease
- Symptoms resolve over weeks to months
  - Average duration of symptoms is 5.3 months

Late Myelopathies
Chronic Progressive Radiation Myelopathy

- Occurs in 1-5% of patients who survive >1 year post XRT
- Can occur after EBRT to treat spinal cord tumors or tumors adjacent to the spinal cord
- It has recently been reported after SRS to treat vertebral body tumors
Chronic Progressive Radiation Myelopathy-Time Course

- CPRM is characterized by a latent period during which the patient is asymptomatic.
- Symptoms can appear within 9-15 months after completion of radiation therapy:
  - It has been reported as early as 1 month post treatment and as late as 6 years.
  - Patients who are retreated tend to have a shorter latency period.
  - Pediatric patients commonly have shorter latency periods.

Hammack, J. Spinal Cord Disease in Patients With Cancer. Continuum Lifelong Learning Neurol 2012; 18(2) 312-327
Goldwein, J. Radiation Myelopathy: A Review. Medical and Pediatric Oncology. 1987;15, 89-95

Time Course

- Clinical onset is usually painless and insidious.
- Occasionally starts as a Brown-Séquard syndrome.
- Typically there is a steady progression of neurological deficits over the course of weeks to months:
  - 6 months.

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Chronic Progressive Radiation Myelopathy Criteria for Diagnosis

- Pallis et al, three criteria for diagnosis:
  - 1. Spinal cord must have been included in the radiation field.
  - 2. Main neurological deficit must be within the segments of the cord exposed to radiation.
  - 3. Metastases or other primary spinal cord lesions must be ruled out as the etiology of neurological impairments.

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Goldwein, J. Radiation Myelopathy: A Review. Medical and Pediatric Oncology. 1987;15, 89-95
The Malignant Spine-Chemotherapy Induced Myelopathy

- Exact pathogenesis is unknown
- IV Administration
  - Cisplatin, BCNU (Carmustine), and Fludarabine have been associated with myelopathy although it is rare.
- Intrathecal Administration
  - Transverse Myelopathy has been associated with Melphalan (most commonly), Cytarabine, and Thiopeta.
  - Anthracycline antibiotics (Adriamycin and Mitoxantrone) and Vinca Alkaloids (Vincristine and Vinblastine) reliably produce myelopathy with intrathecal injection.

The Malignant Spine-Paraneoplastic Myelopathy

- Uncommon and rarely occurs in isolation
- Small cell lung cancer
- Paraneoplastic Encephalomyelitis is most common syndrome
  - Limbic encephalitis
  - Brainstem encephalitis
  - Myelitis
  - Subacute neuronopathy

The Malignant Spine-Myelopathies Not Directly Related to Malignancy

- Acute trauma
- Multiple Sclerosis
- Acute Transverse Myelitis
- Degenerative Diseases
  - Spinal Stenosis
  - Intervertebral Disc Herniation
- Spinal Cord Vascular Disease
  - Anticoagulant Medications
  - Spinal Cord Infection
  - Intraoperative Transfusion
- Nutritional & Metabolic
  - Subacute Combined Degeneration of the Cord (Vit B12 deficiency)
  - Vitamin B deficiency
  - Copper deficiency
  - Toxic Myelopathy
- Neuromuscular Acute Injuries
  - Decompression Myelopathy
  - Myelopathy induced by electric shock
- Motor Neuron Disease
  - Amyotrophic Lateral Sclerosis
  - Primary Lateral Sclerosis
  - Spinal Muscular Atrophy
Myelopathies Not Directly Related to Malignancy

- Spinal Cord Infection
  - Spinal Epidural Abscess
  - Viral
    - HIV Vacuolar Myelopathy
    - CMV
    - Varicella-Zoster
    - HSV
    - HTLV-1 Associated Myelopathy
    - Postpolio Syndrome

- Hereditary Conditions
  - Hereditary Spastic Paraplegia
  - Friedreich Ataxia
  - Ataxinopathies
  - Syringomyelia
  - Simulated Paraplegia

CLINICAL MANIFESTATIONS

The Malignant Spine-Clinical Manifestations

- Pain
- Neurological deficits
- Spine instability
Clinical Manifestations - Pain

- Pain is the most common initial symptom in patients with ESCC
  - 80-90% of patients
  - Median of 2 months before diagnosis
- 16% of patients with leptomeningeal metastases present with pain
- Radiation myelopathy is typically not painful
- 3 classic pain syndromes:
  - Localized spine pain
  - Mechanical pain
  - Radicular pain

Classic Pain Syndromes - Localized Spine Pain

- Often initial pain complaint
  - Present in ESCC, Leptomeningeal disease, and ISCM
- Persistent “gnawing” or “aching” pain emanating from involved spinal segments
- Duration: weeks or longer
- Intensity increases over time
- Often worse when supine
  - Patient sleeps on incline or wakes frequently at night
  - Distension of Batson’s plexus

Localized Spine Pain

- Thought to be caused by periosteal stretching &/or a local inflammatory process 2/2 tumor growth
- Percussion over the spinal processes may illicit tenderness
- Responds well to steroids
Classic Pain Syndromes - Radicular Pain

- Can be present in ESCC, Leptomeningeal disease, ISCM
- “Sharp, shooting, stabbing, intense burning”
- Occurs secondary to nerve root invasion or compression

Diagnosis

- Major differential diagnoses are epidural spinal cord compression and intramedullary spinal cord tumors and metastases

Radicular Pain

- Follows a dermatomal distribution
  - Cervical/Lumbosacral spine radiates unilaterally into the upper or lower extremity
  - Thoracic spine typically bilateral, described as a “tight band” around chest
- ESCC worsens with Valsalva
  - Increases intraspinal pressure
- “Funicular Pain”
  - Compression of the dorsal columns and spinothalamic tract
    - Cervical/high thoracic lesions
    - “Sciatica” type pain and pseudo-claudication
Classic Pain Syndromes - Mechanical Pain

- Mechanical pain is associated with structural abnormalities in the spinal column and is a consistent feature of instability.
- Pain related to axial loading (sitting/standing), relieved when supine
- Usually refractory to steroids and narcotics

Mechanical Pain

- Pain descriptions based on location
  - C1-C2 (atlantoaxial complex): pain with rotation
  - Subaxial cervical spine: late day fatigue or difficulty holding head upright
  - Thoracic spine: pain when supine
    - Supine position can straighten an unstable kyphosis
  - Lumbar spine: pain with axial loading

Pain

- New onset back or neck pain in a patient with known cancer must be considered spinal metastatic disease until proven otherwise.
- Thoracic pain should raise even greater suspicion for the likelihood of cancer.
  - Since complaints of chronic back pain are common there is often a delay in diagnosing spinal metastasis.
  - Levak et al. reported a median of 2 months between reported onset of pain and diagnosis of metastatic spinal cord compression in 319 cancer patients.
Clinical Manifestations - Neurological Deficits

- Can be present in all etiologies of spinal cord injury in the cancer setting
  - Epidural Spinal Cord Compression
  - Leptomeningeal Metastases
  - Primary Intramedullary Tumors and Metastases
  - Radiation Induced Myelopathy
  - Chemotherapy Induced Myelopathy
  - Paraneoplastic Myelopathy

Neurological Deficits

- Sensory impairments
- Motor impairments
- Autonomic dysfunction

Neurological Deficits - Location

- Region of the spine involved - NLI
  - ESCC: thoracic > lumbar > cervical spine
  - Leptomeningeal Metastases: cauda equina
  - ISCM: equally distributed
  - Radiation Myelopathy: area radiated
  - Chemotherapy Induced Myelopathy: along the neuro-axis
- Spinal tracts involved
  - ESCC anterior/lateral aspect of cord
  - Leptomeningeal metastases: dorsal aspect of cord
  - ISCM: dorsolateral aspect of cord
Neurological Deficits - Sensory Impairments

- Dorsal column involvement
- Spinal thalamic tract involvement
- Spinocerebellar tracts
- Spinal nerve root compression

Neurologic Deficits - Motor Impairments

- ESCC, Leptomeningeal Metastases, ISCM, Chemotherapy Induced Myelopathy, Chronic Progressive Radiation Myelopathy
  - In ESCC weakness is the 2nd most common presenting symptom and is present in 35-85% of patients
  - Leptomeningeal Metastases & ISCM motor deficits are an early manifestation
  - Chemotherapy Induced Myelopathy weakness follows onset of pain
  - Chronic Progressive Radiation Myelopathy motor deficits progress to paraparesis or quadriplegia over the course of weeks to months

Motor Impairments

- May present as UMN or LMN type or a combination of both depending on region of the spine involved
- Sphincter Function
  - Usually a late finding in ESCC and Chronic Radiation Myelopathy unless conus medullaris/cauda equina is involved
  - Can be an early finding in Leptomeningeal Metastases and ISCM
Neurological Deficits-
Autonomic Dysfunction

- ESCC, Leptomeningeal Metastases, ISCM, Chronic Progressive Radiation Myelopathy
- Involvement of the sympathetic outflow T1-L2(3)
  - Horner’s syndrome
  - Orthostatic/post prandial hypotension
  - Bradycardia
  - Bowel, bladder, sexual dysfunction
- Involvement of the parasympathetic outflow S2-S4
  - Bowel, bladder, sexual dysfunction
- Bowel and bladder dysfunction is seen in approximately 50% at time of diagnosis

Neurological Deficits-
Patterns

- Posterior Column Syndrome
  - ESCC, Leptomeningeal Metastases, ISCM, Chemotherapy Induced Myelopathy, Chronic Radiation Induced Myelopathy
- Brown Séquard Syndrome
  - ESCC, Leptomeningeal Metastases, ISCM, Chronic Radiation Induced Myelopathy

Neurological Deficits-
Other Findings

- Eruption of herpes zoster from irritation of the spinal dorsal root
- Neuropathic facial pain from involvement of the trigeminothalamic tract in high cervical lesions
NEUROLOGICAL DEFICITS

- The onset of neurological deficits is considered to be a medical emergency.
  - Patients with motor dysfunction inevitably progress to complete paralysis in the absence of intervention.


Neurological Deficits - Time Course

- ESCC rapid progression think aggressive tumor/vascular compromise to the cord
- ISCM neurological deficits occur concomitantly or rapidly after onset of pain
- Chronic Progressive Radiation Myelopathy slow progression of neurological deficits

Hammack, J. Spinal Cord Disease in Patients With Cancer. Continuum CLifelong Learning Neurol 2012; 18(2) 312-327
Clarke, J. Leptomeningeal Metastasis from Systemic ancer. Continuum Lifelong Learning Neurol 2012; 18(2): 328-342

Clinical Manifestation - Spine Instability

- Spine instability
  - Loss of spinal integrity as a result of a neoplastic process that is associated with movement related pain, symptomatic/progressive deformity, &/or neurological compromise under physiologic loads


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Spine Instability

• Determining Instability
  – Location of lesion
  – Spinal alignment
  – Vertebral body involvement
  – Involvement of posterior elements
  – Bone lesion quality
  – Mechanical pain

WORK UP

The Malignant Spine-Work Up

• Strong clinical suspicion
• MRI with and without gadolinium
  – Entire spine
  – Leptomeningeal metastases and ISCM consider addition of brain MRI
• CT myelography
  – If MRI is contraindicated
• CSF cytology
  – Leptomeningeal metastases and ISCM
• Biopsy
  – ESCC if no prior cancer history, or history of limited stage cancer
MANAGEMENT

The Malignant Spine-Tumor Related Treatment Options

- Goals of treatment are centered around pain relief, preservation of neurological function, and maintenance/restoration of spine stability
  - Radiation therapy
  - Surgery
  - Chemotherapy
  - Corticosteroids
  - Bisphosphonates
Treatment Options -
Decision Making

- Patient variables influence decision making
  - Age, tumor characteristics, tumor burden, life expectancy, comorbidities, and functional status

The Malignant Spine -
Treatment of Radiation Myelopathies

- Acute Transient Radiation Myelopathy
  - Symptom management
  - Reassurance

- Chronic Progressive Radiation Myelopathy
  - No effective therapy
  - Corticosteroids are often tried
  - Anticoagulation and hyperbaric oxygen
    - Noted to improve or stabilize symptoms
  - Bevacizumab
    - Monoclonal antibody against vascular endothelial growth factor
    - Anecdotal evidence of benefit

The Malignant Spine -
Role of Rehabilitation

- The overall life expectancy and oncologic prognosis should be taken into account in the rehabilitation of cancer patients.
  - The patient’s medical status can dictate appropriateness for and response to rehabilitation efforts.
  - The patient’s medical condition often follows their oncologic status.
  - Pre-morbid conditions can be exacerbated by cancer care itself or complications from cancer care and heavily impact a patient’s rehabilitation.
- Balance between time devoted to rehabilitation care and time spent with family and loved ones.
Cancer Rehabilitation Approaches-
Dr. J. Herbert Dietz

• Preventive rehabilitation
  – Indicated when disability can be predicted and focuses on reducing the severity and duration of its effect.
• Restorative rehabilitation
  – Attempts to restore pre-morbid function in a patient when a permanent impairment is not expected.
• Supportive rehabilitation
  – Focuses on maximizing function when a permanent impairment exists.
• Palliative rehabilitation
  – Provides comfort and support and reduces complications that may develop when increasing disability is expected from disease progression.

Goals of Rehabilitation

• Functional activities
  – Mobility, transfers, ADLs
• Bowel and bladder management
• Management of pain and spasticity
• Educational training to patient and caregivers
• Equipment
  – Adaptive equipment
  – Wheelchair assessment
  – Adaptive housing
• Psychological counseling
• Nutritional status
• Exploring patient’s financial aid possibilities
• Determine safest disposition
• QUALITY OF LIFE

Communication of Treatment Goals

• Consistent communication between members of the oncology team, rehab team, patient and family members is essential.
  – This ensures that realistic expectations for rehab can be set.
  – This is vital especially during periods when the patient’s clinical status, prognosis, and treatment strategies are changing.
Outcome Data - Rehabilitation Length of Stay


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Abbreviations: NC, not communicated; NRhG, no rehabilitation group; RhG, rehabilitation group.

Outcome Data - Pain


Outcome Data - Ambulation

• Gait score progression on FIM was 38%.
• Acquired functional benefits lasted an average of 3 months.

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Myelopathy in the Cancer Setting—Putting it all Together

• What is the patient’s clinical presentation?
• What is the etiology of the spinal cord injury?
• What is the oncology plan?
• What is the patient’s overall life expectancy and oncologic prognosis?
• What is the best approach/setting for rehab efforts?
• What are realistic goals/what are the patient’s and family’s goals and expectations?
• What factors might interfere with the patient’s functional prognosis?

Putting it all Together

• Consistent communication between all members of the team (oncology, rehab, patient and family members) is ESSENTIAL.
• Balance between time devoted to rehab and time spent with family and loved ones.
Myelopathy in the Cancer Setting-Moving Forward

• “To date, no PM&R therapeutic care model has been designed or validated for patients with metastatic epidural spinal cord compression.”
• “According to the severity of the prognosis correlated with primary cancer and its metastatic potential, only 10-14% of patient with metastatic epidural spinal cord compression and paraplegia or paraparesis have access to rehabilitation care.”
• Further prospective studies are warranted to validate the effect of rehabilitation efforts and update the impact of PM&R in terms of functional outcome and comfort care provided to this population.


Thank you!!!!

Questions, Comments, Concerns???