Introduction to Spine Tumors

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Overview
1. Classification of Spine Tumors
2. Evaluation of patients with Spine Tumors
3. Treatment strategies

Classification
• Spinal Cord or Spinal Column
• Benign versus Malignant
• Anatomically Subclassified
  – Extradural
  – Intradural Extramedullary
  – Intramedullary

Extradural Benign Tumors and Cysts
• Benign Lesions arising from the VB or neural arches
• Relatively uncommon
  ▪ Vertebral Hemangiomas (most common)
  ▪ Osteoid Osteoma/Osteoblastoma
  ▪ Osteochondroma
  ▪ Giant Cell Tumors
  ▪ Langerhans Cell Histiocytosis/Eosinophilic Granuloma
  ▪ Aneurysmal Bone Cyst

Vertebral (Cavernous) Hemangioma
• Most common benign spinal neoplasm
• 10-12% autopsy series
• Hemartomatous proliferation of vasogenic and endothelial tissue in the bone
• 1/3 patients have multiple levels involved
• Usually asymptomatic/incidentally identified
• Rarely may enlarge causing:
  ▪ pain
  ▪ neurological deficit from spinal cord compression
  ▪ pathological fracture
• Symptomatic lesions usually thoracic spine

Vertebral (Cavernous) Hemangioma
• Asymptomatic = no f/u
• XRT often results in sclerotic obliteration
  ▪ Pain (improves over months – yrs)
  ▪ Post op for incomplete removal as 20-30% recurrence within 2 yrs, reduced to 7% with adjuvant XRT
• SRS
• Embolization
  ▪ More rapid pain relief but risk of cord infarction
• Direct Ethanol injection
• Vertebral Augmentation
• Surgery
  ▪ Goal of radical excision and reconstruction
Extradural Benign Tumors and Cysts

- Osteoid Osteoma/Osteoblastoma
  - Irregular woven bone and numerous osteoblasts with increased vascularity
  - Distinguished by size Osteoblastoma >1.5 cm
  - Night time pain, relieved by aspirin
  - Cure = Complete Excision

- Osteochondroma
  - Most common benign bone tumor
  - Considered to be hemartomas of cartilage
  - Often in long bone, 4% in spine, mostly cervical
  - Fibrous capsule, cartilage cap and mature bony stalk
  - Hereditary tendency
  - Surgical resection, rare malignant potential

- Giant Cell Tumors (GCT)/Osteoclastomas
  - Locally aggressive
  - Osteoclast-like giant cells in spinal stroma (neoplastic component)
  - <10% of GCT in spine, 50% in the sacrum
  - High probability of local recurrence
  - Require multiple surgeries or adjuvant radiation
  - Malignant transformation to Sarcoma may occur
  - Curettage only = ~20% recurrence

- Langerhans Cell Histiocytosis/Eosinophilic Granuloma
  - Abnormal histiocytic proliferation and granulomatous lesions
  - Unclear whether it is tumor of inflammation
  - Significant risk of local recurrence
  - Spine involvement typically in pediatric population
  - Immobilization (± radiation)

- Aneurysmal Bone Cyst
  - Small and large cavernous spaces filled with clotted blood fluid
  - Expansile lesion
  - 1% of primary bone tumors
  - 10-30% in the spine (equal distribution throughout spine)
  - 25-50% recurrence if not completely excised

Extradural Benign Tumors and Cysts

- Meningiomas
- Schwannomas
- Neurofibromas
- Paragangliomas
- Ganglioneuromas
- MPNST
- Hemangiopericytoma
- Leptomeningeal Metastasis
  - (to be discussed by Drs. Benzel and Chao tomorrow)

Intradural Extramedullary Tumors

- Astrocytomas
- Ependymomas
- Capillary Hemangioblastomas
- Spinal Cavemosus Angiomas
- Ganglioglioma
- Oligodendrogioma
- PNETs
- Intramedullary Metastases
  - (to be discussed by Dr. Trost tomorrow)

Intramedullary Tumors

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Epidural Malignant Tumors

- Metastases
- Chordoma *
- Plasmacytoma
- Ewing Sarcoma
- Osteosarcoma
- Chondrosarcoma
- Fibrosarcoma
- Lymphoma
  - (*) Covered by Drs. Subramaniam and Saoud tomorrow

Intradural Extramedullary Tumors

- Tumors of various origins (mostly benign)
  - Meningiomas
  - Schwannomas
  - Neurofibromas
  - Paragangliomas
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Epidural Malignant Tumors

- **Plasmacytoma**
  - Collection of malignant hemopoietic cells in marrow
  - Represents solitary lesion, multiple = multiple myeloma

- **Ewing Sarcoma**
  - Uncommon in the spine – 10% (typically long bone)
  - >50% of spine presentation is in sacrum
  - Small round cell sarcoma
  - Aggressive resection/irr/chemo

- **Osteosarcoma**
  - High grade spindle cell neoplasm filled with immature woven osteoid
  - Unusual in the spine (<5%)
  - May develop in post radiation fields

- **Chondrosarcoma**
  - Malignant tumor or connective tissue

- **Fibrosarcoma**
  - Rare tumor
  - Essentially tumor of soft tissue associate with adjacent periosteum

- **Lymphoma**
  - Only 1% of PCNL involve spine
  - Mostly diffuse large B-cell subtype
  - Typically very steroid sensitive

Metastases

- **Cancers** among the leading causes of death worldwide. 8.2 million deaths in 2012
  - WHO estimated 6.2 million people died of Stroke in 2008
  - AIDS-related deaths 2.0 million (1.7 million – 2.4 million) and 1.8 million people died from TB in 2008

The Problem

- Survival and disease control rate steadily improving with
  - 84% of patients surviving 5+ years
  - 40% surviving 10+ years
  - 15% surviving 20+ years

The Implications

- Cancer care of the future needs to consider both the short AND intermediate Consequences and Outcomes of our Interventions
The Issues

- Bone pain is not adequately treated by many physicians
- Patients at times experience sequential complications over a period of several years
- In addition to pain, patients can experience
  - Loss of mobility
  - Skeletal fractures
  - Hypercalcemia
  - Spinal cord and nerve root compression

End Result

Impaired Quality of Life (QOL)

Location of Spinal Metastases

- Bony spine
- Dura/LMD
- Spinal cord (very rare)

Location of the Lesion

- 70% thoracic (most often symptomatic also)
- 20% lumbar & sacral
- 10% cervical
- Body > Pedicle > Posterior Elements (20%)

Histology

Adult:
- Lung (15-20%)
- Breast (15-20%)
- Prostate (15-20%)
- NHL (5-10%)
- Multiple myeloma (5-10%)
- Renal (5-10%)
- Others

Pediatric:
- Neuroblastoma
- Wilms
- Ewings
- Lymphoma
- Sarcoma
Presentation of Spinal Metastases

- PAIN: >90%, persistent, progressive, night pain
- Neurological Symptoms: 10%, weakness, spasticity, bladder or bowel symptoms
- In 50% the primary tumor is unknown

Mechanisms of Spinal Metastasis

- Hematogenous seeding (often multicentric)
  - Arterial
  - Venous via the Batson plexus
- Direct extension or invasion
- CSF seeding
  - Often after surgical manipulation of cranial disease

Pain Characterization

- Biological Pain
  - Nocturnal
  - Resolves with Steroids
- Mechanical Pain
  - Instability related
  - Movement related pain
  - Surgery should be considered

Mechanical Instability

- AA: Rotational pain
- Cervical: Flexion/Extension pain
- Thoracic: Extension (pt sleep upright in chair)
- Lumbar: Mechanical Radiculopathy with axial loading (Searing leg pain on sitting or standing)
  - Needs assessment by spine surgeon

Neurological Symptoms Related to Spinal Cord compression

- Sensory Loss 70 – 80%
- Paraparesis/ Paraplegia > 60%

- 11-34% of patients with spinal cord compression are still ambulatory at diagnosis

Pathophysiology of Spinal Cord Compression

- Compression
- Venous congestion
- Cord edema
- Arterial insufficiency
- Cord infarct
Spinal Cord Compression

• Presents with progressive loss of neurological function
• Complete loss of function for >12hrs - 24hrs results in permanent loss of motor function
• THIS IS AN EMERGENCY! (Radiation Oncologist or Spine Surgeon)

Determinants of Neurological Recovery

• Duration of deterioration
  • acute = poor prognosis
  • gradual = better prognosis
• Degree of deficit
• Location of compression
• Tumor biology

Prognosis

• Median survival for patients with metastatic disease is 10 months
• Death typically results from systemic malignancy
• Spinal vertebral metastases commonly signals disseminated disease
• In the past, ? role for treatment

Prognosis Cont’d

• BUT treatment is warranted especially for Quality of Life (rather than cure)

GOALS

• Preservation or restoration of ambulation
• Bladder control
• Pain Relief

Treatments for Spinal Metastases

• Analgesics, Bracing & Bedrest (?role)
• Radiation/Radiosurgery
• Chemotherapy
• Surgery
  —Curative
  —Palliative
  —Prophylactic
  —Reconstructive

Factors to consider regarding treatment

• Absence or presence of neurologic deficit
• Spinal instability
• Prior tissue diagnosis of primary
• Age, health, life expectancy of patient
• Presence of other metastatic sites
• Relative radiosensitivity
• Prior history of radiation
Medical Treatment of Spinal Tumors

• Analgesia
  — NSAIDS
  — Mild narcotics
  — Morphine with bowel regimen
  — Treatment of neuropathic pain

• Corticosteroids
  — Pain
  — Radiculopathy
  — Myelopathy

Steroids
Can help relieve symptoms by reducing swelling and inflammation around spinal cord.
Dosing – 10-100 mg IV/PO decadron then 4 mg q6h PO and taper every 4 days unless symptoms increase.
25% will remain on chronic therapy
Side effects – GI related (↑ appetite, peptic ulcers)
  Systemic (edema, hypertension, Cushingoid appearance, osteoporosis, electrolyte imbalances)
  Diabetes mellitus
  Psychological (psychoses, depression, insomnia)
  Skin (acne, thinning of skin)

Medical Treatment of Spinal Tumors

• Chemotherapies
• Hormonal therapies
• Biphosphonates

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Radiotherapy for Spinal Tumors

• Historically, laminectomy was the preferred treatment of metastases to spine, particularly those with an epidural component
• In the 60’s and 70’s, radiotherapy became feasible for such tumors and laminectomy and radiotherapy were combined.
• In the 70’s, evidence accumulated that radiotherapy alone was as effective as combined therapy

Goals of radiation therapy

1. Pain control
2. Restore/maintain neurologic function
3. Prevent local progression
4. Provide spinal stability
Radiation therapy

Goal of fractionation is to reduce side effects in adjacent tissue

Potential concerns:
- mechanical stability
- appropriate dosage to treat patient
- large amount of tissue is irradiated
- fractionation may be difficult for some patients

Radiation Therapy

- 25-40 Gy over 10-14 days
- Affected level and 5 cm margin
- Local control determined by dose and tumor type
- The dose delivered to the target is often inadequate, and therefore not recommended in a histological tumor type that is radioresistant
- XRT alone now superseded by SRS and more advanced surgical options

Results from radiation therapy

- Back pain improves in 60-80%
- Improvement in motor/autonomic function in 40-60%.
- <50% regain lost functional capacity
- 80% maintain pre-radiation level of ambulation/motor function
- Complete response varies depending on histology, ranges from 30-80%

Side effects from radiation therapy

- Fatigue
- Erythema of skin
- Esophagitis in thoracic field
- Nausea in abdominal field
- Myelosuppression in pelvic fields
- Post XRT treatment fracture of bone 18% (Tong 1982)

Treatments for Spinal Metastases

- Analgesics, Bracing & Bedrest (?role)
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Surgery’s role

- Tissue confirmation
- Spinal instability
- Bony fragments that impinge on cord
- Previous radiation to affected spine, i.e., lung
- Radioresistant histologies
- Decreased neurologic status during or after radiation
Surgery – Who?

**Ideal**
- Solitary lesion
- Low grade
- Chemoradiosensitive
- Neurologically normal
- Thin and healthy
- Normal bone
- Non-smoker

**Reality**
- Multiple lesions
- High grade
- Life expectancy indeterminate
- Vascular tumor
- Neurologically impaired
- Co-morbidities
- Osteoporosis
- Smoker
- Obesity
- Previous surgery
- Previous irradiation

All patients are different and require individual evaluation.

Surgery – Why?

**Goals**
- Neural Decompression
- Spinal Stability
- Tumor burden
- Neurologic function
- Life expectancy
- Quality of life
- Mobility
- Diminish pain

Surgery – When?

**Neurological deterioration**
- Rapid deterioration
  - Surgical emergency
- Gradual deterioration or complete > 48 hours
  - Urgent investigation, oncology consult, +/- surgery
- Neuro normal
  - Semi-elective
Surgery
Who?
Why?
When?
Which type?

Surgery - Which Type?
Tumor Resection
• Neural decompression
Reconstruction
• Instrumentation
• Fusion
Anterior
Posterior
Combined

Outcome after Surgery
• Pain Relief;
  80 to 90% experience relief of > 80% intensity
• Neurological Recovery
  anterior decompression = 75%
  posterior decompression = 40%
  ambulators = 60 - 95% recover
  paraparetics = 30 - 60% improve
  paraplegics = < 30% improve

Outcome after Surgery
• Mean survival time;
  from diagnosis = 24 months
  from surgery = 16 months
  unknown primary = 6 months
• Complications;
  peri-operative = 30%
  mortality = 5%

Surgical Options
As surgical tools became less invasive and techniques were refined, other approaches were designed to help relieve pressure on the spinal cord.
• Posterior decompression
  - standard approach historically
• Anterior decompression (1980s)
  - best used for tumors causing epidural cord compression

Role of Surgery in Spine Tumors 1970's-2005
• Classic literature
  — Surgery plus XRT no better than XRT
• Surgery consisted of laminectomy alone
  — Not effective for anteriorly situated tumors (most)
  — May not decompress
  — No treatment of the tumor
  — Postoperative instability
Direct Decompressive Surgery

- Relieves compression
- Removes tumor
- Stabilizes the spine

Prospective Randomized Trial: Surgery/RT vs. Radiation Alone

- The surgical group faired better in terms of:
  - Retaining ambulation rate
  - Regaining ambulation rate
  - Neurologic exam
  - Survival
  - Analgesic use
  - Corticosteroids use
- Surgery allows most patients to remain ambulatory for the remainder of their lives
- No excess mortality or morbidity associated with surgery

Spinal Oncology has focused on...

- New instrumentation in spinal reconstruction
- New surgical approaches to the spine (combined anterior/posterior resections)
- Complication avoidance
- Trend toward "minimally invasive" techniques (vertebral augmentation)

Spine Instability Neoplastic Score (SINS)

- To provide a scoring system to accurately and reliably predict the degree of instability in patients with spinal tumors
  - Spine surgeons: a new paradigm for decision making
    - a step toward standardized treatment of spinal metastases
  - Non-surgeons: a tool to help streamline referrals to appropriate oncologic specialists (e.g. surgery vs. radiation therapy)
Surgery and EBXRT Limitations

Surgery
• improves the chance of neurological recovery in patients with high grade cord compression
• restores spine stability
  **BUT**
• Metastatic tumors not resectable for cure
• Recurrences of 57.9% at 6 months and 96% at 4 years with surgery and XRT

Dual Requirement of Effective Spine Metastatic Tumor Treatment

1) **Pain** Palliation (or **Pain** Prevention)
2) **Tumor control** and prevention of neurological compromise

Achieved either through **monotherapy** or as part of **combination/multimodality** treatment

Stereotactic Radiosurgery

• Delivery of an accurate and conformal high radiation dose to the tumor
• Usually a single session (1-5)
• Steep fall-off dose gradients associated with the treatment protects the adjacent normal structures

What does the current evidence support?

• Conventional Radiotherapy
  – 3 randomized trials (high quality evidence)
  – 4 prospective studies (moderate quality evidence)
  – Over 40 non-prospective data (low quality evidence)
  – Includes over 5,000 patients in the literature
• Stereotactic Radiosurgery
  – >60 single institution reports (as of March 2014)
  – No randomized data available to date

Overall Clinical Outcomes: Metastases Evidence in the Literature

• Long-term pain improvement **86% overall**

• Radiographic control
  – Primary treatment **90%**
  – Radiographic progression **88%**

• Clinical improvement after progressive neurological deficit **84%**
**Current Recommendations: Spine Radiosurgery/SBRT**

- "Radiosurgery is safe and effective with durable symptomatic response and local control for even radioresistant histologies, regardless of prior fractionated radiotherapy."

- "Radiosurgery should be considered over conventional fractionated radiotherapy for the treatment of solid tumor spine metastases in the setting of:
  - oligometastatic disease and/or
  - radioresistant histology."

**WE WILL HAVE CLASS 1 EVIDENCE: Radiation Therapy Oncology Group #0631**

- “Phase II/III Study of Image-Guided Radiosurgery/SBRT for Localized Spine Metastases”

- **Phase II Component**
  - 43 patients treated with 16 Gy single dose SBRT
  - (Accrual complete. ASTRO 2011 presentation.)

- **Phase III Component (Currently accruing patients)**
  - 240 patients randomized to 16 or 18 Gy single dose SBRT versus 8 Gy conventional single dose (2:1 ratio)

**Treatments for Spinal Metastases**

- Analgesics, Bracing & Bedrest (?role)
- Radiation/Radiosurgery
- Chemotherapy
- Surgery
  - Curative
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**How best to treat spine metastases?**

**Effective Treatment**

- Often requires
  - Multidisciplinary therapies
  - Understanding of the clinical condition
  - Life Expectancy assessment
  - Specific attention to QOL of the patient