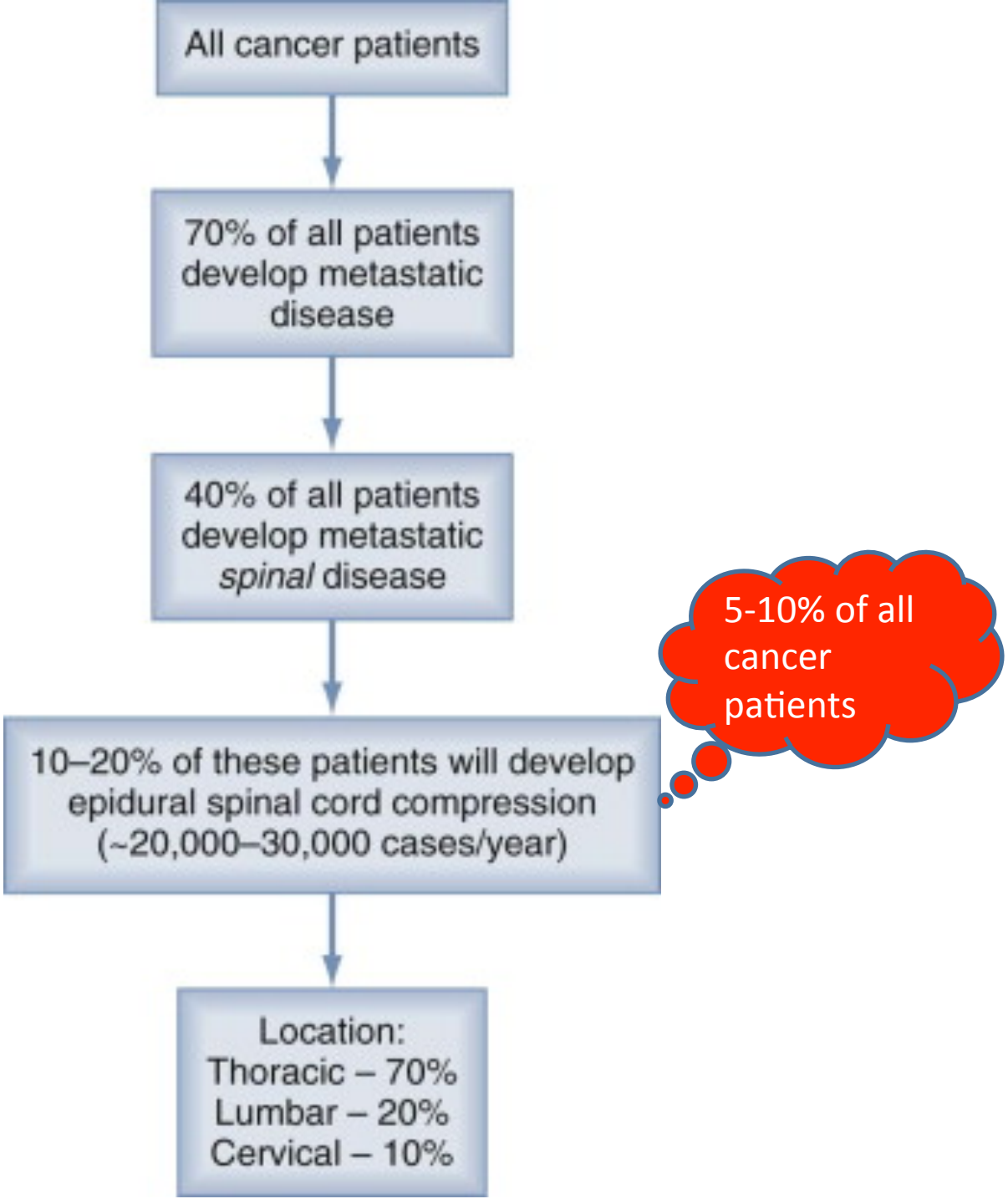
MANAGEMENT OF METASTATIC TUMORS TO THE SPINE


All cancer patients
70% of all patients develop metastatic disease
40% of all patients develop metastatic *spinal* disease
10–20% of these patients will develop epidural spinal cord compression (~20,000–30,000 cases/year)
Location:
Thoracic – 70%
Lumbar – 20%
Cervical – 10%
5-10% of all cancer patients

Introduction

Spine is the most common site of bony metastases

Median survival with spinal metastasis (SM)- 3 to 18 months

The highest incidence of SM is found in the 40–65 age-group as this is the period of highest cancer incidence

Introduction

Vertebral and/or epidural (extradural) involvement is seen in 90–95% of SM

Intradural extra-medullary and intra-medullary seeding of systemic cancer is unusual

Lepto-meningeal disease occurs in about 10% of patients

Introduction

Primary tumors most likely to metastasize to the vertebral column

a. breast (16–37%)

b. prostate (9–15%)

c. lung (12–15%)

d. kidney (3–6%)

e. thyroid (4%).

Metastases from prostate, breast, melanoma, and lung commonly cause spinal metastases in 90.5%, 74.3%, 54.5%, and 44.9% of patients

Introduction

Risk for neurological deficits due to epidural spinal cord compression varies with the site of primary disease:

- ✓ 22% with breast cancer
- ✓ 15% with lung cancer
- ✓ 10% with prostate cancer

Metastatic spinal disease arises in any of three locations:

- ✓ vertebral column (85%)
- ✓ paravertebral region (10% to 15%)
- ✓ rarely the epidural or subarachnoid and intramedullary space (<5%)

Introduction

The posterior half of the vertebral body is involved first, with the anterior body, lamina, and pedicles usually affected later

Multiple lesions at non-contiguous levels occur in 10% -40%

10% patients have an unknown primary (in 50% lung will be the primary source)

Most metastatic lesions are osteolytic. Only 5% of metastases have an osteoblastic response

Pathways of spread

- ✓ arterial route
- ✓ venous routes through the Batson plexus
- ✓ direct invasion through the inter-vertebral
- ✓ lymphatics

Presentation

Night pain or pain when recumbent is a classic feature of spine malignancy (85–96%)

Pain almost always precedes the loss of neurological function

Pain: Tumor related- nocturnal

Mechanical- vertebral destruction

Motor dysfunction is the second most common (35–75%)

Diagnosis

- ✓ Baseline neurologic exam- Grade the patient
- ✓ X-ray- limited role as 30-50% of vertebral body needs to be destroyed before involvement can be seen
- ✓ Bone scans- highly sensitive, identifies areas of increased bone deposition. So, easily detects osteoblastic metastases but can only detect osteolytic lesions if there is a significant bone repair occurring

Diagnosis

- ✓ CT scan- sensitivity and specificity of CT to detect bony involvement ranges between 90% and 100%

- ✓ MRI whole spine (about 15% patients will have other lesions) has the greatest sensitivity (98.5%) and specificity (98.9%) with overall accuracy of 98.7%

Diagnosis

- ✓ CT myelography –when MRI can't be done or when an MRI is not available. Can cause neurological worsening if done in presence of high-grade block rostral to the puncture
- ✓ PET/SPECT
- ✓ Angiography
- ✓ Biopsy

Grading Scales

Frankel Grading Scale

GRADE	DESCRIPTION
A	No motor or sensory function
B	Preserved sensation only, no motor function
C	Nonambulatory, wheelchair bound, some motor function a. Bowel or bladder paralysis b. Neurogenic bowel or bladder c. Voluntary normal bowel or bladder function
D	Ambulatory but with neurological symptoms 1. Requires walker 2. Requires a cane 3. Can walk independently a. Bowel or bladder paralysis b. Neurogenic bowel or bladder c. Voluntary normal bowel or bladder function
E	Normal neurological functions

Frankel HL, Hancock DO, Hyslop G, et al. The value of postural reduction in the initial management of closed injuries of the spine with paraplegia and tetraplegia. I. Paraplegia. 1969;7:179.

Eastern Cooperative Oncology Group (ECOG) Performance Status Grades

GRADE	DESCRIPTION
0	Fully active, able to carry on all predisease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature (light housework, office work)
2	Ambulatory and capable of all self-care but unable to carry out any work activities; up and about >50% of waking hours
3	Capable of only limited self-care, confined to bed or chair >50% of waking hours
4	Completely disabled; cannot carry on any self-care; totally confined to bed or chair
5	Dead

American Spinal Injury Association Impairment (ASIA) Scale

GRADE	DESCRIPTION
A (complete)	No motor or sensory function is preserved through S4-5
B(incomplete)	Sensory but no motor function is preserved below the neurological level and extends through S4-5.
C(incomplete)	Motor function is preserved below the neurological level, and most key muscles below the neurological level have a muscle grade <3
D(incomplete)	Motor function is preserved below the neurological level, and most key muscles below the neurological level have a muscle grade ≥3.
E (normal)	Motor and sensory function are normal.

Gait Scale

Grade	Description
1	Normal
2	Gait with assistance
3	Paresis without gait function but still able to move legs
4	Paraplegia

Management Principles

Options: Surgery, Radiation, Chemotherapy

Early intervention: as neurological outcome after treatment is primarily dependent on the neurological status before treatment

Primary histology and post-treatment ambulatory status - most consistently determine survival (median survival for breast CA- 650 days, lung cancer -120 days)

Decision issues- ambulatory function, pain control, autonomic function (sexual and bowel /bladder control), overall survival, and quality of life

Surgery should only be offered to patients with an estimated life expectancy of greater than 3 to 6 months

Staging

Harrington's scheme *(based on bone destruction & neurological compromise)*

1. no significant neurological involvement
2. involvement of bone without collapse or instability
3. major neurological impairment (sensory or motor) without significant involvement of bone
4. vertebral collapse with pain resulting from mechanical causes or instability, but with no significant neurological compromise
5. vertebral collapse or instability combined with major neurological impairment

Recommendation: Cat 1, 2 & 3 - CT, RT or hormonal Tx

Cat 4 & 5 – Surgery

Harrington KD: Metastatic disease of the spine. *J Bone Joint Surg Am* 1986; 68:1110.

Staging

Based on definition of spinal instability:

1. ***Kostuik et al***: Two-column concept

- ✓ Anterior column - vertebral body, further into ant./post & left/right
- ✓ Posterior column - pedicles, laminae & spinous processes; further into left/right
- ✓ Spine unstable if $\geq$ 3 segments were destroyed

Kostuik JP, Errico TJ, Gleason TF, et al: Spinal stabilisation of vertebral column tumors. *Spine* 1988; 13:250.

Staging

2. ***Tomita et al*** : Instability present if there was-

- ✓ transitional deformity
- ✓ vertebral body collapse greater than 50%
- ✓ three column involvement (as defined by Denis)
- ✓ involvement of the same column in two or more adjacent levels

Tomita K, Kawahara N, Kobayashi T, et al: Surgical strategy for spinal metastases. *Spine* 2001; 26:298.

Staging

3. ***Cybulski*** –

a) Anterior and middle column destruction (> 50% collapse of VB ht.)

b) Collapse of 2 or more adjacent VBs

c) Tumor involvement of the middle and posterior columns

d) Previous laminectomy, with failure to recognize anterior and middle column disease

Recommended- Sx decompression and fixation when any one of above criteria , presence of neural compression in patients with life expectancy> 5–6 months, competent immune and nutritional status, incomplete neurological deficit, and a radioresistant tumor or a tumor that failed to respond to previous treatment

Cybulski GR: Methods of surgical stabilisation for metastatic disease of the spine. *Neurosurgery* 1989; 25:240.

SINS Score

- ✓ Range 0-18
- ✓ 0 - 6 denotes stability
- ✓ 7- 12 denote indeterminate (possibly impending) instability
- ✓ 13- 18 denote instability
- ✓ Patients with SINS scores of 7 to 18 warrant surgery

Fisher CG, DiPaola CP, Ryken TC, et al: A novel classification system for spinal instability in neoplastic disease: An evidence-based approach and expert consensus from the Spine Oncology Study Group. Spine (Phila Pa 1976) 35:E1221-E1229, 2010

Daryl R. Fourney et al: Spinal Instability Neoplastic Score: An Analysis of Reliability and Validity From the Spine Oncology Study Group. JCO 29 (22), 2011

Prognostic Scoring Systems

Tomita Scoring System

1 point - Slow growth: Breast, Thyroid, Prostatic, Testicular CA

2 points -Moderate growth: Renal cell, Uterus, Ovarian,Colorectal CA

4 points = Rapid growth: Lung,Gastric,Esophageal, Nasopharyngeal, Hepatocellular , Pancreas, Bladder, Melanoma,Sarcoma (osteosarcoma, Ewing sarcoma, Leiomyosarcoma) ,Other rare ca., Primary unknown metastasis

Rare CA (4 points) :Inflammatory type Breast CA , undifferentiated Thyroid CA, inflammatory type Renal cell CA

Treatments: Medications

Steroids-

Used in metastatic disease causing spinal cord dysfunction

Rationale- reduces vasogenic edema, protects against lipid peroxidation & hydrolysis, enhances blood flow, prevents ischemia and intracellular calcium accumulation, stabilizes lysosomal membranes, attenuates inflammatory response, and supports cellular energy metabolism

Dosage- Loading doses 10 -100 mg, followed by 4 to 24mg QDS

Treatments: Medications

Sorensen et al. compared high-dose dexamethasone f/b RT with RT alone- 81% patients in the steroid group were ambulatory after treatment compared with 63% in the control group

Heimdal et al. showed that in patients with a complete myelographic block who received a bolus of 100 mg followed by a standard maintenance dose had no better pain relief, ambulation, or bladder function than those who received a 10-mg bolus and the same maintenance therapy

Recommendation- initial bolus of 10 mg followed by 16 mg/day

Sorensen S, Helweg-Larsen S, Mouridsen H: EFFect of high dexamethasone in carcinomatous metastatic spinal cord compression treated with radiotherapy: a randomised trial. *Eur J Cancer* 1994; 1:22.

Heimdal K, Hirschberg H, Slettebo H, et al: High incidence of serious side effects of high dose dexamethasone treatment in patients with spidural spinal cord compression. *J Neurooncol* 1992; 12:141.

Treatments: Medications

Bisphosphonates-

Work by inhibiting osteoclast activity and thus decreasing bone resorption. also have direct tumoricidal effect.

Many RCTs evaluated the use of bisphosphonates in the prevention of skeletal-related events (SREs), defined as pathologic #, spinal cord compression, RT or Surgery for bone metastases, or hypercalcemia. Bisphosphonates showed to decrease the number of and time to an SRE in prostate cancer, breast cancer, multiple myeloma, lung cancer, and renal cell carcinoma

Treatments: Medications

Hormone Therapy

Most commonly for breast and prostate cancer

Breast cancer- Selective estrogen receptor modulators (SERM) such as tamoxifen, and aromatase inhibitors such as letrozole, anastrozole, and exemestane have been shown to be effective

Prostate cancer- androgen suppression with GnRH agonists and/or flutimide are effective

Even if the primary tumor is responsive to hormone therapy, metastases may not possess the same hormone receptors, therefore, may be unresponsive to hormone therapy

Surgery

Indications for surgery

- ✓ Radioresistant tumors (sarcoma, lung, colon, renal cell, breast)
- ✓ Obvious spinal instability
- ✓ Clinically significant neural compression secondary to retropulsed bone or from spinal deformity
- ✓ Intractable pain unresponsive to nonoperative measures
- ✓ Radiation failure (progression of deficit during treatment or spinal cord tolerance reached)

Surgery

Historically, laminectomy was the only surgical treatment offered

Complications (11%)-wound infection/dehiscence and spinal instability

Decompressive laminectomy was prone to failure because in most cases the tumor is ventral to the thecal

Laminectomy can cause/ worsen preexisting spinal instability leading to progressive deformity & pain & neurological compromise

Recommendation- done when pathology is strictly confined to the lamina and spinous process

Ambulatory Outcome after Various Treatments

Treatment	N	Success (%)
Posterior Decompressive Laminectomy Alone (Mean success- 30%)		
Barron ,1959	38	29
Wild, 1963	22	26
Brice and McKissock, '65	139	32
Stark, 1982	32	16
Findlay, 1987	80	24
Sorensen, 1989	105	34

Treatment	N	Success
Radiation Alone (Mean success- 47%)		
Mones et al, 1966	41	34
Khan et al, 1967	82	41
Gilbert et al, 1978	170	49
Constans et al, 1983	108	39
Sorensen et al, 1989	149	38
Ruff & Lanska, 1989	41	73
PDL and Radiation (Mean- 47%)		
Mullan and Evans, 1957	21	43
Wild and Porter, 1963	23	44
Wright, 1963	17	47
Constans et al, 1983	465	46
Sherman, 1986	111	57
Sorensen et al, 1989	91	53

Success is defined as the ability to walk after the operation (i.e., gait was maintained, improved, or regained as a result of the laminectomy)

Surgery

Laminectomy alone or in combination with radiation was no more effective in terms of preserving or restoring neurological function than radiation alone

In a review of 134 patients treated with either a laminectomy (n = 111) or laminectomy with stabilization (n = 23), Sherman and Waddell found that the latter group had better posttreatment ambulatory status (92% versus 57%), sphincter function, and pain control and less recurrent neurological dysfunction

Sherman R, Waddell J:
Laminectomy for metastatic epidural spinal cord tumors. Posterior stabilization, radiotherapy, and preoperative assessment. *Clin Orthop Relat Res* 1986; 207:55.

Surgery

Anterior decompression

One of the first reported series performing anterior spinal decompression was in 1982 by Siegal and coworkers.

Approaches can broadly be classified as anterior (e.g., transthoracic, retroperitoneal) or posterior, including posterolateral trajectories (e.g., laminectomy, transpedicular, costotransversectomy, lateral extracavitary)

Surgery

Consensus and data are lacking as to the optimal surgical approaches and procedures and are at the discretion of the treating surgeon.

Patients with metastatic spinal disease requiring surgical intervention may be treated with either an en bloc spondylectomy (considered in the rare patient with a solitary metastasis and favourable prognosis) or more commonly with an intralesional decompression and stabilization.

Surgical Classification Schemes

Percutaneous vertebral augmentation

1. Vertebroplasty- injection of (PMMA) cement into vertebral body

2. Kyphoplasty

3. Skyphoplasty

Radiation

Indications-

- ✓ Radiosensitive tumors (lymphoma, multiple myeloma, small cell lung carcinoma, seminoma of testes, neuroblastoma, Ewing's sarcoma)
- ✓ Survival <3- 4 months
- ✓ Inability to tolerate an operation, total
- ✓ Neurological deficit for more than 24 -48 hours
- ✓ Multilevel or diffuse spinal involvement

Radiation

Standard radiation portal involves the diseased level with a 5-cm margin, which effectively includes two vertebral bodies above and below

Long course RT: 30- 40 Gy in 20-30 #

Short course RT: 16 Gy in 1-2 # or 20 Gy in 5 # (very sick pts.)

Average pain improvement, ambulatory success, and rescue in recent RT trials are 77%, 63%, and 29%

First Score (predicts survival after RT)

First Score	(%)Survival	
	6 mnths	12 mnths
20-25	4	0
26-30	11	6
31-35	48	23
36-40	87	70
41-45	99	89

Rades D, Dunst J, Schild SE: The First score predicting overall survival in patients with metastatic spinal cord compression *Cancer* 2008; 112:157.

Radiation

Recommendation-

Score 20-30: short-course therapy

Score > 36 points: long-course therapy

Score 31 to 35 points: gray zone

Van der Linden's Scoring System

Prognostic factors	Points
KPS	
80-100	2
50-70	1
20-40	0
Primary tumor	
Breast	3
Prostate	2
Lung	1
Other	0
Visceral mets	
No	1
Yes	0

- ✓ 0 to 3 points- 3 months OS
- ✓ 4 to 5 points- 9 months OS
- ✓ 6 points- 18.7 months OS

Stereotactic Radiosurgery

Indications: No consensus

- ✓ Limited (i.e. 1–3 metastases)
- ✓ ≤ 2 contiguous vertebral bodies involved
- ✓ Limited and/or controlled systemic disease
- ✓ Good performance status
- ✓ Anticipated survival > 3 months

Stereotactic RT

- *Long-term pain control -86%,*
- *Tumor control -90%,*
- *84% of patients with neurological deficits experienced some clinical improvement*

Intramedullary Spinal Cord Metastases

Rare < 5% patients

Most common source- lung carcinoma (esp. SCLC)

When to suspect? -- patient with h/o malignancy and new onset of unilateral motor or sensory impairments

Brown-Sequard syndrome :30–45%

Intramedullary Spinal Cord Metastases

Hallmark - rapid progression of neurological symptoms (primary intramedullary tumors- slow growing and present with a gradual progression of symptoms)

75% patients progressed to full neurological deficit within 1 month of the initial development of neurological symptoms

Intramedullary metastases are generally a late finding

Intramedullary Spinal Cord Metastases

Average survival is less than 1 month

General recommendation-

Sensitive tumors- XRT

Resistant tumors- microsurgical resection (often discrete, well circumscribed tumors) combined with treatment of the primary tumor and other secondary metastases

Patient with suggestive history

- ✓ Confirm with biopsy
- ✓ Grade the patient- Frankel/ ECOG/ ASIA
- ✓ Calculate survival- Tokuhashi/ Tomita/ SINS score
- ✓ Decide mode of treatment that may be offerred- Conservative/ palliative/ excisional
- ✓ Decide the route of surgery

Thank You