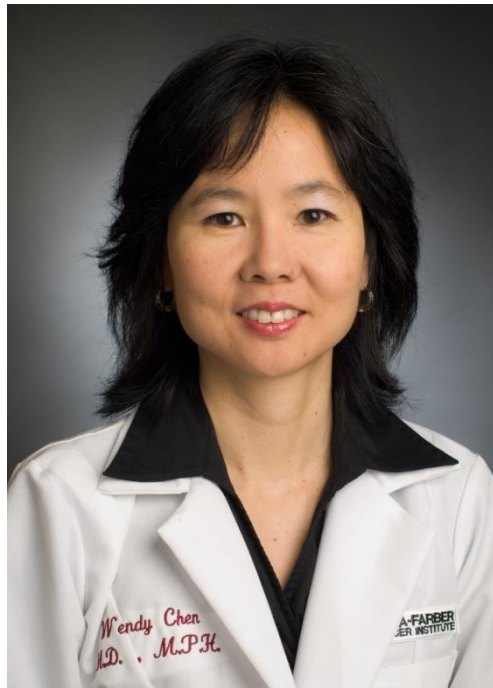


Oncology Pearls

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- Medicine Residency – Brigham and Women's
- Oncology Fellowship – Dana Farber Partners
- Assistant Professor – Harvard Medical School
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 - Clinical focus: Breast Cancer
 - Research focus: Cancer epidemiology

DISCLOSURE

None related to this lecture

OBJECTIVES

- Review “oncology pearls”/ general oncology topics in a case - based format



Case #1

60 y.o. man with 80 pack-yr smoking
hx c/o 1 week history of facial swelling
and cough

Physical examination: distended neck
veins, prominent chest wall venous
distention, facial edema

Chest CT: bulky right hilar/mediastinal
lymphadenopathy

Case #1

- A. Proceed with mediastinoscopy or bronchoscopy to obtain tissue diagnosis
- B. Initiate heparin and radiation with plan to biopsy when swelling improves
- C. Initiate steroids and heparin with plan for biopsy when swelling improves
- D. Initiate heparin and emergent stent placement then biopsy once swelling improves
- E. Explain to patient this is metastatic cancer and he should consider hospice

Oncology pearl

- **Describe the signs and symptoms of and optimal treatment for superior vena cava syndrome.**
- Ref. Friedman T et al. Malignant Venous Obstruction: Superior Vena Cava Syndrome and Beyond. Semin Intervent Radiol 2017; 34:398-408

Pathophysiology of Superior Vena Cava Syndrome

- **Malignancy**

- >50% due to malignancy – tumor causing compression or direct invasion
- Lung cancer (both NSCLC and small cell) and lymphoma most common causes

- **Thrombosis**

- 20-40% due to catheters

Signs and symptoms

- **Physical examination**

- Facial edema and plethora
- Jugular venous distension
- Venous distension of superficial veins on chest

- **Symptoms**

- Shortness of breath
- Cough
- Hoarseness

Grading of SVC syndrome

Grade	Findings	Incidence (%)
0	Asymptomatic	10
1	Mild – edema in head/neck	25
2	Moderate – mild impairment (cough, dysphagia, movement)	50
3	Severe – mild/moderate cerebral or laryngeal edema	10
4	Life threatening – significant cerebral or laryngeal edema	5
5	Fatal – death	<1

Management of SVC syndrome

- **Chest CT with contrast generally preferred**
 - Ultrasound OK if suspect catheter thrombus
- **Tissue diagnosis critical for Rx decisions**
 - **Treatment depends on tumor histology**
 - Chemo-insensitive cancers (e.g. NSCLC) => upfront radiation and/or stent placement
 - Chemo-sensitive tumors (e.g. small cell, lymphoma) => upfront chemo
 - **Indications for stent placement**
 - Life-threatening symptoms (airway obstruction, severe laryngeal edema)
 - Diagnosis not established
 - Refractory/relapsed disease

**Rarely
fatal!**

Case #1 continued

Diagnosed with lung cancer. Treated with pembrolizumab x 3 mths.

Presents with 2 days of dry, non-productive cough. Denies fevers, chills, or dyspnea. Viral panel negative.

Physical exam: Appears well. Lungs clear. Room air O2 sat 96% at rest, but desaturates to 90% with ambulation.

CT scan – scattered patchy ground glass opacities

Case #1 - continued

- A. Bronchoscopy
- B. Empiric broad-spectrum antibiotics
- C. Inhaled steroids and bronchodilator
- D. Trimethoprim-sulfamethaxazole
- E. Prednisone at 1 mg/kg then slow taper

Oncology pearl

- **Recognize potential immunotherapy toxicities**
- Ref: Schneider BJ et al, Management of Immune-Related Adverse Events in Patients Treated With Immune Checkpoint Inhibitor Therapy: ASCO Guideline Update. J Clin Oncol 2021; 39: 4073-4126

Immunotherapy overview

- **Immunotherapy – checkpoint inhibitors**
 - PD1 inhibitors - cemiplimab, nivolumab, pembrolizumab
 - PDL1 inhibitors – atezolizumab, avelumab, durvalumab
 - CTLA4 inhibitors – ipilimumab
- **Wide range of side effects**
 - **Not dose dependent**
 - Varies somewhat with type of agent
 - **Timing highly variable**
 - Can occur months after exposure
 - **Can be fatal!**

Immunotoxicity

- **Gastrointestinal**
 - **Colitis (8-27%)**
 - Diarrhea common, abdominal pain
 - Nausea/vomiting less common
 - **Hepatitis (2-30%)**
 - AST/ALT abnormalities
 - **Pancreatitis (rare)**
- **Pulmonary (1-10%)**
 - **Pneumonitis**
 - Often ground glass opacities, but variable
 - **Can rapidly worsen**

Immunotoxicity

- **Endocrine (common) – can be lifelong**
 - Hypothyroidism/Hyperthyroidism
 - Primary adrenal insufficiency
 - Hypophysitis
 - Diabetes
- **Arthritis/myositis**
- **Dermatologic**
- **Many other rare things**
 - Renal, CNS, hematologic, cardiac, eye, etc

Immunotoxicity management

- **Very steroid responsive**
 - Start prednisone 1 mg/kg then slow taper over more than 1 month
 - Depending upon situation, immunotherapy can be restarted
- **Can worsen rapidly so ensure close follow up**
- **Involve your specialists early!**

Case #2

64 y.o. male with metastatic prostate cancer to bone with metastases to ribs, pelvis, and multiple vertebrae. Currently on docetaxel chemo. Calls c/o of 1-2 weeks increasing mid-back pain. He has no weakness, radicular pain, bowel or bladder difficulties. Neurologic exam is normal.

Case #2

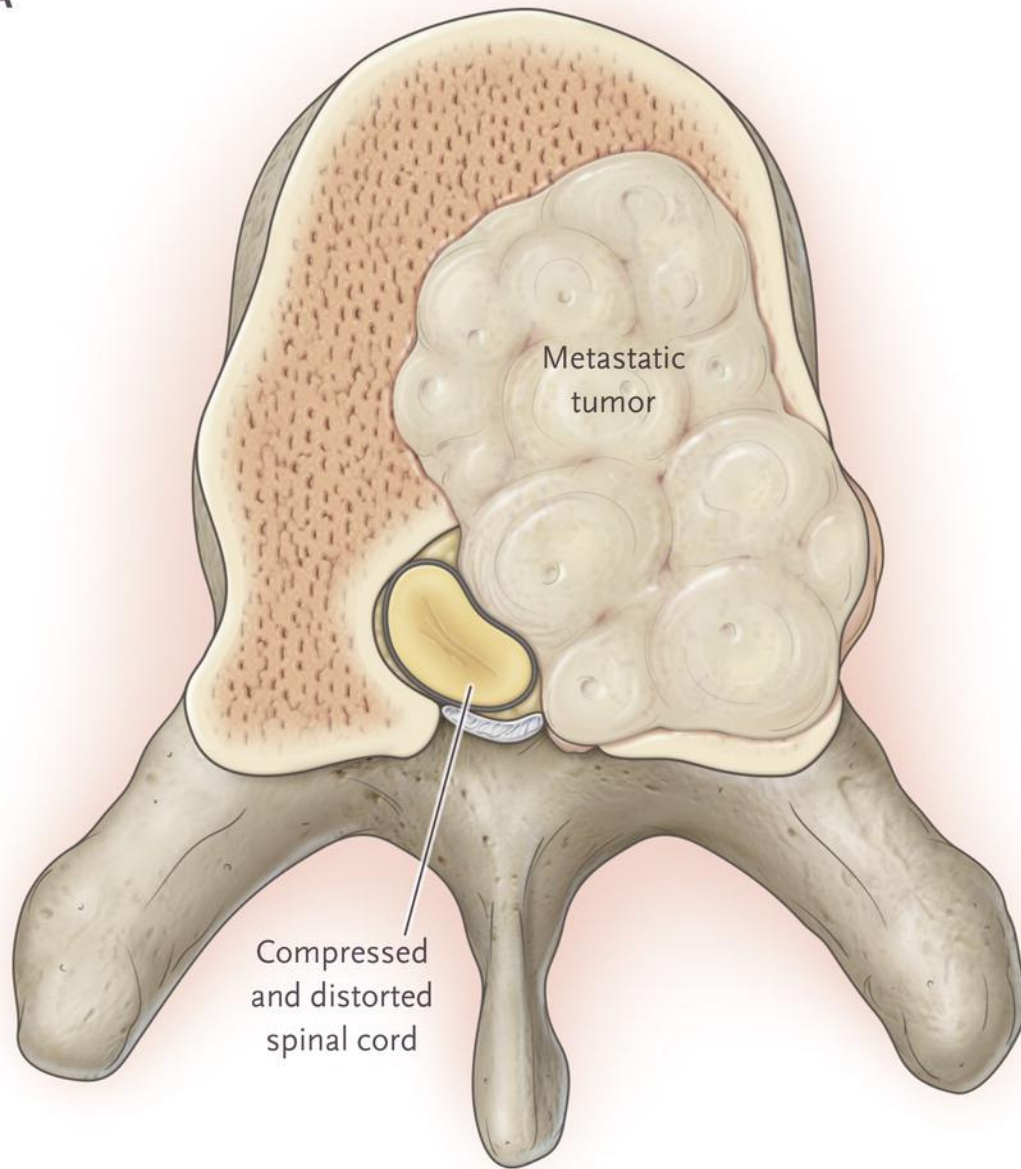
- A. Order a bone scan and CT scan
- B. Administer zoledronate 4 mg IV
- C. Order an MRI of the spine
- D. Radiation oncology consult for radiation to spine
- E. Start prednisone 20 mg

Oncology pearl

- **Describe the signs and symptoms and optimal management of spinal cord compression.**
- Ref: Ropper AE and Ropper AH. Acute spinal cord compression. N Engl J Med 2017; 376: 1358-69

Spinal Cord Compression

- **Initiate treatment early to prevent neurologic deficits**
 - Once neurologic deficits occur, often irreversible
- **Usually epidural compression from vertebral body metastases**
 - Most common tumors: lung, breast, prostate, myeloma, lymphoma, renal cell
 - Thoracic spine most common location (60%)
 - Intramedullary metastases less common

A**B**

Symptoms

- **BACK PAIN!**
 - New or worsening back pain with known vertebral mets mandates further evaluation
 - Pain may be radicular, but not always
- **Numbness/paresthesias**
- **Weakness**
- **Bowel and bladder symptoms occur late**
- **Neurologic exam may be normal**
 - Key is early diagnosis
- **MRI imaging of choice**

Treatment

- **Corticosteroids to ↓ edema**
 - Only short-term benefit
 - Should not be used if diagnosis unknown
 - 4-10 mg IV dexamethasone then 4 mg po q 6hrs
- **Radiation 1st line treatment for most**
- **Upfront surgery reserved for:**
 - Unknown diagnosis
 - Progression during or after radiation
 - Spinal instability
 - One RCT showed improved function with immediate surgery for less radiosensitive tumors with single area of compression

Case #3

62 y.o. woman presents to ED with temperature of 101.4°F, malaise, and cough 15 days after receiving chemotherapy for refractory lymphoma. Physical exam is unrevealing for source. WBC is 6400 cells/mm³ with 45% polys. CXR is negative. Cultures are obtained.

Case #3

- A. Admit patient and start cefepime
- B. Admit patient, start cefepime and G-CSF
- C. Admit patient and observe
- D. Discharge patient home on oral quinolone and G-CSF
- E. Discharge patient home on oral quinolone

Oncology pearl

- **Describe the optimal management of febrile neutropenia.**
- Ref: Taplitz RA et al. Outpatient management of fever and neutropenia in adults treated for malignancy: American Society of Clinical Oncology and Infectious Diseases Society of America Clinical Practice Guideline Update Summary. Journal of Oncology Practice 2018; 14: 250-255.

Fever and Neutropenia

Fever

- Oral temperature $> 38.3^{\circ}\text{C}$ (101°F) or 38.0°C (100.4°F) for > 1 hr

Neutropenia

- Absolute neutrophil count < 500 cells/ μL or ANC $< 1,000$ with predicted nadir of < 500 in next 48 hrs

Fever and Neutropenia

- **Risk for occult infection and mortality ↑ as ANC falls < 1,000/mm³**
 - Greatest risk with ANC < 500/mm³
 - Mortality rate for solid tumors less than heme malignancies
- **Growth factors (GCSF)**
 - Modestly ↓ duration of neutropenia and hospitalization
 - ⇒ No impact on mortality
 - ⇒ No significant benefit to empiric use of GCSF in uncomplicated F & N

Risk Factors for F&N

- Rapid decline in ANC
- Prolonged duration of neutropenia (>7-10d)
- Leukemic induction
- Uncontrolled cancer
- Hematologic cancers

Typical infectious sources of F&N

- Catheters
- Skin
- Respiratory tract
- Sinuses
- GI tract

=>Source identified in less than 30% of cases

- *Endogenous flora in 80% of cases*

Likely Organisms

- **Gram-positive infections (50-60%)**
 - Staph epidermidis
 - Streptococcus
 - Enterococcus faecalis/faecium
- **Gram-negative rods (more likely to cause death)**
 - Enterbacteriaceae (E. coli, Klebsiella)
 - Pseudomonas aeruginosa

Routine evaluation

- History and Physical exam
- CBC, chemistries, LFTs, urinalysis
- Blood/sputum/urine cultures
- Chest imaging if respiratory symptoms
- Viral testing if appropriate

Treatment

Empiric antibiotics: broad spectrum with gram positive and gram negative coverage (especially Pseudomonas)

- 3rd generation cephalosporin (cefepime)
 - Depends upon local hospital bacteriology
- **Alternatives:**
 - Imipenem cilastatin or meropenem
 - Higher rate C.diff colitis than cephalosporin
 - Beta-lactam allergy: aztreonam+vanco or cipro+clinda
 - <1% cross-reactivity between 3rd generation cephalosporin and PCN/1st gen cephalosporin

Vancomycin for F & N

- Empiric initial use does not improve morbidity or mortality
- Encourages development of vancomycin resistant Enterococcus
- Reserve for high suspicion of line/skin infection, mucositis, h/o MRSA, severe PCN allergy along with quinolone or aztreonam

“Low risk” F & N

- **Outpatient antibiotic treatment reasonable for low risk (Cipro/levo + Amox/Clav)**
 - anticipated duration of neutropenia < 7 days
 - solid tumor
 - clinically stable
 - no major comorbidities
 - adequate oral intake
 - malignancy responding to current treatment
 - observe for a few hours

Case #4

68-year-old woman with metastatic lung cancer is brought to ED with confusion. Serum calcium is 16.2 mg/dl and creatinine is 1.0 mg/dl. Four liters of normal saline and IV furosemide are administered. What is the next most appropriate therapeutic intervention that should be undertaken first?

Case #4

- A. Another 2 liters normal saline infusion IV and furosemide
- B. Denosumab 120 mg IV
- C. Zoledronate 4 mg IV
- D. Chemotherapy for lung cancer

Oncology pearl

- **Describe optimal management of hypercalcemia.**
- Ref: Guise T and Wysolmerski J. Cancer-associated hypercalcemia. N Engl J Med 2022; 386:1443-1451

Hypercalcemia

- Occurs in solid and hematologic cancers
 - Most common: breast, lung, myeloma
 - Incidence ↓↓ among metastatic pts because bisphosphonates routinely used for prevention of complications due to bone mets
 - Urgent rx for hypercalcemia important for palliation, but long-term control requires effective anti-cancer therapy



Causes of Hypercalcemia

- **Humoral hypercalcemia of malignancy**
 - Tumors secrete PTHrP
 - May not have bone mets
- **Local osteolytic hypercalcemia**
 - Extensive bone mets - commonly breast, myeloma
- **1,25 (OH)₂D-production by tumor**
 - Rare and occurs only in lymphoma
- **Ectopic PTH**
 - Extremely rare – isolated case reports

Management of hypercalcemia

- **IV normal saline volume repletion**
- **Inhibit osteoclastic activity**
 - Bisphosphonates (2-4 days for max effect) or denosumab
- **Calcitonin**
 - Less potent and short duration of action but rapid onset so only useful for very high calcium levels
- **Treat underlying cancer**

Bisphosphonates versus denosumab

- **Oral bisphosphonates less potent so not used for hypercalcemia Rx**
- **Zolendronate vs. Denosumab**
 - Both associated with osteonecrosis of jaw
 - Denosumab slightly superior or equivalent
 - Can be associated with refractory hypocalcemia
 - Can be used in severe renal impairment
 - Considerably more expensive (\$\$\$)
 - Rebound hypercalcemia if stopped after longer use

Case #5

Which of the following pairs a proven cancer prevention action and the cancer it prevents?

- A. Tobacco cessation and bladder cancer
- B. Hepatitis C vaccine and hepatocellular carcinoma
- C. Decreasing soy consumption and breast cancer
- D. Human papilloma virus and uterine cancer

Oncology pearl

- Recognize important epidemiologic associations for cancer



Important associations

Tobacco

- Head and neck
- Pancreas
- Bladder
- Lung
- Esophagus
- Kidney

Ionizing Radiation

- Thyroid
- Hodgkin's
- Breast
- Lung
- Leukemia

Infectious causes

- Hepatitis B and C => hepatocellular cancer
- Epstein-Barr virus => post-transplant lymphoma and nasopharyngeal cancer
- Human papilloma virus => cervical and anal cancer (90%), vaginal/vulvar, penile, oropharyngeal

MENINGIOMA

THYROID GLAND

BREAST
IN POSTMENOPAUSAL WOMEN

OESOPHAGUS

LIVER

STOMACH
CARDIA

GALLBLADDER

KIDNEY

OVARY AND
ENDOMETRIUM

MULTIPLE MYELOMA

COLORECTUM

PANCREAS

**OBESITY
INCREASES
THE RISK OF
THESE
CANCERS**

Case #6

38 y.o. male presents with chest pain and shortness of breath. CXR shows mediastinal mass suggestive of cancer. Which of the following blood tests would be most helpful to identify the primary site?

Case #6

- A. PSA (prostate specific antigen)
- B. CEA (carcinoembryonic antigen)
- C. CA 19-9
- D. hCG (human chorionic gonadotropin)

Oncology pearl

- **How to evaluate cancer of unknown primary**
- Ref: Raghav K. Cancer of unknown primary site. N Engl J Med 2025; 392: 2035-2047

Approach to unknown primary

- **Chest/abdominal/pelvic CT with contrast**
 - Preferred to PET-CT
- **Focused tumor markers**
 - Often non-specifically elevated
 - Man with adenocarcinoma and bone mets - PSA
 - Man with mediastinal/midline carcinoma - hCG and AFP for germ cell tumor
- **Immunohistochemistry + molecular profiling/next generation sequencing**

Histology of unknown primary

- **Adenocarcinoma (50-60%)**
 - Lung, hepatobiliary, pancreatic, renal most common
- **Poorly differentiated cancer (30%)**
 - Lymphoma, melanoma, sarcoma, germ cell
- **Squamous cell carcinoma (5-10%)**
 - Cervical => head and neck primary
 - Inguinal => genital or anorectal primary
- **Other tumors (5%)**
 - Neuroendocrine, melanoma, germ cell, etc

Find non-metastatic cancers

- **Woman with axillary lymph nodes**
 - Node positive breast cancer
- **Neck nodes with squamous cell ca**
 - Locally advanced head and neck
- **Young man with mediastinal/retroperitoneal LN**
 - Germ cell tumor
- **Woman with peritoneal disease**
 - Stage III ovarian cancer

Find treatable metastatic cancer

- **Breast**
- **Ovarian**
- **Prostate**
- **Germ cell**
- **Lymphoma**
- **Melanoma**
- **Head and neck**
- **Colorectal**



Case #7

45 y.o. premenopausal women has severe hot flashes during the day and frequent night sweats. She has a history of a stage I ER negative breast cancer diagnosed two years ago treated with lumpectomy and radiation. She is not on hormonal therapy. Which of the following is the best choice for treating her hot flashes?

Case #7

- A. Clonidine
- B. Elinzanetant
- C. Soy protein
- D. Pregabalin

Oncology pearl

- **Counsel cancer survivors regarding hot flash treatment**
- Ref: Hickey M et al. Managing menopause after cancer. Lancet 2024; 403: 984-96.

Hot flash treatment

- Placebo-controlled RCT key since placebo has 25-30% response rate
 - RCTs show 30-50% ↓ in frequency and intensity of hot flashes with:
 - SSRI's (paroxetine, fluoxetine)
 - SNRI's (venlafexine)
 - Gabapentin
 - Oxybutynin
 - Elinzanetant/Fezolinetant
- => *No consistent effect of soy protein, black cohosh***

NK1/NK3 antagonist

- **KNDy (kisspeptin, neuokinin, dynorphon) expressing hypothalamic neurons important for thermoregulation**
 - Low estrogen => ↑↑ KNDy neuron activity => ↑↑ neurokinin B
- **Drugs targeting NK pathway ↓↓ hot flashes**
 - Fezolinetant – NK3 antagonist
 - Monitor LFTs
 - Elinzenetant – NK1/NK3 antagonist
 - Also helps with sleep and no LFT abnormalities



Menopause sx – breast cancer survivors

- **Menopause symptoms common among breast ca survivors**
 - Treatment induced menopause and side effects
- **Two RCT of HT for breast cancer survivors**
 - Both showed ↑↑ recurrence risk
- **No systemic HT for br ca survivors**
 - Systemic absorption low for most vaginal HT, but minimize use if ER positive cancer

Take home messages

- Treatment of SVC syndrome depends on histology
- High suspicion for cord compression with bone mets
- Immunotoxicity can impact many different organs with varying manifestations
- Remember common epidemiologic cancer risk factors
- Many options for menopausal symptoms for breast cancer survivors, but trials should be placebo controlled

Thank You!

