Board Review Pearls Paraneoplastic Syndromes and Solid Tumors

Goals

To Highlight topics that are likely to be high yield for board testing

Not to cover all solid tumors, as for some there is much less board testable material

Disclosure: I am not an oncologist

- 1) A 50 yo man presents with a bulge in his left scrotal area. He has noticed it for the past 3 days. Exam reveals a left varicocele. Labs: HB 15 HCT 45, Ua 10-30 RBC's

What is the most likely diagnosis?

A) Renal cell cancer
B) Renal vein thrombosis
C) Prostate cancer
D) Inguinal hernia
E) DVT

Paraneoplastic Syndromes Renal Cell Ca

- Sudden onset of varicocele (2% of males with renal cell)
- Fever (20%)
- Hypertension
- Erythrocytosis (3%)
- Non-metastatic hepatic dysfunction (15%)

- 2) A 67 year old man has the sudden appearance of 30 lesions on his back and chest. These are new for him (no prior similar lesions). What diagnosis is of greatest concern?
- A) Cutaneous lymphoma
- B) HIV
- C) Gastric Cancer
- D) Testicular Cancer
- E) Multiple Myeloma

Leser-Trelat

Sudden appearance of seborrheic keratoses

Malignancies Associated:

- **Non-Hodgkin's Lymphoma**
- **GI Adenocarcinomas**
- **Miscellaneous**

- 3) A 48 yo woman with metastatic breast cancer reports she has been unable to use her fingerprint log in for her cell phone and has been unable to do the same at the fitness club she is a member. Which of the following drugs has she been treated with that explains this?
- A) Abemaciclib
- B) Capecitabine
- C) Doxorubicin
- D) Eribulin
- E) Carboplatin

Capecitabine Associated Loss of Fingerprints (Adermatoglyphia)

- 20 cases reported in literature^ (one prospective study showed loss of fingerprints in 14%(9/66) of patients treated with capecitabine*)
- All had hand –foot syndrome, loss of fingerprints not associated with severity grade of hand-foot syndrome
- ^Cureus 2017, 9(1):e969
- * JAMA Oncol 2017,3:122-123

4) 64 yo gentleman with 60 pack-year h/o ongoing tobacco use presents to clinic with complaint of progressive weakness.

AOX4. T 37ºC, BP 125/62, HR 94, RR 18, O_2sat 92% on ambient air. Bilateral ptosis. Lungs clear. No lymphadenopathy. Proximal weakness in bilateral upper and lower extremities with absent reflexes. Reflexes improve after isometric exercise. CXR shows a centrally-located, 4-cm lung nodule.

What is the most likely cause of this patients weakness

A) Lambert-Eaton syndrome
B) Hypercalcemia
C) Hyponatremia
D) Cerebral metastases
E) Spinal cord metastases

Neurologic Paraneoplastic Syndromes SCLC

Syndrome	Features
Lambert-Eaton Myasthenic Syndrome	• Proximal muscle weakness and absent reflexes that improve after isometric exercise • Autoantibodies to calcium channels
Peripheral Neuropathy	• Peripheral neuropathy
Encephalomyelitis	• Disorders of temporal, limbic, brainstem, cerebellum, spinal cord, dorsal root ganglia, and/or autonomic nervous system • Anti-Hu (aka ANNA-1) antibodies
Cortical Cerebellar Degeneration	• Dizziness, nausea, ataxia, diplopia, dysarthria, dysphagia • Anti-Hu (aka ANNA-1) antibodies

5) 84 yo gentleman with 65 pack-year h/o tobacco use and known metastatic lung cancer on no specific cancer-related therapy due to poor performance status presents to the emergency department with confusion and abdominal pain. He is visiting Seattle from out of town (working on his Bucket List) and comes with no records. Serum calcium is elevated at 12 mg/dL (8.9-10.3 mg/dL).

What is the most likely cancer type?

A. Small cell lung cancer
B. Adenocarcinoma of the lung
C. Squamous cell lung cancer
D. Carcinoid of the lung

Paraneoplastic Syndromes

Tumor	Syndrome	Features
Squamous Lung	Hypercalcemia*	• Excess PTHrP and/or bone destruction
Various Lung	Polymyositis/ Dermatomysitis	• Proximal weakness • Elevated serum muscle enzymes
	Digital clubbing	• Flattening of angle between nail base and cuticle
	Hypertrophic osteoarthropathy	• Clubbing plus periosteal proliferation of tubular bones • Symmetric, painful arthropathy of ankles, knees, wrists, elbows

* Treat underlying cancer, give IV fluids and IV bisphosphonate, consider IM/SQ calcitonin

Paraneoplastic Syndromes SCLC

Cushing syndrome (2-5%)- hypokalemia, hypertension, muscle weakness

SIADH (16%)- Hyponatremia

6) 70 yo gentleman with 55 pack-year h/o tobacco use and 6 months of cough and weight loss presents with 1 week of hemoptysis. CXR shows a R upper lobe mass. CT chest/abdomen confirms 6cm R upper lobe pulmonary mass with mild mediastinal lymph node enlargement. CT-guided biopsy of lung mass reveals adenocarcinoma of lung. PET/CT shows large uptake in RUL lung mass and low level uptake in mediastinal lymph nodes. MRI of brain and mediastinoscopy with lymph node sampling show no cancer. Performance status is good.

What is the most appropriate treatment option?

A. Surgery
B. Surgery with subsequent chemotherapy
C. Chemotherapy
D. Immunotherapy

Non-Small Cell Lung Cancer

- 80-90% of all lung cancers (squamous cell, large cell, adenocarcinoma, undifferentiated)

- Surgery can be curative so staging is key
  - CT chest/abdomen with PET
  - Mediastinoscopy with lymph node sampling if +CT/PET
  - MRI brain if neuro symptoms or worse than stage I disease

- Stage I: single tumor ≤5cm, no lymph node involvement

- Stage II: tumor >5 but ≤7cm or + regional (peribronchial/ hilar) lymph nodes, tumor near carina

- Stage III: + mediastinal lymph nodes or tumor >7 cm

- Stage IV: ipsilateral malignant pleural/pericardial effusion or metastatic disease

Non-Small Cell Lung Cancer – Treatment

Stage	Treatment *
I	Surgical resection for cure then consider adjuvant chemotherapy
II	Surgical resection for cure then adjuvant chemotherapy +/- radiation
III	Surgery then chemotherapy and radiation OR Chemotherapy and radiation without surgery
IV	Chemotherapy integrated with palliative care (with radiation only for symptom management)

* Do NOT treat poor performance status persons with chemotherapy regardless of stage except perhaps for tumor mutation-specific therapy

7) A 75 yo man presents to the ED with a 3 week history of facial swelling and headache, and a 2 week history of dyspnea. He has a 100 pk year history of cigarette smoking.

PE: BP 110/70 P105 T 36.8 O2 92%

Diffuse facial erythema present and neck veins are dilated bilaterally.

CT:9cm medial right lung mass and large mediastinal lymphadenopathy. Severe SVC compression is present.

What is the most appropriate management?

A) Biopsy of lung mass
B) Immediate radiation therapy
C) Placement of SVC stent
D) Begin carboplatin
E) Begin pembrolizumab

Superior Vena Cava Syndrome

Malignancy associated SVC caused by direct invasion for SVC by tumor, or compression by tumor/lymph nodes

Symptoms/Signs: Facial swelling/headache/dyspnea/dilated chest veins

Most common tumors :NSCLC (50%),SCLC (25%),NHL (10%)

Intravascular devices associated with 20-40% in cancer patients

Treatment: Make a diagnosis first! Only exception is if patient has major pulmonary compromise/cerebral edema, then urgent stent placement

8) 50 yo woman of East Asian decent presents with several months of cough. She has never smoked and she has no known pulmonary disease. No nausea. CXR shows a L peripheral lung mass. CT chest/abdomen shows 4-cm L lung mass, hilar and mediastinal lymph node enlargement, and pleural effusion. A CT biopsy of the mass shows adenocarcinoma. Which of the following is the most appropriate management?

A. PET Scan

B. Surgical resection

C. EGFR mutation testing

D. Carboplatin plus docetaxel

E. Hospice referral

Lung Tumors in Non-Smokers

- Differential diagnosis
  - Non-small cell lung cancer
  - Carcinoid
  - Metastatic malignancy from non-lung source
- Adenocarcinoma of the lung with epidermal growth factor receptor (EGFR) mutation
  - Most common in women of East Asian decent
  - Better prognosis than non-EGFR mutation adenocarcinomas
  - Treat with EGFR-tyrosine kinase inhibitors such as erlotinib (Tarceva®), gefitinib (Iressa®), afatinib (Gilotrif®), osimertinib (Tagrisso®)

Specific Therapy - NSCLC Mutations

- Epidermal growth factor receptor (EGFR) mutations
  - Erlotinib (Tarceva®)
  - Gefitinib (Iressa®)
  - Afatinib (Gilotrif®)
  - Osimertinib (Tagrisso®)

EGFR tyrosine kinase inhibitors

- Anaplastic lymphoma kinase (ALK) mutations
  - Crizotinib (Xalkori®)
  - Ceritinib (Zykadi™)
  - Alectinib (Alecensa®)

ALK inhibitors

- ROS1 oncogene rearrangement
  - Crizotinib (Xalkori®)
  - Ceritinib (Zykadi™)
- BRAF mutation
  - Dabrafenib (Tafinlar®) plus trametinib (Mekinist®)
- Programmed death 1 ligand (PD-L1) expression
  - Pembrolizumab (Keytruda®)

National Comprehensive Cancer Network (NCCN) Guidelines. 7/2018. www.nccn.org.

9) 60 yo woman with a hx of metastatic melanoma presents to ED with 5 day history of diarrhea. She has 8-9 loose stools daily, with some abdominal cramping. She has no recent antibiotic use, travel or history of bowel disease. She has just received the 4th of 4 doses of ipilimumab therapy. PE- T 37 BP 120/80 P 100

Abd- soft non tender, increased bowel tones

Labs: HB 13 HCT 39 WBC 9500 (65% polys) AST 170,ALT 140, Bun 29 Cr 1.3

Which of the following is the most appropriate next step in management?

A) Oral vancomycin

B) GCSF

C) High dose IV steroids

D) Supportive care

Checkpoint Inhibitors

PD1 inhibitors

Nivolumab

Pembrolizumab

CTLA-4 inhibitors

Ipilimumab

Toxicities- Rash(common),hepatitis, enterocolitis, thyroid disease (hyper or hypo)

More common with Ipilimumab

Immune mediated- serious toxicity should be treated with stopping drug and giving corticosteroids

Chemotherapy Side Effects You Need To Know

- Peripheral neuropathy- Platinum compounds, Vinca alkaloids (ie vincristine/vinblastine), Taxanes (paclitaxel/docetaxel)
- Cardiomyopathy- Anthracycline, cyclophosphamide, trastuzumab

10) 84 yo gentleman with known metastatic prostate cancer presents with several month history of back pain and 1 week of lower extremity weakness. No trauma. On physical exam, point tenderness over T12 vertebral body, decreased bilateral LE strength, increased bilateral LE reflexes, and bilateral extensor plantar reflexes. MRI of thoracic and lumbar spine shows radiographic lesion typical of metastatic prostate cancer at T12 with associated spinal cord compression

What is the most appropriate initial treatment?

A. Radiation therapy
B. Corticosteroids plus radiation therapy
C. Bisphosphonate
D. Chemotherapy
E. Corticosteroids

Spinal Cord Compression

- Most common breast, lung, and prostate cancer
- Symptoms/signs may include
  - Pain
  - Weakness
  - Hyperreflexia/extensor plantar reflexes
  - Bowel/bladder incontinence
- Diagnosis via MRI of entire spine
- Treatment
  - Corticosteroids immediately
  - Surgery if needed for urgent decompression
  - Radiation therapy
  - Chemotherapy for sensitive tumors

Cauda Equina Syndrome

- Saddle anesthesia
- LE weakness
- Radicular pain
- Bowel/bladder dysfunction

11) 67 yo gentleman undergoes colonoscopy for bright red blood per rectum and is found to have a 3-cm adenocarcinoma located 8 cm from the anal verge. Contrast-enhanced CT of chest/abdomen/pelvis shows no evidence for metastases. Endorectal ultrasound reveals full thickness involvement of the rectum with no lymph node involvement (T3N0M0).

What is the most appropriate treatment?

A. Surgery
B. Surgery with subsequent chemotherapy and radiation therapy
C. Chemotherapy/radiation, then surgery, then subsequent chemotherapy
D. Chemotherapy
E. Chemotherapy and radiation therapy

Rectal Cancer

- Endorectal US or pelvic MRI to assess tumor depth

Stage	TNM	Treatment
I	T1-2, N0	Surgery
II	T3-4, N0	Radiation and chemotherapy before surgery and chemotherapy after surgery
III	Any T, N1-2	Radiation and chemotherapy before surgery and chemotherapy after surgery
IV	M1	Surgery for palliation or oligometastatic liver or lung disease and/or chemotherapy

12) 42 yo HIV-positive gentleman presents with rectal pain and bleeding. Physical exam reveals a 2-cm mass in the anal canal. Colonoscopy shows no other masses. Biopsy of the anal mass reveals invasive squamous cell carcinoma. Contrast-enhanced CT of chest/abdomen/ pelvis shows no evidence for metastases. Endorectal ultrasound confirms a 2.3-cm mass in the anal canal with no perirectal lymph node involvement.

What is the most appropriate treatment?

A. Surgery
B. Surgery with subsequent chemotherapy and radiation therapy
C. Radiation therapy
D. Radiation therapy and chemotherapy

Anal Cancer

- Squamous cell or epidermoid tumor
- Risk factors
  - Human papilloma virus (HPV)
  - Human immunodeficiency virus (HIV)
- Treatment
  - Initial combined radiation and chemotherapy with curative intent
  - Surgery if radiation/chemotherapy fails

National Comprehensive Cancer Network (NCCN) Guidelines. 7/2018. www.nccn.org.

- 13) A 34 yo man presents with sore throat that has been present X 3 months. He was treated with 2 courses of antibiotics without improvement. On exam he has a erythematous lesion adjacent to his R tonsil. He has a 4cm anterior R cervical lymph node. Bx shows squamous cell cancer. What is the most likely risk factor in this patient?
- A) Tobacco use
- B) Marijuana use
- C) Alcohol use
- D) HPV

Head and Neck Cancer

- Squamous cell cancer in older patients more likely tobacco/alcohol related
- Tonsilar cancer, younger patients favor HPV etiology
- Outcomes much better in younger patients with HPV related cancer
- Multiple unilateral nodes < 6cm considered N1 disease with HPV cancers
- Treatment with radiation therapy/surgery alone or in combination with cisplatin based chemo based on staging

14) 67 yo gentleman presents with decreased energy, dull R upper quadrant pain and weight loss over 6 months. Vitals normal. Temporal wasting, hepatomegaly, fluid wave and lower extremity edema present. Rest of exam is normal. Chem8 normal. CBC with mild anemia. Albumin low. Alkaline phosphatase and bilirubin elevated. PSA normal. CT of chest/abdomen/pelvis demonstrates ascites and multiple hypodense lesions replacing >50% of the liver. Needle biopsy of liver lesion shows moderately differentiated adenocarcinoma. Upper endoscopy and colonoscopy normal. Empiric chemotherapy for which of the following primaries is appropriate?

A. Lung
B. Prostate
C. Testicular
D. Gastrointestinal

Cancer of Unknown Primary

- Biopsy and obtain immunohistochemical markers
- CT chest/abdomen/pelvis

Scenario	Treat Empirically For
Women with isolated malignant axillary lymphadenopathy	Breast cancer
Women with abdominal carcinomatosis and ascites	Ovarian cancer
Young men with tumor of mediastinum/retroperitoneum	Testicular cancer
Adenocarcinoma predominately below the diaphragm	Gastrointestinal cancer
Adenocarcinoma predominately above the diaphragm	Lung cancer

Petrakis D, et al. Cancer Treat Rev. 2013;39(7):701-8.

Key Solid Tumor Information For Boards

- Know your paraneoplastic syndromes!

Hypercalcemia-squamous cell over small cell

Know Side effects of Chemotherapy/Immune Therapy drugs

Rash/diarrhea checkpoint inhibitors, causes of neuropathy/cardiomyopathy

Know how different forms of lung cancer are treated

ANSWERS

1) A- Renal cell cancer
2) C-Gastric cancer
3) B- Capecitabine
4) A-Lambert-Eaton syndrome
5) C-Squamous Cell lung Cancer
6) B-Surgery with subsequent chemotherapy
7) A- Biopsy of lung mass
8) C- EGFR mutation testing
9) C-IV high dose steroids
10) B- Corticosteroids + radiation
11) C-Chemotherapy/radiation, then surgery, then subsequent chemotherapy
12) D- Radiation and chemotherapy
13) D-HPV
14) D- Gastrointestinal