Oncology Test Review

Lise Harper, MD MPH

February 25, 2020

Question 1:

- Answer: D, resection of all lesions

Treat oligometastatic liver metastases of colorectal cancer

- 71 y/o M, stage II rectal CA that was resected 3 years ago
- Surveillance CT shows 3 new hyperdense lesions in the left lobe of the liver c/w metastatic disease, largest 4 cm
- CT C/A/P with contrast otherwise unremarkable

- Liver is the primary metastatic site for patients with colon cancer

- Complete resection of metastatic foci to the liver or lung leads to cure in 25% of patients
- Criteria for resection: 3 lesions or less
- 3 conditions in which resection not an option:
  - Tumor involvement of the common artery or portal vein or CBD
  - More than 70% liver involvement, more than 6 involved segments, or involvement of all 3 hepatic veins
  - Predicted inadequate hepatic reserve after resection

Colorectal cancer surveillance

- Surveillance for colorectal CA
  - CEA at 6 month intervals
  - Annual CT C/A/P for 5 years following therapy
  - Colonoscopy 1 year after resection and then in 3 years and then every 5 years

- Other answers:
  - Hepatic artery embolization
    - Useful for more vascular tumors – HCC or neuroendocrine
  - Needle biopsy
    - Clinical presentation compelling enough to diagnose recurrent colorectal CA
  - Palliative chemo not appropriate as this is a potentially curable CA

Question 2:

- Answer B, bilateral salpingo-oophorectomy by age 40 - 45 years

Manage a *BRCA2* mutation carrier with prophylactic bilateral salpingo-oophorectomy

- 38 y/o F questioning her risk of ovarian CA
- Mother and maternal grandmother diagnosed with breast CA at ages 40 and 38 respectively
- She tested positive for BRCA2 gene mutation and underwent b/l prophylactic mastectomies at age 35

- BRCA2
  - ~ 17% lifetime risk of ovarian CA
  - BSO recommended by age 40-45 years of age
- BRCA1
  - ~ 44% lifetime risk of ovarian CA
  - BSO recommended by age 35-40 years of age

Managing patients with BRCA1 and BRCA2

- Breast CA screening
  - MRI at age 25
  - Mammography at age 30
- Risk of breast CA
  - 12% of women in the general population will develop breast CA at some point in their lives
  - BRCA1 – 72%
  - BRCA2 – 69%
- Other answers:
  - Annual pelvic exam and CA-125 screening
    - Not found to be effective
  - BSO now
    - This patient desires further childbearing and is only 38 y/o, so can safely delay until 40-45 y/o once childbearing is complete
  - OCP use
    - Decreased the risk of ovarian CA as much as 50% and can be used in BRCA1 and BRCA2 carriers, but is not an adequate substitute

Question 3:

- Answer A, continue tamoxifen for 5 more years

Treat early-stage hormone receptor–positive breast cancer with tamoxifen in a premenopausal patient

- 48 y/o F seen in f/u for breast CA
- Diagnosed at age 43 with low-risk, stage IIA invasive ductal cancer, ER+ PR+ and *HER2* –
- Completed 5 years of tamoxifen and has tolerated it well
- She continues to have menstrual periods and takes no other medications

- 10 years of tamoxifen compared with 5 years reduces breast CA mortality by one third in the first 10 years and by one half after 10 years
- Major AEs w/ 5 additional years of tamoxifen use was a small increase in the risk for endometrial CA with no increase in endometrial CA deaths
  - There were no increases in fatal pulmonary emboli, stroke, or ischemic heart disease

Hormone receptor therapy

- Tamoxifen side effects:
  - Endometrial cancer in women older than age 55 years, hot flushes, vaginal discharge, sexual dysfunction, venous thromboembolic events, and stroke
- Aromatase inhibitor side effects:
  - Arthralgia, vaginal dryness, sexual dysfunction, and higher risks of osteoporosis, fractures, cardiovascular events, and hyperlipidemia
  - Compared to tamoxifen, AIs have a lower risk of venous thrombosis and endometrial cancer

- AIs prevent conversion of adrenal androgens to estrogen but do not inhibit ovarian estrogen production
  - Therefore, they are not effective in premenopausal women unless ovarian suppression is given concomitantly

Question 4:

- Answer A, exemestane

Provide chemoprevention in a patient at high risk for breast cancer

- 55 y/o F with recent diagnosis of lobular carcinoma in situ and atypical lobular hyperplasia
- She is postmenopausal and wishes to decrease her risk of breast CA
- Her medical history is significant for a left calf deep venous thrombosis at 25 years of age concurrent with oral contraceptive use

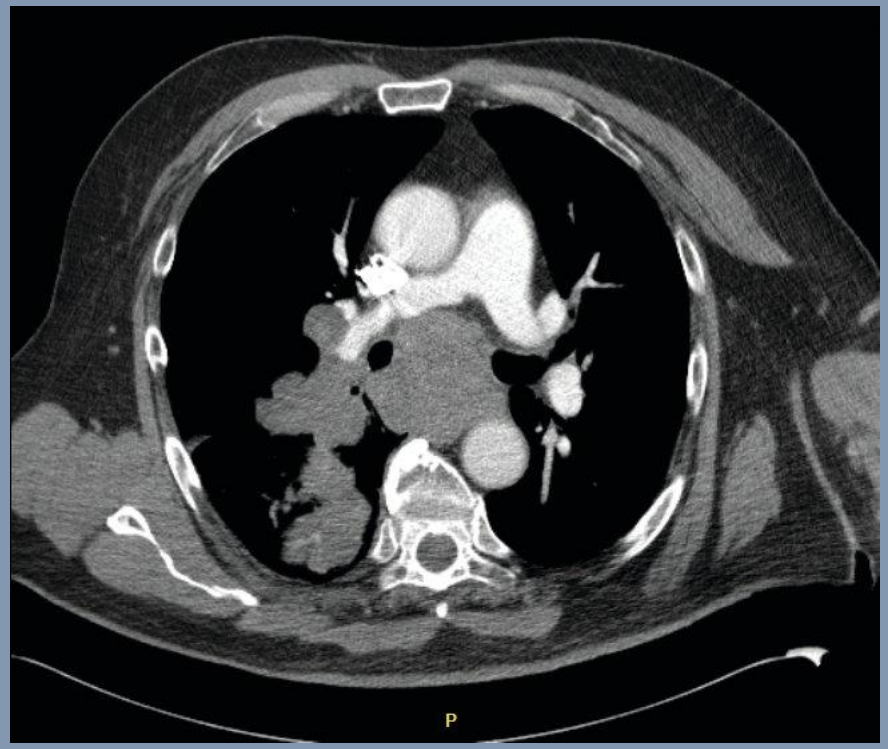
- Lobular carcinoma in situ and atypical hyperplasia are associated with a 30% to 35% lifetime risk of breast cancer and these pts are candidates for chemoprophylaxis with antiestrogens
- Antiestrogen options include:
  - Tamoxifen in both premenopausal and postmenopausal women and
  - Raloxifene and aromatase inhibitors (such as exemestane or anastrozole) in postmenopausal women

Question 5:

- Answer C, small cell lung cancer

Diagnose small cell lung cancer

- 67 y/o M with weakness and nausea
- 22.7 kg (50 lb) weight loss
- 30-pack-year history of smoking
- Lung examination reveals decreased tactile fremitus above the lower portion of the right lung as well as dullness to percussion and decreased breath sounds
- Laboratory studies reveal a serum sodium concentration of 127 mEq/L (127 mmol/L)



Small cell lung cancer

- SCLC is a neuroendocrine tumor
  - 15% of all lung cancers
  - Predominantly in smokers
  - Adjacent to the central airways with extensive LAD and distant metastasis at diagnosis
  - SIADH due to ectopic production of antidiuretic hormone (ADH) is most often due to a SCLC; rarely seen with other lung tumors
    - It occurs in approximately 10% of patients and results in hyponatremia
- Staging
  - CT C/A/P
  - Whole body bone scintigraphy
  - MRI brain
- Most patients with SCLC do not meet criteria for 1˚ surgery
- Treat with cisplatin-based therapy
  - Radiation if limited disease
  - No radiation if extensive disease
- Prophylactic brain radiation

Paraneoplastic syndromes

Table 1. Paraneoplastic Syndromes Associated with Small Cell Lung Cancer

Paraneoplastic Syndrome	Hormone/Antibody
Endocrine	
Cushing's disease	Adrenocorticotropic hormone
SIADH	Antidiuretic hormone
Acromegaly	Growth hormone–related peptide
Neurologic	
Lambert-Eaton syndrome	Anti-VGCC
Encephalitis	Anti-GAD65, CRMP5
Cerebellar degeneration	Anti-HuD, Anti-Yo
Stiff-person syndrome	Anti-amphiphysin
Retinal blindness	Anti-recoverin
Opsoclonus/myoclonus	Anti-Ri

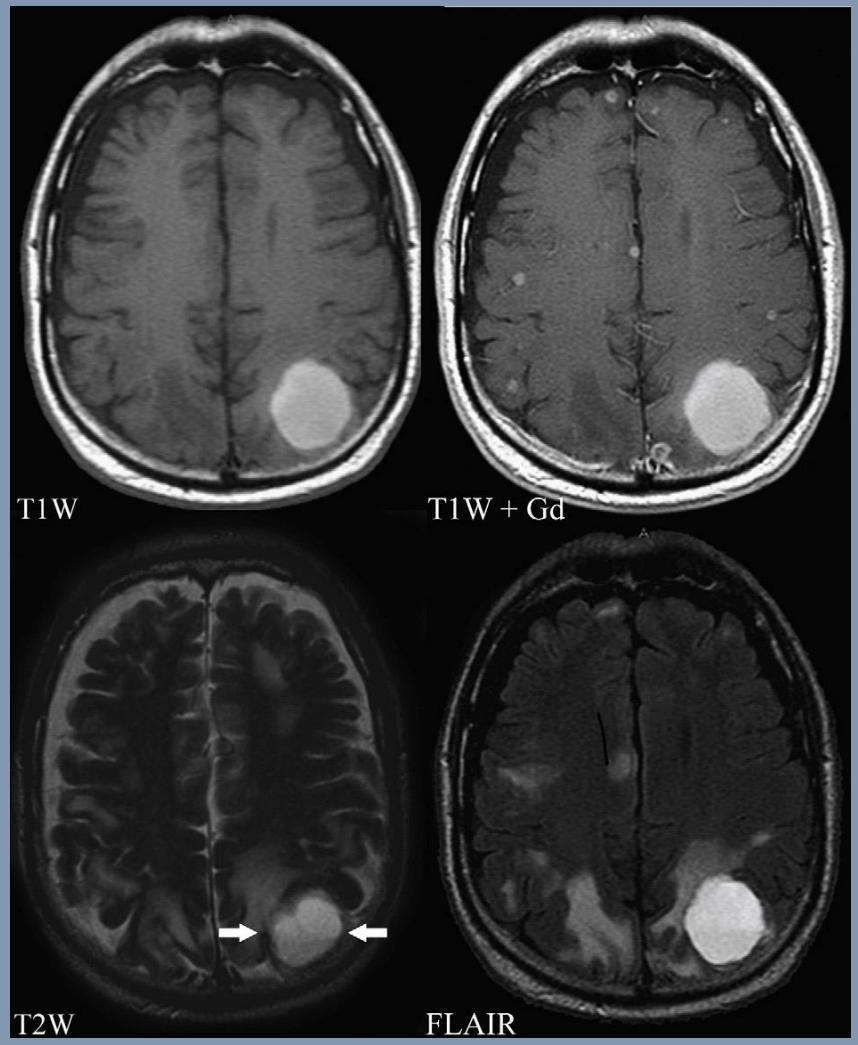
- Squamous cell
  - PTHrP related hypercalcemia
- Adenocarcinoma
  - Trousseau's syndrome/CA-related hypercoagulability syndromes

Question 6:

- Answer C, surgical resection of brain lesion

Treat melanoma with a solitary brain metastasis

- 42 y/o F w/ new-onset seizure
- Hx of malignant melanoma resected 7 years ago; 3.2-mm depth of invasion by Breslow microstaging
- Medications are dexamethasone and levetiracetam
- Brain MRI shows a 3.5-cm left frontal lesion consistent with metastatic disease; CT scan of the chest, abdomen, and pelvis is negative



Treat melanoma with a solitary brain metastasis

- As depth of invasion increases, risk of nodal and distant mets increases
- Surgery has a role for distant mets
- Resection provides a tissue diagnosis and provides the best long-term local cure
- Surgery associated with overall survival of 15.8 mos compared to 6.9 mos with systemic therapy alone
- 4 year overall survival
  - Surgery group 20.8%
  - Systemic therapy alone 7%

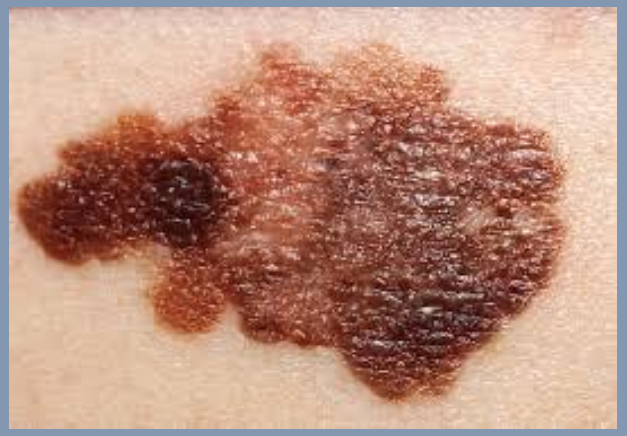
- Other answers:
  - Ipilimumab and nivolumab
    - Not first line due to resectable isolated mets
  - Stereotactic radiosurgery to the brain lesion
    - Gamma knife provides high rates of local control, however surgical resection would provide better long term control
  - Vemurafenib plus cobimetinib
    - Effective for BRAF-mutated melanoma
  - Whole brain radiation therapy
    - Reserved for patients with multiple mets

Question 7:

- Answer E, follow up in 12 months

Treat superficial melanoma

- 34 y/o F diagnosed with malignant melanoma
- 2 weeks ago underwent resection with wide excision and pathologic evaluation showed malignant malignant melanoma
  - Lesion was 1.2 cm invading 0.4 mm by Breslow microstaging



- Prognosis is related to the depth of invasion, either by Clark level (I to V) or by Breslow's depth
- High mitotic rate, lymphovascular invasion, and the presence of bleeding or ulceration are poor prognostic signs
- Surgical resection margins
  - 1-cm margins for lesions < than 1 mm in thickness
  - 1 mm and 2 mm in thickness should be resected with a 2-cm margin provided that skin graft is not needed
  - > 2 mm in thickness should be resected with 2-cm margins
- Early-stage patients can be assessed clinically and do not need radiographic staging (for example, CT and PET) and surveillance

Melanoma characteristics

Table 1. Characteristics of Normal Moles, Atypical Moles, and Melanomas

Lesion	*Age at onset*	*Location*	*Number*	*Size*	*Color*	*Morphology*
Normal moles	After 6 months, usually by 20 years of age	Anywhere	Few to hundreds	Usually < 6 mm	Evenly distributed, with only 1 or 2 shades of brown	Round, oval, symmetrical, with smooth and well-demarcated borders
Atypical moles	After 6 months, usually by 20 years of age	Anywhere, but most common on the trunk, especially the back	1 to hundreds	Usually ≥ 6 mm, although they may be smaller	Variegated, with more than 2 shades of color, most commonly brown or tan, but possibly including pink or black	Round, oval, asymmetrical, with pebbled surface and irregular or poorly demarcated borders
Melanoma	Usually adulthood, may occur in children with giant congenital moles or atypical mole syndromes	Anywhere, including sun-protected areas; most common on the trunk in men and legs in women	1	Usually ≥ 6 mm, although they may be smaller	Variegated, with more than 2 shades of color, often very dark brown to black, that may have changed over time	Asymmetrical, with irregular or poorly demarcated borders

Adapted with permission from Cyr PR. Atypical moles. Am Fam Physician. *2008;78(6):737, with additional information from references 10, 12, and 13.*

Question 8:

- Answer C, history, physical and gynecologic exam every 3 months

Manage posttreatment surveillance for a patient with cervical cancer

- 42 y/o F w/ stage IIA cervical CA s/p pelvic radiation, weekly cisplatin and cervical brachytherapy
- Responded well to therapy and pelvic exam without e/o tumor

- Guidelines for post-treatment surveillance:
  - H&P q3-6 mos for 2 years, then q6-12 mos for years 2-5
  - Higher risk pts (such as those treated with chemo or radiation) should be evaluated q3 mos for 2 years then q6 mos for years 2-5
  - Lower risk disease (treated with surgery alone) should be evaluated q6 mos for 2 years and then annually through year 5

Cervical cancer

- Most common symptoms of early cervical CA are abnormal or heavy vaginal bleeding or vaginal discharge
- Advanced cervical cancer symptoms include pelvic or back pain and bowel or bladder symptoms
- Select patients with cervical cancer confined to the cervix can be treated with surgery that preserves fertility
  - < 2 cm with no LN mets
- Patients with bulky or locally advanced cervical cancer are treated with cisplatin-based chemotherapy and radiation instead of surgery

Cervical cancer screening

TABLE 2

Age-Based Cervical Cancer Screening Recommendations for Average-Risk Women

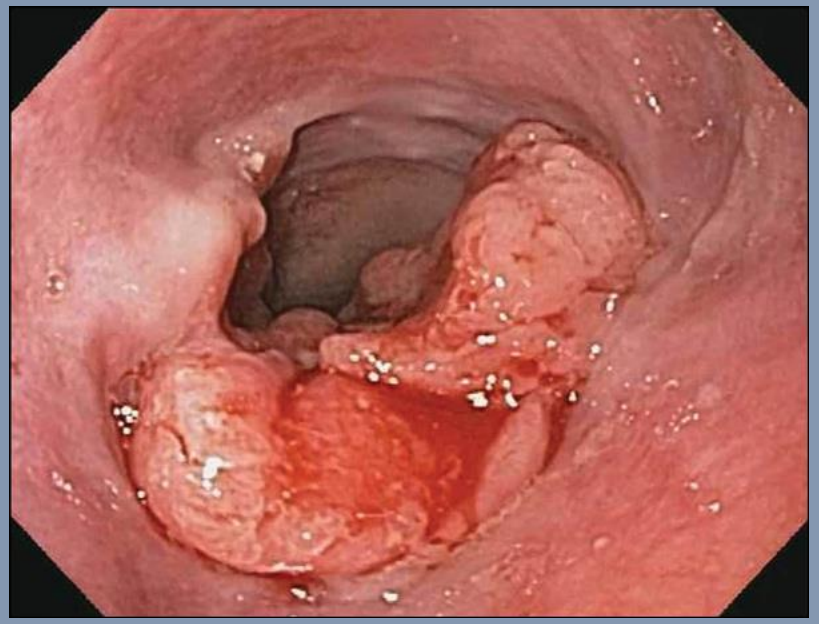
	Recommendations		
Patient age	**ACS, ASCCP, and ASCP 2012[16]**	**USPSTF and AAFP* 2012[17-19]**	**ACP 2015[20]**
Younger than 21 years‡	Screening is not recommended	Screening is not recommended	Screening is not recommended
21 to 29 years	Cytology alone every three years	Cytology alone every three years HPV testing (alone or in combination with cytology) is not recommended in women younger than 30 years	Cytology alone every three years
30 to 65 years§	Cotesting every five years (preferred) Cytology alone every three years (acceptable) Primary HPV testing† is not recommended in most clinical settings	Cytology alone every three years is recommended For women who want to extend the screening interval, cotesting every five years is an option Primary HPV testing in women older than 30 years is not addressed	Cytology plus HPV testing every five years
Older than 65 years‖	Screening is not recommended in patients with an adequate history of negative screening results and no history of CIN2 or higher within the past 20 years	Screening is not recommended in women older than 65 years with an adequate history of negative screening results and who are not otherwise at high risk of cervical cancer	Screening is not recommended in women older than 65 years with an adequate history of negative screening results

Question 9:

- Answer B, assess tumor tissue for *HER2* amplification

Evaluate metastatic gastroesophageal junction adenocarcinoma for *HER2* amplification

- 48 y/o M with 2 mos of progressive dysphagia, first with solids, progressed to liquids
- On PE, 1.5 cm supraclavicular LN and palpable liver edge
- CT C/A shows a mass in the lower third of the esophagus just proximal to the gastroesophageal junction; the liver has multiple hypodense lesions consistent with metastases
- EGD reveals a near-obstructing lesion in the distal esophagus; biopsy shows adenocarcinoma



Evaluate metastatic gastroesophageal junction adenocarcinoma for *HER2* amplification

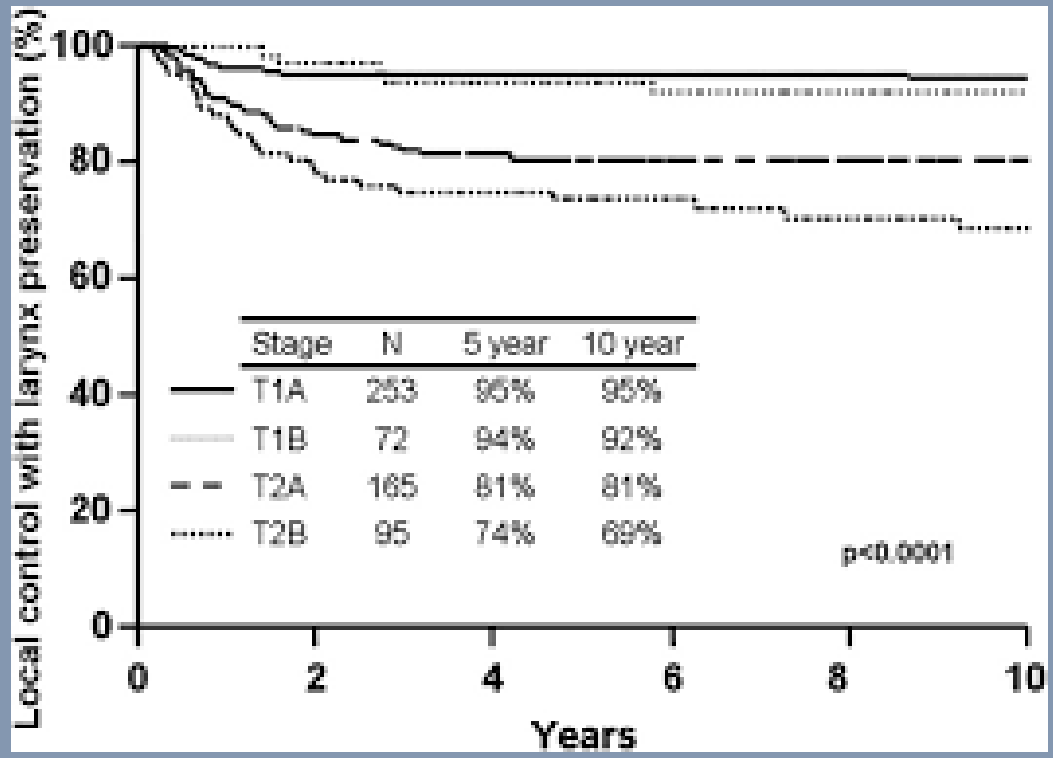
- 25% of gastroesophageal cancers demonstrate *HER2* amplification
  - Superior response to chemotherapy when anti-*HER2* monoclonal antibody trastuzumab is added to standard chemotherapy
- Other answers:
  - *BRAF* mutation status is important in melanoma
    - 40% of pts will have *BRAF*-mutated tumors that are highly likely to respond to TKIs targeting *BRAF*
  - *RAS* mutation status is relevant to the use of anti-epidermal growth factor receptor (*EGFR*) monoclonal antibodies in colorectal cancer

Question 10:

- Answer C, radiation therapy

Treat early stage laryngeal cancer

- 70 y/o M with 2 mos of hoarse voice
- 50-PY smoking hx
- Laryngoscopy reveals small R vocal cord mass
- CT neck shows a small lesion on the R vocal cord without e/o left-sided involvement, cartilage involvement or LAD



Head and neck cancer

- Risk factors are tobacco use followed by ETOH; together there is a synergistically increased risk
- HPV is an increasing RF and associated with a better prognosis
- Presenting symptoms:
  - Persistent or progressive LN enlargement, unilateral hearing loss, unilateral ear pain, nasal obstruction, oral pain, nonhealing oral ulcers, dysphagia, odynophagia, and hoarseness
- Diagnosis: H&P, direct laryngoscopy with FNA, tumor staining for p16 (HPV)
- Treatment:
  - 1/3 of pts present with early stage disease
  - Early stage treated with either surgery of radiation
    - Surgery for oral, RT for laryngeal
  - Adjuvant RT for locally advanced H/N cancer +/- adjuvant chemo if high risk features:

T3 or T4 tumor
Positive or close resection margins
Lymph node extracapsular extension
≥2 positive lymph nodes (N2 or N3)
Perineural invasion
Lymphovascular invasion

Question 11:

- Answer B, low dose chest CT scan

Perform lung cancer screening after treatment for head and neck cancer

- 61 y/o F with stage IVA hypopharyngeal squamous cell CA s/p combined cisplatin + RT 1 year ago
- 30-PY smoking hx, quit 1 year ago
- Exam reveals induration and limited ROM, no palpable LAD
- TSH normal
- Recent laryngoscopy showed no recurrent CA

Key Points for Practice

- Low-dose CT is recommended annually for asymptomatic adults 55 to 77 years of age who have smoked at least 30 pack years, and who continue to smoke or have quit within the past 15 years.
- Low-dose CT screening is not recommended in patients who do not meet the age and smoking criteria, even if they are considered high risk by clinical risk prediction calculators.
- Evidence-based tobacco cessation treatments should be provided to current smokers undergoing low-dose CT screening for lung cancer.

From the *AFP* Editors

Question 12:

- Answer C, CT scan of the abdomen

Diagnose renal cell carcinoma in a patient with erythrocytosis

- 58 y/o F w/ 6 months of headaches and facial redness
- On exam, BP 160/85, HR 96, RR 20 and she has facial plethora and palmar erythema

Laboratory studies:	
Erythropoietin	Markedly elevated
Hemoglobin	18.1 g/dL (181 g/L)
Leukocyte count	5400/µL (5.4×10^9/L) with a normal differential
Liver chemistry tests	Normal
Platelet count	250,000/µL (250×10^9/L)
Urinalysis	Normal

- Classic triad: flank pain, hematuria, palpable abdominal mass in ~9%
- Erythrocytosis is a common paraneoplastic syndrome associated with kidney cancer
  - Elevated erythropoietin level
- With polycythemia vera, you would evaluate with bone marrow biopsy and *JAK-2* mutation but the erythropoietin level is typically low or undetectable; it is also associated with leukocytosis, thrombocytosis and hepatosplenomegaly

Paraneoplastic syndromes in RCC

Paraneoplastic syndrome	Key Features
Anemia	Seen in 29-88% of pts with advanced disease and often precedes the diagnosis of RCC by several months
Hepatic dysfunction	Stauffer syndrome when it occurs in the absence of liver mets; may be related to tumor production of cytokines, such as GM-CSF and IL-6; may resolve with nephrectomy
Hypercalcemia	3 mechanisms: (1) lytic bone metastases, (2) over-production of PTHrP, (3) increased production of prostaglandins that promote bone resorption
Erythrocytosis	Present in 1-5% of pts with RCC and related to production of erythropoietin
Secondary (AA) Amyloidosis	Present in up to 5% of pts with RCC and reflects a chronic inflammatory response
Thrombocytosis	Associated with a poor prognosis; mechanism possibly related to IL-6 production by the tumor
Polymyalgia Rheumatica	Symptoms do not respond to prednisone, but are corrected by nephrectomy

Question 13:

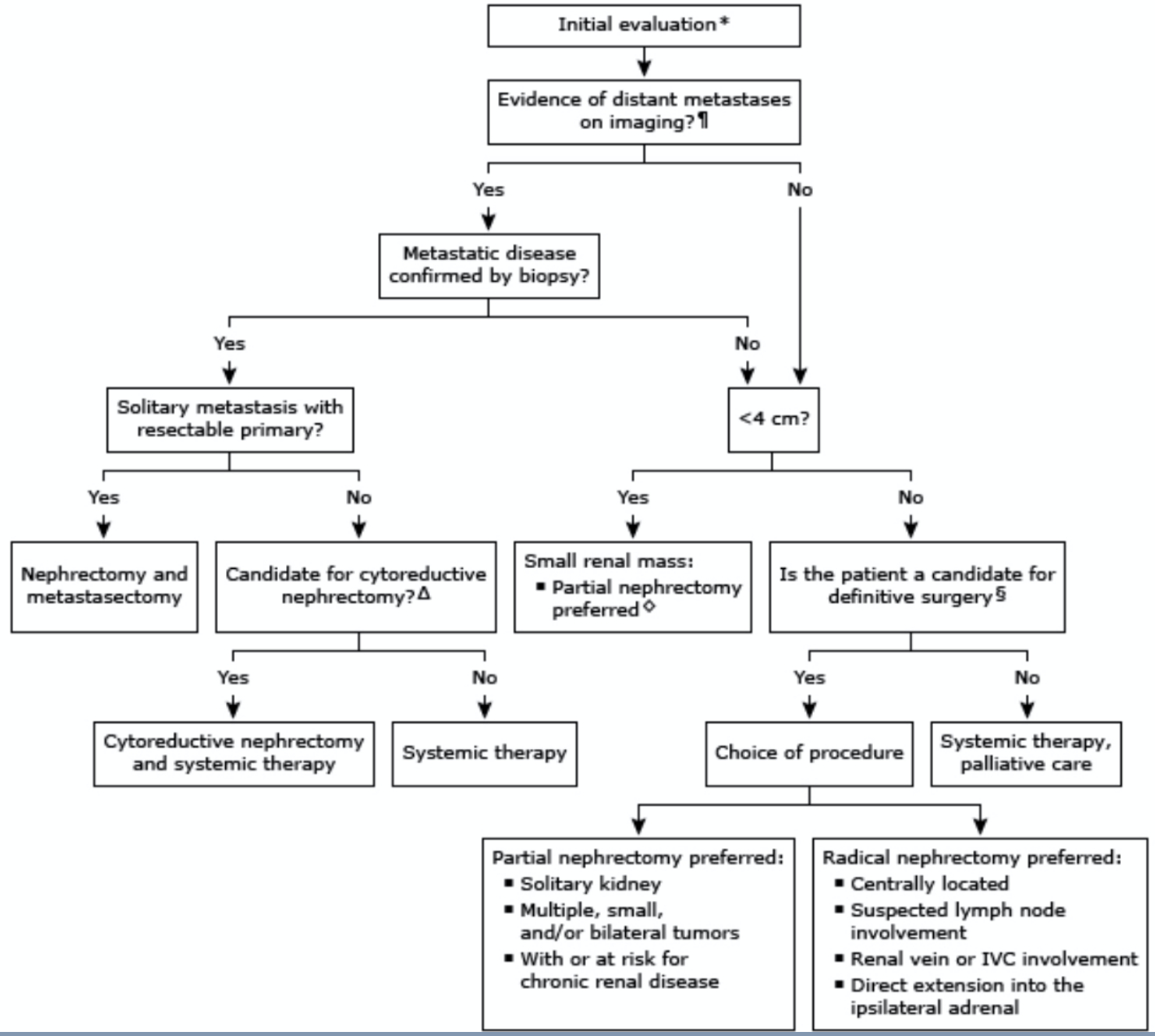
- Answer A, left radical nephrectomy

Treat metastatic renal cell carcinoma

- 50 y/o F w/ 4 months of left flank pain and 4 kg weight loss
- PE with left flank tenderness on palpation
- Laboratory studies reveal a hemoglobin level of 10.1 g/dL (101 g/L)
- CT scan of the chest, abdomen, and pelvis reveals a 10-cm left kidney mass with radiographic features suggesting renal cell carcinoma and a 1.2-cm single pulmonary nodule

- Most likely diagnosis is metastatic kidney cancer based on identification of a large kidney mass associated with a suspicious pulmonary nodule and anemia
- Debulking nephrectomy improves survival in patients diagnosed with metastatic kidney cancer, particularly in those with limited metastatic disease
- Nephrectomy both confirms the diagnosis and also serves as treatment for her metastatic kidney cancer
- Metastasectomy should be considered for removal of the isolated pulmonary lesion

Initial evaluation and treatment of renal cell carcinoma



Question 14:

- Answer B, intravesicular bacillus Calmette-Guérin (BCG)

Treat superficial bladder cancer

- 81 y/o M w/ 2 months of gross hematuria; former cigarette smoker
- Ultrasound of the kidneys, ureters, and bladder is unremarkable
- Cystoscopy reveals a lesion along the bladder wall. Transurethral resection of the bladder tumor reveals high-grade, stage T1 transitional cell carcinoma

- Initial treatment for high-grade or recurrent low-grade bladder cancer is transurethral resection of the bladder tumor followed by intravesical chemotherapy and periodic cystoscopy
- Most important RF: smoking
- Most common presenting symptom: gross hematuria
- Other answers:
  - Cisplatin-based chemotherapy has no role in the treatment of non–muscle invasive cancer
  - Partial cystectomy is not needed for the treatment of early-stage, non–muscle invasive bladder cancer; though has a role in selected patients with muscle-invasive cancer

Question 15:

- Answer A, dexamethasone

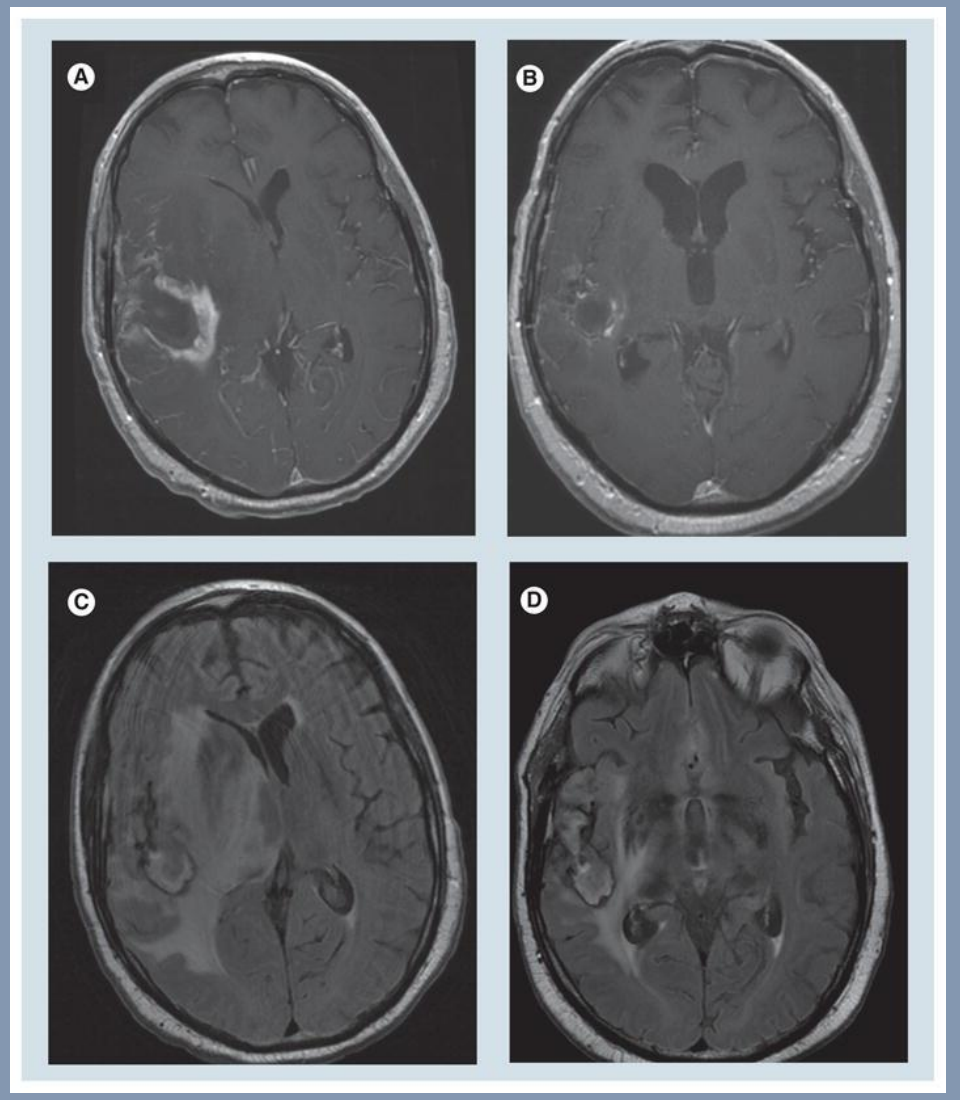
Treat symptomatic brain metastases

- 40 y/o F seen in the ED with 2 weeks of worsening headache and imbalance
- She has metastatic hormone receptor–negative, *HER2*-positive breast cancer with bone metastases and is being treated with paclitaxel, trastuzumab, and pertuzumab
- On exam, BP 168/66, HR 104, past-pointing on finger-to-nose testing and truncal ataxia
- Non-con head CT shows a 1.5 cm left cerebellar mass with surrounding edema and a 1 cm frontal mass with edema without midline shift

- Patients with symptomatic brain metastases should be initially treated with glucocorticoids
- Neurologic symptoms improve in 75% of patients, usually reducing intracranial pressure and improving neurologic symptoms within hours
- For moderate to severe symptoms, initial loading dose is 10 mg IV, followed by 4 mg IV q6h

Treat symptomatic brain metastases

- Other answers:
  - Levetiracetam
    - 25% of patients with brain metastases have seizures; prophylactic antiepileptic therapy not recommended in patients who have not had seizures
  - Mannitol
    - Mannitol and mechanical hyperventilation would be used in patients with severe edema at risk for herniation
  - Urgent neurosurgery
    - Neurosurgical decompression would be recommended in patients with severe edema or impending herniation
  - Whole brain radiation
    - Stereotactic radiation preferred, though following glucocorticoid treatment



Question 16:

- Answer B, immediate decompressive surgery

Treat neoplastic epidural spinal cord compression

- 60 y/o F seen in the ED with 4 weeks of mid-thoracic back pain and 1 week of leg weakness and numbness in her lower abdomen and legs without bowel or bladder incontinence
- She has hormone receptor-positive, *HER2*-negative breast CA with mets to spine, ribs and pelvis
- Currently on letrozole and palbobiblib
- There is a sensory level at the T8 vertebral body; bilateral, proximal, and distal lower-extremity weakness; hyperactive knee and ankle reflexes; and bilateral plantar extension responses
- MRI scans show a large lytic lesion in the T6 vertebral body, with an epidural mass causing compression of the spinal canal
- Dexamethasone followed by decompressive surgery for acceptable surgical candidates and with an expected survival of at least 3 months
- Neoplastic epidural spinal cord compression (ESCC) develops in approximately 2.5% of patients with metastatic cancer
  - Most common types of CA: lung, breast, and prostate cancer; myeloma; and lymphoma
  - ~ 85% of ESCC cases are due to epidural extension from vertebral body metastases
  - Lymphomas are more likely to involve a paraspinal mass that extends through the neural foramina to cause cord compression
  - Pain, often worse with recumbency, is present in more than 80% of patients and usually precedes neurologic symptoms by several weeks

Treat neoplastic epidural spinal cord compression

- Study published in the Lancet in 2005 of 101 patients with epidural spinal cord compression
  - Patients who received surgery followed by radiotherapy had better outcomes and lower morbidity and mortality than those who received radiotherapy alone
  - Primary outcome - ability to walk

Direct decompressive surgical resection in the treatment of spinal cord compression caused by metastatic cancer: a randomised trial

Roy A Patchell, Phillip A Tibbs, William F Regine, Richard Payne, Stephen Saris, Richard J Kryscio, Mohammed Mohiuddin, Byron Young

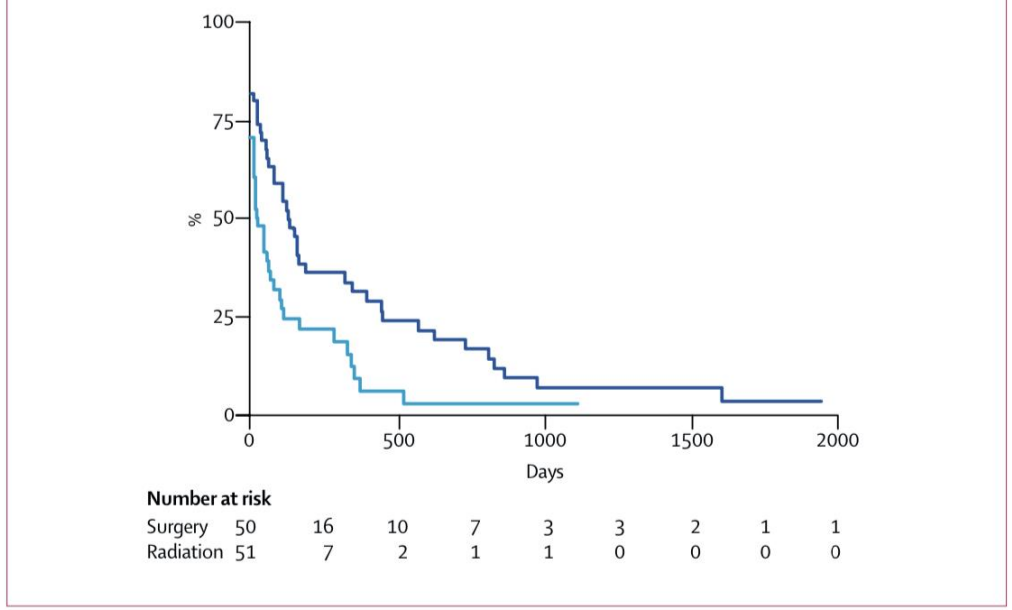


Figure 2: Kaplan–Meier estimates of length of time all study patients remained ambulatory after treatment

Question 17:

- Answer C, start G-CSF on day 2 of her subsequent cycles of therapy

Prevent chemotherapy-induced neutropenia

- 26 y/o F hospitalized with T 38.6 °C (101.5 °F) 10 days after 1st cycle of R-CHOP for diffuse large B-cell lymphoma, no other symptoms of infection
- WBC count 1100/µL (1.1×10^9/L) with 10% neutrophils, platelet count of 144,000/µL, and hemoglobin level of 11.2 g/dL
- Blood and urine cultures pending, CXR unremarkable
- Broad spectrum antibiotics started

- Neutropenic fever (per IDSA)
  - Single fever of ≥ 101 °F (38.3 °C), or
  - Temp ≥ 100.4 °F (38.0 °C) sustained over a 1 hour period, and
  - A current or anticipated absolute neutrophil count < 500 cells/µL (0.5×10^9/L)
- Neutropenia typically occurs 5 to 15 days after administration of chemotherapy

Prevent chemotherapy-induced neutropenia

Recommendations for the Use of WBC Growth Factors: American Society of Clinical Oncology Clinical Practice Guideline Update

- Primary prophylaxis with a CSF starting with the first cycle and continuing through subsequent cycles of chemotherapy is recommended in patients who have an approximately 20% or higher risk for febrile neutropenia based on patient-, disease- and treatment-related factors. Primary CSF prophylaxis should also be administered in patients receiving dose-dense chemotherapy when considered appropriate. Consideration should be given to alternative, equally effective, and safe chemotherapy regimens not requiring CSF support when available. (Type: evidence based, benefits outweigh harms. Evidence quality: high. Strength of recommendation: strong.)
- Secondary prophylaxis with a CSF is recommended for patients who experienced a neutropenic complication from a prior cycle of chemotherapy (for which primary prophylaxis was not received), in which a reduced dose or treatment delay may compromise disease-free or overall survival or treatment outcome. In many clinical situations, dose reduction or delay may be a reasonable alternative. (Type: evidence based, benefits outweigh harms. Evidence quality: high. Strength of recommendation: strong.)
- CSFs should not be routinely used for patients with neutropenia who are afebrile. (Type: evidence based, benefits outweigh harms. Evidence quality: high. Strength of recommendation: strong.)

Prevent chemotherapy-induced neutropenia

Table 1. Patient Risk Factors for Febrile Neutropenia

Risk Factor
In addition to chemotherapy regimen and type of malignancy, consider the following factors when estimating patient's overall risk of febrile neutropenia[22-25]:
Age ≥ 65 years
Advanced disease
Previous chemotherapy or radiation therapy
Preexisting neutropenia or bone marrow involvement with tumor
Infection
Open wounds or recent surgery
Poor performance status or poor nutritional status
Poor renal function
Liver dysfunction, most notably elevated bilirubin
Cardiovascular disease
Multiple comorbid conditions
HIV infection

- Other answers:
  - Reduce the chemo dose - may compromise outcome
  - Start G-CSF now – little benefit; neutrophil count may improve quicker, but there is minimal proven benefit and no demonstrated reduction in mortality
  - Start levofloxacin prophylaxis – for high-risk patients with ongoing neutropenia
    - Those undergoing allogeneic hematopoietic cell transplantation or receiving induction chemotherapy for acute leukemia

Question 18:

- Answer D, now

Screen for breast cancer in a patient with previous chest wall radiation

- 27 y/o F with hx of stage IIB Hodgkin lymphoma at age 19 treated with mantle and para-aortic radiation
- No family hx of breast or ovarian CA
- On exam, healed right supraclavicular incision from a previous lymph node biopsy

- Cumulative breast cancer incidence by age 40 to 45 years ranges from 13% to 20% among those with hx of chest wall radiation
- Risk varies with dose of radiation and increased risk begins within 8 years following treatment

Screen for breast cancer in a patient with previous chest wall radiation

- International Late Effects of Childhood Cancer Guideline Harmonization Group:
  - For women who received chest wall radiation before the age of 30 years, screening should begin at age 25 years or 8 years after completion of radiation therapy, whichever is last
- National Comprehensive Cancer Network:
  - Annual mammography and MRI starting after age 25 for patients receiving radiation between ages 10 and 30, beginning 8 to 10 years after irradiation
- Other answers:
  - Age 30 - breast cancer screening should start at age 27 years (8 years after radiation or age 25 years, whichever is last), not 30 years
  - Age 40 and 50 – for average risk individuals, breast cancer should start screening every 2 years by age 50 years, with the option to start mammographic screening between ages 40 and 50 years being an individualized decision

Question 19:

- Answer B, a germ cell chemotherapy regimen

Treat midline poorly differentiated carcinoma of unknown primary site

- 29 y/o M 2 mos of night sweats, fever, abdominal fullness and fatigue
- On PE, abdomen is distended with diffuse tenderness
- CBC, bili, Cr, alk phos, AST/ALT, α-fetoprotein, and β-human chorionic gonadotropin levels, are normal
- CT w/ contrast C/A/P shows bulky RP LAD (the largest mass 10 cm in diameter) with smaller but still enlarged mediastinal LAD
- Biopsy specimen of the most accessible enlarged LN shows poorly differentiated carcinoma; testicular US is unremarkable

- Cancer of unknown primary (CUP): a diagnosis of exclusion established in patients with a solid metastatic tumor after a detailed medical history and physical examination have been done and imaging studies or other diagnostic studies have not identified a primary tumor site
- 20% of patients with CUP fall into identifiable subgroups with a more favorable prognosis and who can benefit from a specific treatment strategy

Treat midline poorly differentiated carcinoma of unknown primary site

- Pt is a M with poorly differentiated CUP, predominantly midline
- In the absence of an identified primary tumor, he should be treated presumptively for metastatic germ cell tumor despite normal testicular examination/US and the absence of germ-cell specific markers, such as α-FP and β-HCG
- An unrecognized germ cell tumor may still exist and treatment should be with a platinum-based chemotherapy regimen

- Other answers:
  - GI cancer chemo regimen: CUP c/w GI primary would be predominantly below the diaphragm with liver or peritoneal involvement
  - Radiation therapy and tumor debulking of the LAD
    - Not appropriate given the extent of retroperitoneal and mediastinal lymphadenopathy

Cancer of unknown primary

Treatments for specific subsets of patients with CUP

Histologic type	Clinical feature	Treatment recommendation
Adenocarcinoma	Women with isolated axillary adenopathy	Treat as stage II breast cancer
	Women with peritoneal carcinomatosis	Treat as stage III ovarian cancer
	Men with elevated PSA or blastic bone metastases	Treat as advanced prostate cancer
	Colon cancer profile	Treat as advanced colon cancer
Adenocarcinoma or PDC	Single metastatic lesion	Definitive local therapy (resection and/or radiation therapy)
Squamous cell carcinoma	Cervical adenopathy	Treat as head and neck cancer with involved neck nodes
	Inguinal adenopathy	Inguinal node dissection
		Consider concurrent radiation therapy/chemotherapy (as in locally advanced cervical or anal cancer)
Poorly-differentiated carcinoma	Young men with midline tumor or elevated hCG/AFP	Treat as extragonadal germ cell tumor
Poorly-differentiated neuroendocrine carcinoma	Diverse clinical presentations	Treat with platinum/etoposide or paclitaxel/platinum/etoposide

Approximately 20 percent of patients with carcinoma of unknown primary (CUP) fit into one of these subsets with specific treatment implications.

Question 20:

- Answer A, active surveillance

Manage very-low-risk prostate cancer with active surveillance

- 60 y/o M with family hx of prostate CA
- Pt proceeds with prostate CA screening and laboratory studies reveal a serum prostate-specific antigen level of 5.1 ng/mL (5.1 µg/L)
- Biopsy of the prostate reveals cancer in two cores of the right lobe (Gleason score, 6), with less than 10% cancer in each core

- Recent literature supports the use of active surveillance
  - Scheduled assessments that include digital rectal examination, PSA measurement, and prostate biopsy
  - The purpose of active surveillance is to identify early cancer progression to limit treatment to those most likely to benefit
  - Appropriate only for men with low-risk or very-low-risk prostate cancer who have a life expectancy of at least 10 years
- Although no randomized data are available to support this strategy, available data indicate that the 15-year metastasis-free survival in appropriately selected patients is up to 97%

Manage very-low-risk prostate cancer with active surveillance

Very low	Stage T1c, serum PSA <10 ng/mL (10 μg/L), Gleason score ≤6, fewer than 3 biopsy cores positive, ≤50% cancer in each core, PSA density <0.15 ng/mL/g
Low	T1-T2a, Gleason score ≤6, PSA <10 ng/mL (10 μg/L)
Intermediate	T2b-T2c OR Gleason score 7 OR PSA 10-20 ng/mL (10-20 μg/L)
High	T3a OR Gleason score 8-10 OR PSA >20 ng/mL (20 μg/L)
Very high	T3b-T4, primary Gleason pattern 5, >4 cores with Gleason score 8-10

[a]T1 = tumors that are not palpable or seen on imaging; T1a (<5% of specimen) and T1b (>5% of specimen) are discovered incidentally in a pathologic specimen resected for benign disease; T1c discovered in prostate biopsy for elevated serum PSA.

T2 = palpable tumors; T2a involves <50% of one lobe; T2b involves >50% of one lobe; T2c are in both lobes of the prostate.

T3a extends through the prostate capsule; T3b involves the seminal vesicles.

T4 tumors are fixed to adjacent structures.

- Other answers:
  - Bone scan – not indicated in the asymptomatic patient due to very low likelihood of occult metastatic disease
  - Leuprolide – indicated for treatment of metastatic disease; can be combined with RT for high-risk or very-high-risk prostate CA
  - Observation – “watchful waiting” appropriate for elderly males with significant comorbidities that limit life expectancy

ACP statement on prostate cancer screening

- **Guidance Statement 1:**ACP recommends that clinicians inform men between the age of 50 and 69 years about the limited potential benefits and substantial harms of screening for prostate cancer. ACP recommends that clinicians base the decision to screen for prostate cancer using the prostate-specific antigen test on the risk for prostate cancer, a discussion of the benefits and harms of screening, the patient's general health and life expectancy, and patient preferences. ACP recommends that clinicians should not screen for prostate cancer using the prostate-specific antigen test in patients who do not express a clear preference for screening.
- **Guidance Statement 2:**ACP recommends that clinicians should not screen for prostate cancer using the prostate-specific antigen test in average-risk men under the age of 50 years, men over the age of 69 years, or men with a life expectancy of less than 10 to 15 years.