

Case I

Patient Description

- 48 year old, black male with history of HIV and Kaposi's sarcoma presents with left sided abdominal pain, fever and fatigue worsening over past month
- On lamivudine/zidovudine, efavirenz, TMP-SMX, azithromycin, but on no KS therapy

Patient Description

- Enlarged inguinal nodes bilaterally, palpable spleen, diffuse abdominal pain with some guarding, no palpable masses, active BS, no rectal masses and hemoccult negative.
- Few scattered KS lesion on lower extremities bilaterally, no edema
- Remainder of exam normal

Patient Description

- CD4+ count 56 cells/mm³; plasma HIV RNA 1000 copies/mL
- Liver enzymes mildly elevated, creatinine normal, amylase normal
- Hb 9.7 g/dL; Hct 29.3%; WBC 3000/mm³; platelet count 120,000; MCV 90 fL; retic 0.014

**What is your initial
diagnosis**

Possible Diagnosis

1. GI Kaposi's sarcoma with GI bleed
2. Non-Hodgkin's lymphoma
3. Abdominal abscess, MAI or others
4. CMV colitis
5. Anal cancer
6. Progressive HIV/AIDS

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6. Progressive HIV/AIDS

**What additional test would
you do first?**

Additional Tests

1. CT abdomen
2. Biopsy lymph node
3. Repeat VL and HIV genotype
4. Culture blood and stool, endoscopy
5. Stool occult blood, bone marrow, further heme work up
6. Chest X-ray and Chest CT if appropriate

Additional Tests

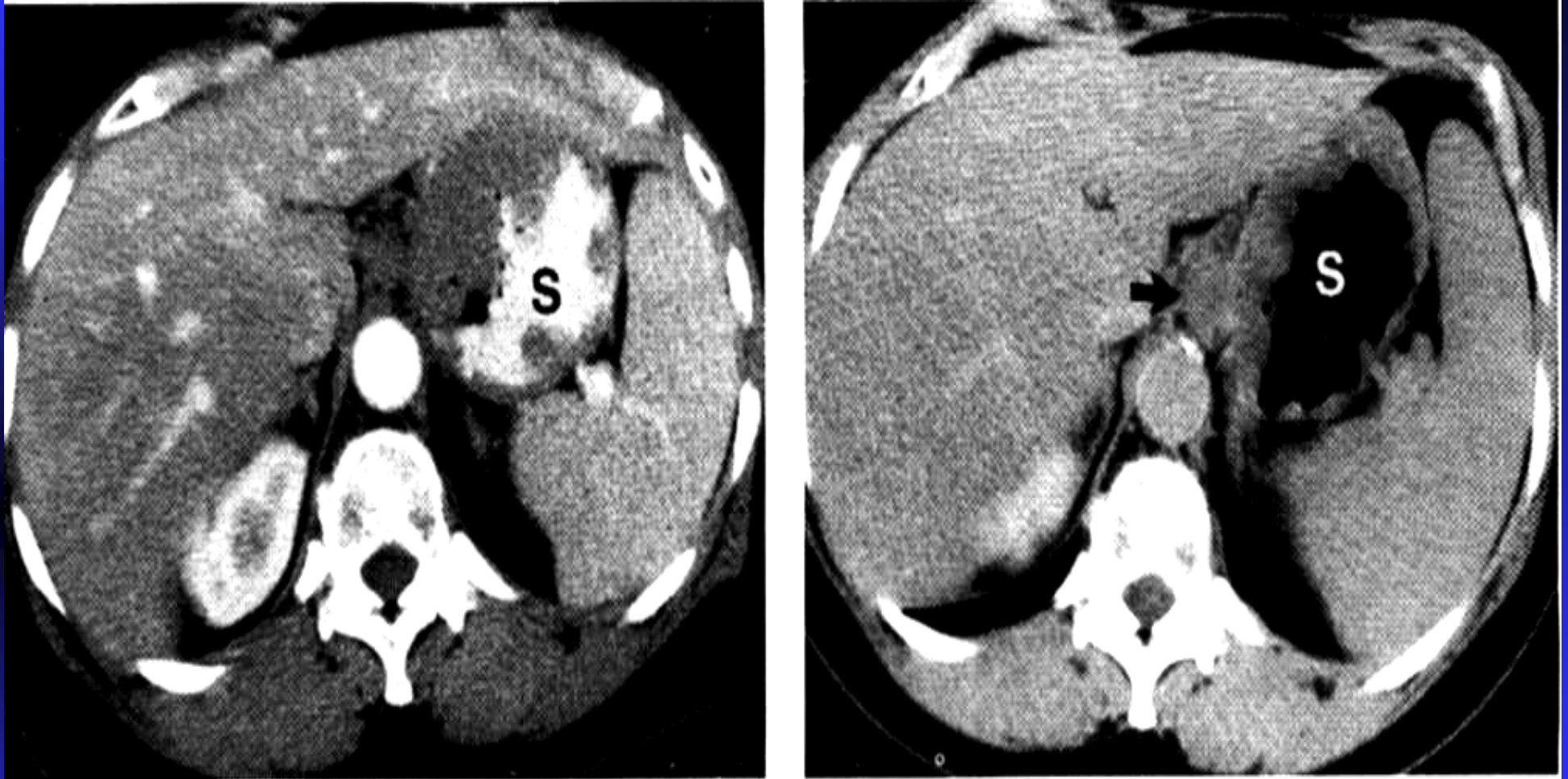
1. **CT abdomen**
2. Biopsy lymph node
3. Repeat VL and HIV genotype
4. Culture blood and stool, endoscopy
5. Stool occult blood, bone marrow, further heme work up
6. Chest X-ray and Chest CT if appropriate

Laboratory Findings

- Urinalysis normal, bilirubin normal, urine hemosiderin negative, LDH 500 IU/L, G6PD level normal, ferritin level elevated.
- Stool occult blood positive, blood cultures X 3 neg, MAC cultures neg, AFB negative, stool cultures neg, CXR normal
- CT scan abdomen - ordered
- HIV drug genotype - ordered
- Bone marrow aspiration and biopsy- ordered

Laboratory Findings

- CT scan of abdomen shows large gastric mass, enlarged perigastric and periaortic nodes, a few liver nodules and small amount of ascites
- Gastroscopy shows large gastric ulcerated mass, no active bleeding
- Histology reveals large B-cell NHL, CD-20+, no CMV or KS



Gastric lymphoma. Persistent gastric wall thickening (S). Enlarged spleen and an enlarged Lt. gastric lymph node (arrow)

Clinical Decision Point

- The patient has no CNS symptoms, CBC has not changed. Staging work up includes:
- CT of chest - no abnormalities
- LP with CSF cytology - neg for lymphoma
- Bone marrow aspiration and biopsy
 - ◆ **hypocellular, normal iron stores, no lymphoid infiltrates, normal lymphocyte flow panel, no granuloma or infection seen**

**How would you proceed
now?**

Clinical Decision

1. Chemotherapy (e.g CHOP-R or EPOCH-R)
2. Hydrate, allopurinol, follow electrolytes, creatinine, phosphorus, calcium
3. Intrathecal cytosine arabinoside X 4
4. Continue TMP-SMX, azithromycin
5. Begin prophylaxis with ciprofloxacin
6. Follow CBC, +/- G-CSF, +/- rEPO
7. Change ART
8. All of the above

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7. Change ART
8. **All of the above**

Clinical Course

- Patient tolerates chemotherapy with EPOCH-R, however after two cycles, Hb now 8.0 g/dL.

What do you do?

1. Repeat bone marrow aspirate and biopsy
2. Give iron and folic acid
3. Check EPO level and give recombinant erythropoietin alpha
4. Stop AZT and switch to new ARV
5. Transfuse 2 units of PRBC and schedule endoscopy

Clinical Course

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3. **Check EPO level and give recombinant erythropoietin alpha**
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Clinical Course

- EPO level 125, rEPO administered at 40,000 IU per week with supplemental iron and folic acid.
- After three cycles of EPOCH, patient has achieved a complete remission. Treatment continues for 6 cycles. CBC returns to normal.

Clinical Course

- 6 months later, he is again noted to have Hb 9.5 g/dL, WBC 2300/mm³ and platelets 65,000/mm³ and enlarged femoral nodes
- **What do you do?**

What do you do?

1. Work up anemia, DC TMP-SMZ, retreat with epoetin alfa and follow nodes
2. Assume recurrent lymphoma and retreat with EPOCH-R
3. Assume lymphoma and treat with alternate regimen
4. Assume progressive KS and treat with liposomal doxorubicin
5. Biopsy lymph node and bone marrow

What do you do?

1. Work up anemia, DC TMP-SMZ, retreat with epoetin alfa and follow nodes
2. Assume recurrent lymphoma and retreat with EPOCH-R
3. Assume lymphoma and treat with alternate regimen
4. Assume progressive KS and treat with liposomal doxorubicin
5. **Biopsy lymph node and bone marrow**

Clinical Course

- Biopsy of lymph node and bone marrow shows high grade B-cell (CD20+) NHL, large cell type
- Patient treated with ESHAP, G-CSF, epoetin alfa and prophylactic antibiotics (ciprofloxacin)
- Complete remission achieved after 5 cycles, patient treated for 8 cycles and continues to be followed.

Key Points

- **AIDS patients can have multiple cancers**
- **Evaluate for multiple etiologies for anemia in advanced AIDS patients**
- **Consider use of Epoetin alfa when risk of further myelosuppression is great**
- **Early relapse in AIDS/NHL should be treated with non-cross resistant salvage chemotherapy**
- **Use prophylactic antibiotics and hematopoietic growth factors in AIDS patients on chemotherapy, especially if receiving Rituximab**

Case 2

Patient Description

- 57 year-old white male with HIV infection since 1985, currently on tenofovir/emtricitabine, darunavir/ritonavir, TMP-SMX, azithromycin, valgancyclovir and fluconazole
- CD4 count 12, VL >150,000 copies/mL, Hb 9.2 g/dL, Hct 28 %, platelet count 111,000/mm³
- Presents with low grade fevers, progressively worsening personality changes for past month and mental confusion and lethargy for past week

Patient Description

- He suffers grand mal seizure on day of admission
- MRI scan of brain shows single contrast-enhancing lesion in the basal ganglion with surrounding edema
- **What do you suspect is the most likely diagnosis?**

Possible Diagnosis

1. CMV encephalitis
2. Toxoplasmosis
3. PML
4. CNS lymphoma
5. Fungal abscess
6. Infectious meningitis

Possible Diagnosis

1. CMV encephalitis
2. Toxoplasmosis
3. PML
4. ***CNS lymphoma***
5. Fungal abscess
6. Infectious meningitis

Clinical Decision Point

- Patient loaded with Phenytoin and started on dexamethasone 10 mg QID
- Which diagnostics study would produce the greatest likelihood of a diagnosis?

Clinical Decision Point

Which diagnostics study would produce the greatest likelihood of a diagnosis?

- 1. Toxoplasma serology**
- 2. Brain biopsy**
- 3. LP with CSF cultures and cytology**
- 4. LP with toxo titer, CMV and EBV PCR**
- 5. Blood cultures for bacteria, fungi, AFB, viruses**
- 6. Bone marrow aspiration and biopsy**
- 7. None of the above**

Clinical Decision Point

Which diagnostics study would produce the greatest likelihood of a diagnosis?

1. Toxoplasma serology
- 2. *Brain biopsy***
3. LP with CSF cultures and cytology
4. LP with toxo titer, CMV and EBV PCR
5. Blood cultures for bacteria, fungi, AFB, viruses
6. Bone marrow aspiration and biopsy
7. None of the above

Clinical Course

- CSF cultures and cytologies negative; CMV and EBV CSF PCR sent
- Blood cultures sent, preliminary negative
- Toxo IgG+ but IgM negative
- Stereotactic biopsy under MRI guidance shows immunoblastic lymphoma, EBV+, CD20+, HHV-8 negative
- Retic count 0.14, LDH 140 IU/L, ferritin normal

Clinical course

- Bone marrow obtained, hypocellular with all marrow elements present, no granuloma or lymphoma, few intracellular inclusions seen, cultures pending
- **What is your preferred therapeutic approach?**

Clinical Course

Therapeutic approach?

1. Refer for radiation therapy
2. Call oncologist for high-dose MTX with leukovorin rescue
3. Change antiretroviral therapy, if possible, continue TMP-SMX, azithromycin
4. Begin GCV 5 mg/kg BID
5. Begin epoetin alfa 40,000 IU QW with iron and folate, and G-CSF
6. Nothing, just continue dexamethasone and anticonvulsants and provide palliation

Clinical Course

Therapeutic approach?

1. Refer for radiation therapy
2. *Call oncologist for high-dose MTX with leukovorin rescue*
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4. Begin GCV 5 mg/kg BID
5. Begin epoetin alfa 40,000 IU QW with iron and folate, and G-CSF
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Clinical Course

- Patient responds to HDMTX with leukovorin rescue. Hct increases to 38% on EPO. GCV instituted for EBV-8 and with response dose reduced to 5 mg/kg TIW
- ART changed to raltegravir, TMC-125 EAP and enfuvirtide
- 6 months later, he is still in remission. His mental status improves but not completely
- 12 months later he relapses, responds transiently to radiation therapy but ultimately succumbs to tumor progression and respiratory failure.

Key Points

- **CNS changes in AIDS may be due to multiple causes**
- **PCNSL is rare in the HAART era, but can occur late in disease**
- **Biopsy of brain lesion for diagnosis**
- **If inaccessible for biopsy, EBV PCR on CSF and/or genetic studies on lymphocytes may be helpful**
- **Treatment best with HDMTX w/wo XRT**
- **Prognosis is unfortunately very poor, but improving**

Case 3

Patient Description

- 49 year old, white male with recently diagnosed HIV and presumed Kaposi's sarcoma presents to you for treatment of his KS
- He has been treated by his primary physician with lamivudine/zidovudine, efavirenz for 6 months, but has received no specific KS therapy

Patient Description

- On examination he has several scattered dark colored lesion on his lower extremities and feet bilaterally and localized edema at sites of several larger lesions
- Remainder of exam normal, including stool negative for occult blood
- CD4 count is 220 and viral load is <200 copies/ml
- Hb is 10.8, Hct 34, WBC 5,600, platelet count 145,000. LFTs are normal. CXR is clear

How would you proceed?

What would you do?

1. Order upper and lower endoscopy to r/o GI involvement with KS
2. Order whole body PET-CT
3. Biopsy the skin lesion
4. Begin liposomal doxorubicin for KS
5. Change efavirenz to lopinavir/ritonavir
6. 4 + 5

What would you do?

1. Order upper and lower endoscopy to r/o GI involvement with KS
2. Order whole body PET-CT
3. **Biopsy the skin lesion**
4. Begin liposomal doxorubicin for KS
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Laboratory Findings

- **Skin biopsy confirms Kaposi's sarcoma**
- **CT scan of chest and abdomen show small retroperitoneal lymphadenopathy but no visceral lesions**
- **Repeat CD4 count 329, VL <50 copies**
- **Ferritin, Fe/TIBC, folate, and calcium normal, corrected retic count 0.01**
- **The patient says that he would like something done for his leg lesions**

**How would you proceed
now?**

Clinical Decision Point

What do you do?

1. You indicate that he should not do anything at this point as ART can cause KS to regress
2. Change efavirenz to lopinavir/ritonavir
3. You begin treatment with liposomal doxorubicin
4. You begin topical 9-cis retinoic acid for the larger lesions
5. Refer to radiation therapy for treatment of his large lesions and edema
6. 2 + 4

Clinical Decision Point

What do you do?

1. You indicate that he should not do anything at this point as ART can cause KS to regress
2. Change efavirenz to lopinavir/ritonavir
3. You begin treatment with liposomal doxorubicin
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6. **2 + 4**

Clinical Course

- Patient tolerates change in ART and notices some local control of his KS lesions, but eventually he notices that the leg lesions have become more confluent and locally infiltrative with brawny edema
- He also notices some lymphadenopathy in his groin and some mild testicular swelling
- There are no new cutaneous lesions
- Six months later his testicular swelling is more pronounced and he begins to have pain in his extremities

Clinical decision point

What do you do?

1. Recheck his viral load and CD4 count as his HIV disease must be progressing
2. Refer him for biopsy of his lymph node to R/O NHL
3. Order CT or MRI of abdomen
4. Biopsy his skin lesion
5. Begin liposomal doxorubicin
6. 1 + 2
7. 3 + 5

Clinical decision point

What do you do?

1. Recheck his viral load and CD4 count as his HIV disease must be progressing
2. Refer him for biopsy of his lymph node to R/O NHL
3. Order CT or MRI of abdomen
4. Biopsy his skin lesion
5. Begin liposomal doxorubicin
6. 1 + 2
7. **3 + 5**

Clinical Course

- CT of the abdomen shows retroperitoneal adenopathy and enlarged inguinal nodes
- Testicular ultrasound shows testicular edema but no masses
- Alpha fetoprotein and beta hCG are normal
- Patient begun on liposomal doxorubicin q2 weeks with reduction in testicular and lower extremity edema and less pain after 2 cycles of therapy

Clinical Course

- After 6 cycles of liposomal doxorubicin the leg lesions are under better control, but still present
- He develops a non-productive cough, mild SOB and low grade fevers over course of a month
- You order a chest X-ray which shows some mediastinal adenopathy, blunting of both costophrenic angles and slightly enlarged cardiac silhouette

What is your diagnosis and what do you do?

1. Pulmonary KS, Order bronchoscopy for endobronchial lesions and transbronchial biopsy
2. Pulmonary TB or bacterial pneumonia or PCP, Order bronchoscopy with bronchoalveolar lavage
3. Non-Hodgkin's lymphoma, Order CT scan of chest and abdomen and biopsy inguinal lymph node
4. Non-Hodgkin's lymphoma or KS, Order pericardiocentesis under ultrasonic guidance

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4. **Non-Hodgkin's lymphoma or KS, Order pericardiocentesis under ultrasonic guidance**

Clinical Course

- Pericardiocentesis shows an exudate with many lymphoblastic appearing cells which are CD20+, EBV+, HHV-8+ and culture negative for TB, bacteria or fungus
- Flow cytometry confirm malignant anaplastic B-cells, negative for epithelial markers, c/w primary effusion lymphoma
- PET CT showed hypermetabolic lymphadenopathy in the mediastinum but not in the abdomen
- Bone marrow biopsy did not show NHL
- CSF was negative for malignant cells

Clinical Course

- Patient was begun on EPOCH-R and GCV
- Tumor initially regressed and patient's symptoms improved
- However after 3 cycles of therapy, the effusions returned, requiring 2 additional pericardiocentesis
- Chemotherapy was changed to R-CODOX M, but the tumor continued to progress and the patient expired after deciding against further intervention

Key Points

- **Kaposi's sarcoma continues to remain both a local and systemic problem in the HAART era**
- **Progression of KS can occur even with good virologic control of HIV**
- **Other HHV-8 related tumors may occur in individuals with KS**
- **Treatment of Primary Effusion Lymphoma is difficult and may require more aggressive treatment**

Case 4

Patient Description

- 42 year old, white gay male with recently diagnosed HIV infection presents to your office for the first time.
- He is on efavirenz/tenofovir/emtricitabine (Atripla) and has a CD4 count of 320 (22%) and a viral load <50 copies/ml

Patient Description

- As part of your routine work up, in addition to a complete history and physical examination,
what do you also order?
 1. CXR and EKG
 2. Immunization with Pneumococcal vaccine, hepatitis A and B vaccine, influenza vaccine
 3. PSA and flexible sigmoidoscopy
 4. Perform anal pap test
 5. All of the above

Patient Description

- As part of your routine work up, in addition to a complete history and physical examination,
what do you also order?
 1. CXR and EKG
 2. Immunization with Pneumococcal vaccine, hepatitis A and B vaccine, influenza vaccine
 3. PSA and flexible sigmoidoscopy
 4. **Perform anal pap test**
 5. All of the above

Patient Description

- Routine labs, CXR and EKG are normal
- Anal pap test shows moderate dysplastic changes
- You refer for high-resolution anoscopy and biopsy which show grade 3 ASIL

How would you proceed?

1. Refer to surgery for AP resection and lymph node sampling
2. Refer to radiation therapy
3. Perform infrared coagulation
4. Do nothing and repeat HRA and biopsy in 6 months
5. Refer for electrocauterization
6. Treat with imiquimod

How would you proceed?

1. Refer to surgery for AP resection and lymph node sampling
2. Refer to radiation therapy
3. Perform infrared coagulation
4. Do nothing and repeat HRA and biopsy in 6 months
5. Refer for electrocauterization
6. Treat with imiquimod

Clinical Course

- He undergoes IRC which he tolerates well. Follow up exam in 1 month shows good healing. He is asked to return in 3 months for repeat exam
- He is lost to follow up and returns to you 3 years later stating he was in Iraq with a contract security firm
- He has been poorly compliant with his HIV medications, as he did not want his employer and associates to know of his HIV status which would have threatened his employment

Patient Description

- He appears in good health. His physical exam is normal.
- CD4 count is 179 (15%) and his viral load is 230,000 copies/ml
- You refer him for high resolution anoscopy and biopsy which reveals a 2.0 cm mass in the posterior anus, which is biopsied and found to be invasive poorly-differentiated squamous cell carcinoma

Patient description

- PET-CT scan of abdomen shows locally invasive cancer in the anus with perianal adenopathy but no other hypermetabolic areas in the abdomen or retroperitoneum
- Chest CT scan shows no abnormalities
- LFTs, CBC are normal
- Repeat CD4 count is 150 (14%) and viral load is 210,000. Genotype shows 184V, 103N, 181C mutations

Clinical Decision Point

1. Refer to surgery for tumor resection and lymph node dissection
2. Change ART to lopinavir/ritonavir and abacavir/lamivudine
3. Refer to medical oncology for chemotherapy
4. Refer to radiation therapy
5. 1 + 2
6. 2 + 3
7. 2 + 3 + 4

Clinical Decision Point

- Refer to surgery for tumor resection and lymph node dissection
- Change ART to lopinavir/ritonavir and abacavir/lamivudine
- Refer to medical oncology for chemotherapy
- Refer to radiation therapy
- 1 + 2
- 2 + 3
- **2 + 3 + 4**

Clinical Decision

- Patient has antiretroviral drugs changed, which he tolerates well
- He is also started on TMP-SMZ
- He receives 2 cycles of cis-platinum and 5FU and then begins concurrent chemo-radiotherapy for 4 additional cycles
- He also receives prophylaxis with ciprofloxacin
- Follow CBC, G-CSF +/- rEPO as needed

Clinical Course

- Patient tolerates chemoradiotherapy, but develops some localized pain and diarrhea requiring symptomatic therapy
- Hb falls to 8.2 g/dl and rEPO is administered at 40,000 IU per week with supplemental iron and folic acid
- Repeat PET-CT and HRA shows complete remission and Hb returns to 11.0 after chemoradiation completed
- Plasma HIV RNA <50 copies/ml and CD4 count 80, confirmed on repeat testing

What do you recommend now?

1. Follow up every 3-6 months with repeat HRA and PET-CT for 1 year
2. Change antiretroviral therapy because of lower CD4 count
3. Institute additional prophylaxis for MAC and fungus
4. Consolidation chemotherapy with 2 additional cycles of chemotherapy
5. 1 + 3
6. 2 + 3
7. 1 + 4

What do you recommend now?

1. Follow up every 3-6 months with repeat HRA and PET-CT for 1 year
2. Change antiretroviral therapy because of lower CD4 count
3. Institute additional prophylaxis for MAC and fungus
4. Consolidation chemotherapy with 2 additional cycles of chemotherapy
5. **1 + 3**
6. 2 + 3
7. 1 + 4

Clinical Course

- Patient now works in the USA and returns regularly for follow up
- CD4 counts gradually increases to 200 after 6 months
- At 9 months patient develops a non-productive cough and some weight loss
- CXR shows multiple diffusely scattered pulmonary nodules with hilar adenopathy
- PET-CT shows retroperitoneal adenopathy and perianal adenopathy

Key Points

- Patients with HIV should undergo anal PAP testing at first presentation and q6 month if abnormality detected
- Local ablative therapy is effective for most HSIL, but progression can occur
- Treatment for invasive anal CA consists of concurrent chemoradiotherapy
- Recurrence after remission can occur and if disseminated, may have poor prognosis
- Be on alert for possible chemo-ART drug interactions and plan accordingly