43 - Non-AIDS-Defining Complications of HIV/AIDS

Speaker: Michael Saag, MD

IDBR INFECTIOUS DISEASE BOARD REVIEW AUGUST 17-21, 2024

Non AIDS-Defining Complications of HIV/AIDS

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- **Disclosures of Financial Relationships with Relevant Commercial Interests**

  - None

CASE 1

PREVIEW QUESTION

- 55 year old man presents with R hip pain
- H/o COPD requiring steroids frequently
- HIV diagnosed 17 years ago
- On TDF / FTC / EFV for 10 years; originally on IND / AZT / 3TC
- Initial HIV RNA 340,000; CD4 43 cells/ul
  - Now HIV RNA < 50 c/ml; CD4 385 cells/ul
- Electrolytes NL; Creat 1.3; Phos 3.5 Ca 8.5
- Mg 2.1, alk phos 130; U/A neg
- R Hip film unremarkable

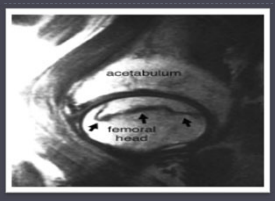
QUESTION #1

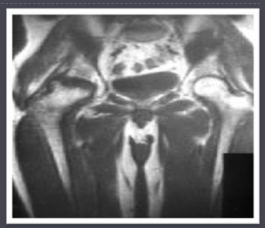
PREVIEW QUESTION

Which if the following is the most likely underlying cause of his hip pain?

A. Osetonecrosis of Femoral Head
B. Fanconi's syndrome
C. Vitamin D deficiency
D. Tenofovir bone disease
E. Hypogonadism

Osteonecrosis





This image demonstrates a classic segmental area of osteonecrosis with a dark line denoting the border between dead bone and living bone.

M. Levine. Ostoenecrosis of the hip- emedicine.com

Avascular necrosis in HIV

- Reported prior to the HAART era; increasing in HAART era.
- Rates of AVN 4.8/1000 person years >> general population.
  - Age ~ 35 yrs
  - Male predominance
  - H/o IDU
  - Increased duration of HIV
  - Low CD4
  - Elevated lipids
  - Glucocorticoid steroid use
  - Alcohol use

Monier et al, CID 2000;31:1488-92, Moore et al, AIDS 2003

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CASE 2

- 46yowf c/o (CD4 582, VL <50 c/ml) c/o 1 week cramps in calves, tingling in hands, feet
- Today awoke and can't move except hands/feet
- No F/C, chest pain, SOB, incontinence
- + chronic diarrhea 4x/day
- Chronic fatigue, poor appetite
- Meds
  - TDF/FTC/EFV (2008), on TDF/FTC/Elv/cobi since 2014
  - zoloft, buproprion, norco, prilosec, trazodone, pravachol ibuprofen

CASE 2: Exam

- VS: T 98.2 P 79 BP 112/73
- RR 16, O2 sat 97%
- Pertinent findings
- Neuro: CNII-XII intact, strength 1+ all extremities except 4+ hand/wrist and ankles.
- NI reflexes. Alert, oriented.

CASE 2: Labs

137 | 116 | 5 Gluc 83
1.6 | 18 | 1.0 AG 3

Ca 8.3 Phos 1.8 Mg 2.1
Lactate 1.5 CK 186
UDS +cocaine/benzo/opiate
UA: 1.015 pH 6.5 2+ pro
Neg: gluc/ketones

QUESTION #2

Which of the following is the most likely diagnosis?

A. Cocaine toxicity
B. Nucleoside-induced myopathy (ragged red fiber disease)
C. Serotonin Syndrome
D. Statin toxicity
E. Fanconi's syndrome

Fanconi syndrome

- Type II RTA
- Generalized proximal tubule dysfunction
- Hypophosphotemia, renal glucosuria, hypouricemia, aminoaciduria
  - Not all have present at once
- Osteomalacia can occur
- Recovery is the rule; can take months

CASE 3

- 35 year old man presents with complaints of increasing fatigue, headache, SOB / DOE
- HIV diagnosed 4 mos ago with PCP; intolerant to TMP/SMX
- Now on TAF / FTC / BIC + PCP Prophylaxis with Dapsone
- Claims adherence to all meds;
  "Doesn't miss a dose!"
- Normal PE
- Pulse Ox 85%; CXR no abnormalities
- ABG: 7.40 / 38 / 94/ 96% (room air)

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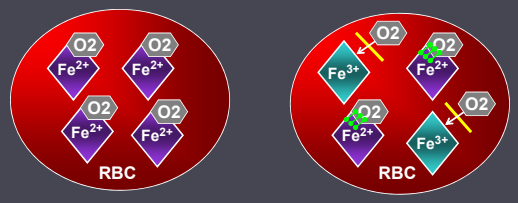
QUESTION #3

Which of the following is the most likely underlying cause of his symptoms?

A. Recurrent PCP
B. IRIS Reaction
C. Drug toxicity
D. Pulmonary Embolus
E. Patent Foramen Ovale

Hemoglobin and Methemoglobin



CASE 4:

In a 40 yo male PWH non-smoker, non-diabetic with LDL cholesterol 125 mg/dl, HDL 45 mg/dl, with an ASCVD score of 1.5%, should he be started on a statin ?

A. Yes
B. No
C. Not sure

REPRIEVE Study (started in 2015)

- 7769 HIV+ men and women (30%) age 40 – 70 yo
- Low to moderate risk for statin use
- All patients on ARV Rx with CD4 > 100 cells / ul
- Randomized to pitavastatin vs placebo
- Study stopped by DSMB
- Findings:
  - 35% reduction in CV events

CASE 5

- 25 year old black woman presents with fatigue
- History of IV Heroin use; intermittently takes TDF/FTC PreP
- Exam no edema
- Work up in ER shows creatinine 8.4 BUN 79; mild anemia; mild acidemia
- In ER 10 weeks earlier; normal renal function
- U/A high grade proteinuria
- US of kidneys: Normal to increase size; no obstruction
- Rapid HIV test positive

QUESTION #5

Which of the following is the most likely cause of her renal failure?

A. Volume depletion / ATN
B. Heroin Associated Nephropathy
C. HIVAN
D. Membranous glomerulonephritis
E. Tenofovir Toxicity (PrEP)

Bonus Question #1:

In a patient with HIV Associated Nephropathy, which of the following is the most effective intervention to prevent progression to ESRD?

A. An ACE inhibitor
B. Corticosteroids
C. High Molecular Weight Dextran
D. Antiretroviral Therapy
E. A calcium channel blocker

CASE 6

- 55 year old man presents with complaints of fever / volume depletion
- HIV diagnosed in ER on rapid test
- Lymphadenopathy / splenomegaly / few petechiae / Oriented X 3
- HIV RNA 340,000; CD4= 3 cells/ul
- On no medications

Hb 8.2 gm/dl; Plt count 21,000; Creatinine 2.0

Rare schizocytes on peripheral blood smear

QUESTION #6

Which of the following is the most effective intervention to increase the platelet count?

A. Splenectomy
B. Corticosteroids
C. Plasmapheresis
D. Ethambutol + Azithromycin
E. Antiretroviral Therapy

CASE 7

- 45 year old recently diagnosed with HIV
- HIV RNA 140,000; CD4= 230 cells/ul
- Baseline labs:
- Hb 11.2 gm/dl; AST 310 / ALT 120

140 | 101 | 5 Gluc 100

4.2 | 28 | 1.1 eGFR = 65 ml/min

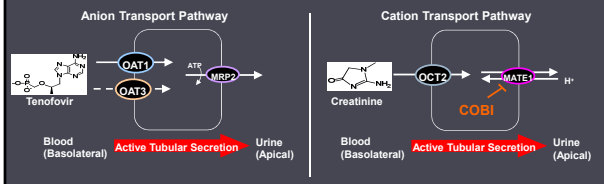
- Started on TAF/FTC+ Dolutegravir; No other medications
- Returns 4 weeks later, labs unchanged except creatinine now 1.3 mg/dl (eGFR 55)

QUESTION #7

Which of the following is the most likely cause of her increased creatinine / reduced eGFR?

A. Glomerular lesion
B. Proximal Tubule damage
C. Proximal Tubule inhibition
D. Distal Tubule damage
E. Distal Tubule inhibition

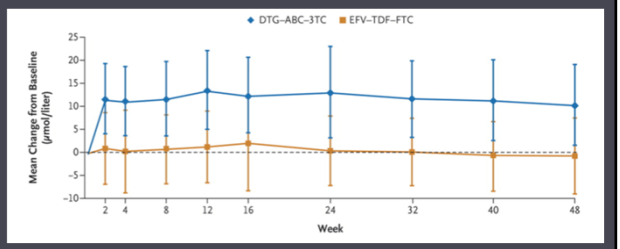
Tenofovir and COBI Interact with Distinct Renal Transport Pathways



The active tubular secretion of tenofovir and the effect of COBI on creatinine are mediated by distinct transport pathways in renal proximal tubules

Ray A, et al. Antimicro Agents Chemo 2006;3297-3304
Lepist E, et al. ICAAC 2011; Chicago. #A1-1724

Changes in eGFR



Walmsley, et al. N Engl J Med. 2013;369:1807-18.

CASE 8

- 26 year old presents with cryptococcal meningitis and newly diagnosed HIV (Rx with AMB +5FC; to fluconazole)
- HIV RNA 740,000; CD4= 23 cells/ul
- Baseline labs:
- CSF: 2 lymphocytes / protein 54 / glu 87 (serum 102)
  OP = 430 mm H_20
  Started on TAF/FTC /Bictegravir at week 2
- Returns 6 weeks later, Fever 103 and a mass in supra-clavicular region (3 x 4 cm)

QUESTION #8

Which of the following is the most likely cause of the new mass?

A. B Cell Lymphoma
B. Multicentric Castleman's Disease
C. IRIS reaction to cryptococcus
D. Mycobacteria Avium Complex
E. Bacterial Abscess from prior PICC line

IRIS

- Immune Reconstitution Inflammatory Syndrome
- Occurs 4 – 12 weeks after initial ARV administration
- Most often in patients with advanced HIV infection
- High viral load / low CD4 count
- TB, MAC, crypto, PML, KS are most common OIs
- Is **NOT** related to type of ARV therapy

CASE 9

- 48 yo Male presents with newly diagnosed HIV infection
- Asymptomatic
- **Initial: HIV RNA 160,000 c/ml**
  CD4 count 221 cells/ul
- Other labs are normal; Started on ARV Rx with DTG + TAF/FTC
- Returns for a 3 month follow up visit
- **HIV RNA < 20 c/ml; CD4 390 cells/ul**

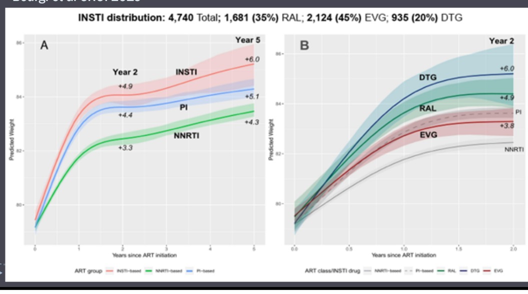
QUESTION # 9

Which of the following will most likely be present on his 3 month visit from use of dolutegravir:

A. Morbilliform skin rash (extremities)
B. 3 kg weight gain
C. Mild cognitive impairment
D. Depression
E. Anemia

Change in Weight Overtime – NA-ACCORD

Bourgi et al CROI 2019



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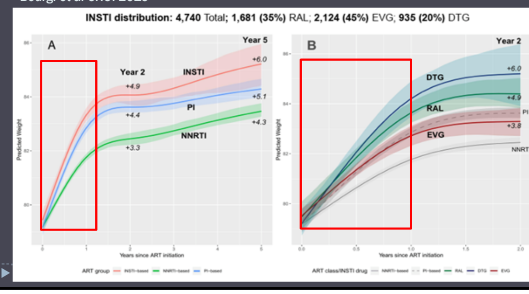

Change in Weight Overtime – NA-ACCORD

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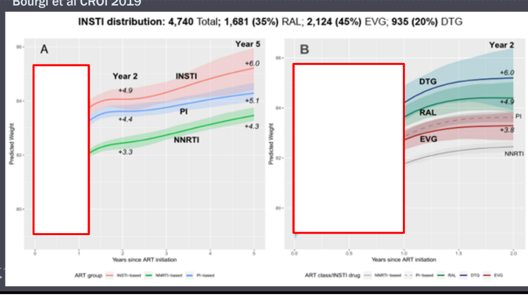

CASE 10

- 48 yo Male presents with newly diagnosed HIV infection
- Asymptomatic except for weight loss / fatigue
- Initial: HIV RNA 160,000 c/ml
  CD4 count 221 cells/ul
- Other labs are normal; Started on ARV Rx
- Returns for a 3 month follow up visit
- HIV RNA < 20 c/ml; CD4 390 cells/ul

QUESTION # 10

Assuming he remains undetectable, you tell him that his risk of transmitting HIV to his seroneg partner via sex is:

A. Virtually zero risk (< 0.2%)
B. Very low risk (< 2%)
C. Possible (<10 %)
D. It depends on which ARV regimen he's on

PARTNERS Study

- 548 heterosexual and 972 discordant gay couples followed up to 8 years
- Seropositive partner had VL < 200 c/ml
- 77,000 sexual acts without condoms
- Zero transmissions (from seropositive partner)
- Upper bound of 95% CI: 0.23 /100 CYFU
- Sexual Transmission from a person with Undetectable Viral Load is Effectively Zero

Rodger AJ, et al. Lancet 393: 2428-38, 2019

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U=U: Undetectable=Untransmittable

CASE 11

- 58 yo MSM Male presents for routine evaluation
- On ARV Rx:
- HIV RNA < 20 c/ml; CD4 590 cells/ul
- He is sexually active with 3 to 4 different partners / year
- Receptive and insertive anal intercourse
- A routine annual anal PAP is collected and shows LSIL

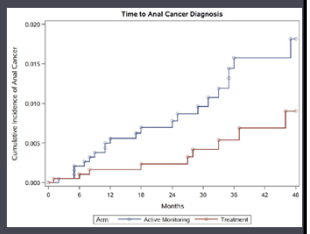
QUESTION # 11

Which of the following should be performed?

A. High Resolution Anoscopy with Biopsy
B. Digital Rectal Exam; if negative monitor for 1 yr
C. Sigmoidoscopy
D. Colonoscopy
E. Monitor only; repeat anal PAP in 6 months

Treatment of HSIL reduces risk of anal cancer by 57%

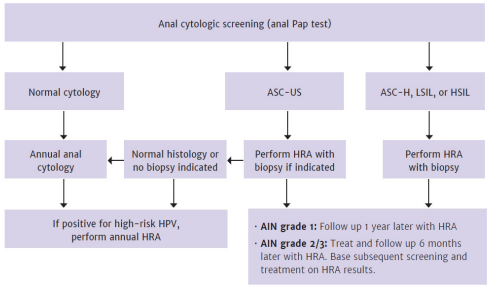
- **30 anal cancers diagnosed** in median f/u of 25.8 months
  - 9 in Treatment arm (173/100,000 PY)
  - 21 in Active Monitoring arm (402/100,000 PY)
- 8 study-related serious AEs:
  - 7 in treatment arm (3 pain, 3 abscess, 1 skin ulceration)
  - 1 in monitoring arm (infection)



Anal dysplasia

Palefsky J, et al. N Engl J Med 2022; 386:2273-2282

Figure 1. Follow-up of Anal Cytologic Screening Results



Recommendations: Screening

- ☑ Clinicians should promote smoking cessation for all patients with HIV, especially those at increased risk for anal cancer. (A3)
- ☑ For all patients aged ≥35 years with HIV, clinicians should recommend and perform DARE annually to screen for anal pathology (B3)
- ☑ Clinicians should evaluate any patient with HIV who is <35 years old and presents with signs or symptoms that suggest anal dysplasia. (A3)
- ☑ Clinicians should conduct or refer for HRA and histology (via biopsy) in any patient with abnormal anal cytology. (A2)
- ☑ Clinicians should refer patients with suspected anal cancer determined by DARE or histology to an experienced specialist for evaluation and management. (A3)

7/31/2024 NYSDOH AIDS Institute Clinical Guidelines Program

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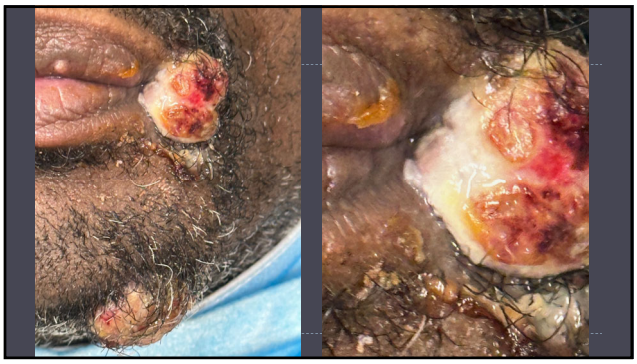
CASE 12

- 30 yo Male presents with new lesions on his buttocks, groin, back, and face
- MSM; reports fever
- Denies sexual activity in the last 12 weeks
- HIV RNA 68,000 c/ml (off ARV now)
  CD4 count 250 cells/ul
- UDS + methamphetamine



QUESTION # 12

In addition to STI screening and Mpox culture, which of the following would you do?

A. Treat for molluscum contagiosum
B. Start tecovirimat at this visit
C. Wait for cultures, if positive for mpox, start tecovirimat
D. No specific mpox Rx; give JYNNEOS vaccine now instead
E. Administer Benzathine Penicillin