TB or Not TB
That is the Question

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Case: Mr. DN 42 yr. Male

- HIV on ART since 2006 and HPT - perindopril
- 1/12 prior to admission -fever, cough and cervical L/N
- Started on
  - Rifafour 4 daily, pyridoxine 25mg daily
  - LPV/r 2 bid, TDF/FTC 1QD, purbac D/S 1QD.

Current Presentation

- Worsening symptoms
- Tremor, difficulty mobilizing and difficulty walking
- Pale, anicteric, acyanotic, hydration was good, large lymph-nodes bilaterally post triangle, submandibular nodes and R supra-clavicular -largest ~5 x 3cm.
- CVS & Resp.: normal
- Abdomen: 6cm hepa, no spleen, no ascites.
- CNS: speech was slow, dysarthric, pill rolling tremor, increased tone, cogwheel rigidity, bradykinesia, hypokinesia, bradyphrenia.

Laboratory Results

- CD4: 81cells/uL
- FBC: 8.2/305/18.61
- U&E: 138/3.9/105/15/5.5/81
- CCa 2.80, PO4 1.13, Mg 0.76
- LFT: 71/19/21-3/127/302/22/32
- RPR, HAV, HBV, HCV, all neg,
- Sputum (Dec 2013) Smear neg, GXP R sen., culture positive
- CT Head/MRI: N, CSF: P 6, LC 4, prot.1.38, G 2.7 (B/S 5.4), CRAG neg.

Summary

- Advance HIV disease
- Failing first line treatment
- Recent commenced on 2nd line HAART
- PTB - smear/culture positive for sensitive TB
- Presumed L/N TB
- Parkinsonism

Cause of Parkinsonism

- TB meningitis
- Cryptococcal Meningitis
- Drugs
- HIV
- Toxoplasmosis
- Lymphoma
- Parkinsons Disease

Parkinsonism and HIV

- OI's and Malignancies rarely cause parkinsonism.
- Incidence of parkinsonism 0.6% (14/2460) pre-HAART (1986–1999) & 0.2% (2/970) post-HAART (2000–2007).
- Movement disorders - 3% at tertiary centers
- Prospective studies - 50% of patients with AIDS develop some movement disorder.

Parkinsonism and HIV

- Movement disorders include
  - Hemiballism-hemichorea
  - Tremor
  - Dystonia
  - Chorea
  - Myoclonus, tics
  - Parkinsonism
- Management:
  - Symptomatic treatment often disappointing
  - **HAART : mainstay of treatment**

Progress

- Continued ATT, aluvia adjusted to **4 bd**, truvada 1 daily, purbac D/S 1 daily
- perindopril 8mg/d, Epilim 800mg bd
- 5mg weekly taper of pred from 20mg/d
- 16/01/2014 (3/52) discharged with persisting signs of parkinsonism but able to mobilize with less difficulty

Readmission: 12/02/2014

- One month later- persistent V & D
- Acidotic and confused.
- FBC- 8.2/12.67/336
- U&E- 132/**6.0**/96/**9**/**53.8**/**1327**
- LFT- 77/19/20-8/129/417/5/14,
- CCa- 2.84, PO4 2.32, Mg 1.26
- CD4 59, viral load 384cpm
- U/S kid: R- 12.4cm, L 11.9cm increased echogenicity.

Approach

- Institute renal replacement treatment
- Look for underlying cause
- Address the underlying cause
- Remove/avoid other nephrotoxic agents

Cause of Renal Failure?

- Hypertension
- Aluvia
- Tenofovir
- INH
- Rifampicin
- PZA
- HIVAN
- Sepsis

TDF and Kidneys

- Mitochondrial toxicity
- Risk factors:
  - GFR <90 mL/min
  - Comorbidities DM, HPT
  - Ritonavir-boosted PI
  - Concomitant nephrotoxic drugs
  - advanced age, low body weight,
  - Low CD4 count
- Associated with: PCT dysfunction, ARF, CRF
- Studies suggest 1/5 tubular defect, 1/100 RF-excluded high risk patients - underestimate

Approach

- Institute renal replacement treatment
- Look for underlying cause
- Address the underlying cause
- Remove/avoid other nephrotoxic agents
- Adjust all medication for RF

Choose the drugs that need Dose Adjustment

- Aluvia
- INH
- RIF
- 3TC
- ABC

Renal Dosing of NRTIs

NRTI	Glomerular Filtration Rate			
	>50	50-25	10-25	<10
AZT	300mg bid	300mg bid	300mg bid	300mg/d
d4T	30mg bid	15mg bid	15mg /d	15mg /d
3TC	300mg/d	150mg/d	100mg/d	25/50mg/d
TDF	300mg/d	300mg Q48	300mg Q72	Don't use
ABC	600mg/d	600mg/d	600mg/d	600mg/d

Progress

- Dialysis dependent for about 4/52, 134/5.5/99/16/11.7/221 (eGFR 28)
- Discharged on ABC 600mg QD, 3TC 100mg QD, LPV/r 800/200 bid, rifinah 2 daily, pyridoxine 25mg daily
- Aspiration of L/N- AFB smear positive, culture positive, sensitive to H/R

2nd April (1/12 later) Readmitted

- Profound weakness, body aches and pains, unsteady, neck mass increasing in size
- Drowsy, dehydrated, signs of parkinsonism resolved, lymph-nodes distinctly larger

Blood results

- FBC: 5.3/11.82/513
- U&E: 133/5.5/101/19/14.3/203 (eGFR 31)
- LFT: 94/18/31-28/185/546/10/26,
- CCa 3.48, PO4 1.44, Mg 0.98, PTH 6 (15-65)
- CD4 172, Viral load 150 cpm , CXR clear, U/S increased L/N compression of left ureter $\Rightarrow$ hydronephrosis of left kidney.

Causes of HyperCa in Our Patient

- Malignancy
- Ectopic production of 1,25$(OH)_2$ vitamin D
- 1° hyperparathyroidism
- 3 ° hyperparathyroidism
- Drugs
- Adrenal insufficiency
- Renal failure

TB IRIS with Hyper Ca

- TB - more common cause of IRIS
- Pathogen specific IR $\Rightarrow$ improved granuloma formation to control/eradicate infection.
- The macrophages in the granuloma have increased 1α-hydroxylase activity $\Rightarrow$ overproduction of 1,25 $(OH)_2D$ $\Rightarrow$ increased gut reabsorption of calcium $\Rightarrow$ hypercalcemia

What is the management of Hyper Ca in our Patient?

- Hemodialysis
- Rehydration
- Rehydration with forced diuresis with loop diuretics
- Rehydration forced diuresis with thiazide diuretics
- Rehydration + steroid therapy
- Rehydration + bisphosphonates

Management of Hyper-Ca.

- Rehydrate with saline
  - Increases GFR
  - Reduces Ca. reabsorption in PCT and DCT
  - Use loop diuretics in pts at risk of fluid overload
- Steroids:
  - decreases 1,25 $(OH)_2D$ within 3 days- drop in Ca.
- Bisphosphonates- no role

Management and Progress

- Rehydrated
- Transfused
- L/N biopsy- no malignancy
- High dose steroids IVI followed by oral
- Aluvia 4 bd, 3TC 300mg QD, ABC 600mg QD
- Rifinah 2 QD, pyridoxine 25mg QD, Prednisolone 90mg QD, purbac D/S 1 QD

Last follow-up 8/07/2014 (2 ½ mths)

- FBC- 10.9/8.29/330
- U&E- 140/4.0/100/18/**11.9**/105
- LFT- 82/35/11-9/102/543/22/18
- CCa- 2.43 PO4- 0.87, Mg 0.83
- CD4 129 (9%), Viral load <40cpm

Conclusion

- Movement disorders in HIV
- TDF induced RF
- TB IRIS with hypercalcemia