Rifampin-induced Nephrotoxicity in a Tuberculosis Case

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Background and Rationale

- Rifampin causes an acute interstitial nephritis (AIN), an allergic response. It is idiosyncratic, and non-dose dependent.
- Acute kidney injury due to rifampin is rare, occurring in 0.1% of TB patients, thus making diagnosis difficult (*Manika K et al, Renal Fail. 2014*).
- Nevertheless, early diagnosis is important to prevent progression to end-stage renal disease. Of the four drugs used in initial phase of TB treatment, namely isoniazid (INH), rifampin (RIF), pyrazinamide (PZA), ethambutol (EMB)—two (RIF and PZA) can cause AIN.
- We describe in this case report a TB patient who developed acute kidney injury and how we came to attribute this to RIF.

Presentation of Case

- A 38-year male from Mexico arrived in United States 1996
- Left wife and 2 year old child behind
- Worked as a painter
- Cigarette smoker for 10 years, one pack a day
- Was drinking beers, up to 10 cans a day
- Ill for 3 months
  - Cough
  - Night sweats, Fever
  - Loss of appetite
  - Hoarseness voice
  - A 50 lb. weight loss

Diagnosis

Date	Test	Result
8/18/14	Chest radiograph	Bilateral Infiltrates Cavitary Disease
8/27/14	Sputum	AFB smear 3+ GeneXpert MTB/RIF Positive
9/03/14	T.SPOT.TB	Negative
9/08/14	Sputum Culture	M. *tuberculosis*
9/15/14 10/2/14	Drug S usceptibility Testing	Sensitive to INH, RIF, EMB Resistant PZA
9/19/14	Genotyping	GENType G03500; M. *bovis* Lineage
8/29/14	HIV	Negative



Chest Radiograph 8/18/2014

Bilateral extensive disease
Multiple cavities
Tracheal deviation to the left

Treatment Plan

9 Months Course of Treatment

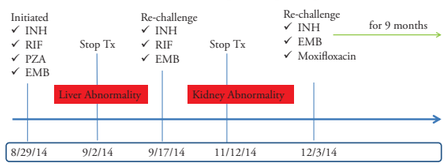
- 2 months initiation phase; isoniazid, rifampin, pyrazinamide, ethambutol
- 7 months continuation phase; isoniazid and rifampin

Counseled on drinking and smoking

Developing Acute Kidney Injury (1)

- Case initiated four drug therapy 8/29/14
- AST=101 on day he started treatment; AST =41 at baseline ten days earlier
- Although he was referred to TB clinic from a walk-in clinic 8/18/14, he delayed coming in
- Treatment was stopped 9/3/14 because AST = 118, and ALT=73
- Re-challenged with Isoniazid, Rifampin, and Ethambutol 9/17/14 Pyrazinamide was dropped
- Organism was reported resistant to pyrazinamide on 10/2/14

Timeline on TB Drug Therapy Regimens

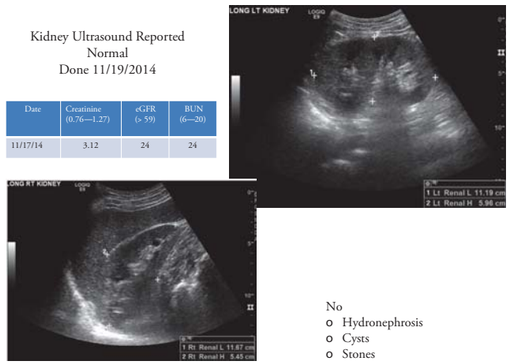


Trends in Laboratory Results: Renal Function and Liver Function (1)

	Renal Function			Liver Function			
Date	Creatinine (0.57—1.0)	eGFR (> 59)	BUN (6—20)	AST (0—40)	ALT (0—32)	Bilirubin, Total (0.0—1.2)	
August 18	0.64	111	15	41	28	0.4	← Baseline
29	0.65	123	12	101	73	0.3	← Initiated Tx
September 3	0.54	133	12	118	70	0.3	← Stopped Tx
8	0.5	137	9	68	69	0.3	
11	0.5	137	12	53	53	0.3	
17	0.64	124	14	46	35	0.4	← Re-challenge with IRE No PZA
19	0.54	133	11	44	32	0.6	
October 2	0.51	136	9	56	38	0.3	
November 10	2.45	32	22	26	10	0.2	← M.*tb* resistant to PZA
12	2.92	26	24	23	10	0.2	← Stopped IRE

Kidney Ultrasound Reported Normal
Done 11/19/2014

Date	Creatinine (0.76—1.27)	eGFR (> 59)	BUN (6—20)
11/17/14	3.12	24	24



No
- Hydronephrosis
- Cysts
- Stones

Developing Acute Kidney Injury (2)

- Creatinine and eGFR dramatically increased on 11/10/15
- Medications were stopped
- AKI attributed to rifampin
- Nephrologist was consulted 11/18/14, steroids not recommended
- Consulted Heartland National TB Center, San Antonio TX, on treatment regimen 11/25/14

Guidance from Blood Count, Hepatitis Screening, and Urinalysis

Blood Count	AKI (11/13/14)
WBC (3.4—10.8/uL)	5.8
Hemoglobin (12.6—17.7 g/dL)	10.3
Neutrophils (%)	68
Lymphocytes (%)	11
Monocytes (%)	13
Eosinophils (%)	7
Basophils (%)	1
Neutrophils (Absolute) (1.4—7.0/uL)	3.9
Lymphocytes (Absolute) (0.7—3.1 /uL)	0.7
Monocytes (Absolute) (0.1—0.9/uL)	0.7
Eosinophils (Absolute) (0.0—0.2/uL)	0.4
Basophils (Absolute) (0.0—0.2/ uL)	0.1

Urinalysis 11/13/14	
Specific Gravity	5.5
Protein	1+
Glucose	1+
WBC	0-5
RBC	0-2
Eosinophil	Negative
Creatinine	97.6

Hepatitis Panel 9/3/14	Results
Hep A, Ab, IgM	Negative
HBsAg Screen	Negative
Hep C Virus Ab	Negative

Trends in Laboratory Results: Renal Function and Liver Function (2)

	Renal Function			Liver Function			
Date	Creatinine (0.76—1.27)	eGFR (> 59)	BUN (6—20)	AST (0—40)	ALT (0—32)	Bilirubin, Total (0.0—1.2)	
December 2	1.66	52	19	29	20	0.2	← Re-challenge INH, EMB Moxifloxacin
8	1.61	53	15	40	21	0.3	
March 20	1.10	85	15	30	23	0.3	
27	1.09	86	13	31	19	0.3	
April 3	1.04	91	13	38	24	0.3	
10	1.03	92	17	32	24	0.4	
24	0.96	100	12	38	23	0.3	

Update May 13, 2015

- Pleasant, good rapport with clinic nurse
- History of falling out of bed in a dream 2 weeks ago; injured left elbow, swollen not tender. Watching for moxifloxacin adverse effects

Discussion

- A 38-year old male developed AKI attributed to rifampin
- He had received 50 doses of rifampin before AKI manifestations
- A baseline complete metabolic panel (CMP) was essential in recognizing AKI; covers both liver and renal function
- A CMP test costs us $3.90. Should this be routine, irrespective of risk factors indication?
- Alcohol most likely contributed to abnormal AST and ALT the day he initiated treatment Fortunately he has abstained from drinking and smoking after counseling
- This is a case of pulmonary tuberculosis due to *Mycobacterium bovis*. Patient admitted to drinking unpasteurized milk while in Mexico. There are 7 cases with genotype GO3500 in TB GIMS (CDC) database since 2005; California (4), Arizona (1), Texas (1), and Arkansas (1)

Conclusions

- Rifampin-induced renal toxicity is a rare but serious adverse effect among patients on anti-tuberculosis treatment
- Our patient has recovered his renal function upon discontinuation of the offending agent, rifampin, without using corticosteroids
- More reports are needed