Drug induced acute interstitial nephritis

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INTRODUCTION

- Acute interstitial nephritis (AIN) causes decline in renal function and usually characterized by an inflammatory cell infiltrate in the interstitium of the kidney.
- It is usually caused by infections, medications (PPI, NSAIDs, antibiotics etc), autoimmune or neoplastic disorders.
- AIN causes nonspecific signs and symptoms of acute renal failure such as nausea, vomiting and malaise. However, about 10% of patients can present with classic triad of rash, fever, and eosinophilia.
- Patient may be oliguric or nonoliguric and hematuria can be seen in about 5% of patients.
- AIN can be found in about 15% of patients hospitalized for acute renal failure.
- In patients with biopsy proven AIN, the recommended treatment is removal of the offending agent and glucocorticoid therapy.
- Withdrawing the offending medications early (within two weeks of onset of AIN) can help recovery to normal/near-normal renal function than patients who remain on the precipitating medication for longer period of time and should be done immediately if concerned about AIN.
- The studies has showed that up to 40% of patient have achieved partial renal recovery.

BRIEF SUMMARY OF CASE

- We present the case of a young male with acute interstitial nephritis secondary to omeprazole with biopsy proven AIN.
- The patient presented with extremely elevated BUN and creatinine which required hemodialysis.
- AIN thought to be secondary to omeprazole and/or amoxicillin, less likely azithromycin.
- Since there was no evidence of chronic changes (scarring), the patient was discharge with nephrology follow up outpatient with an anticipation of renal recovery.

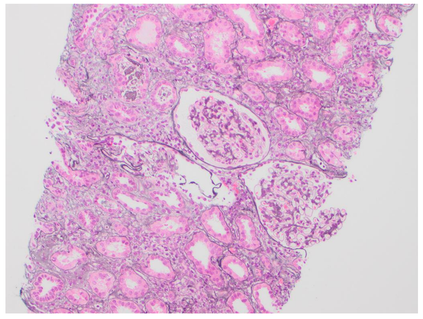
LEARNING OBJECTIVE

- Early diagnosis of acute interstitial nephritis and removing the precipitating medications can prevent progression to chronic kidney disease or end stage renal disease.
- Even if there is no evidence of chronic changes or scarring on biopsy, the renal function may not fully recover.

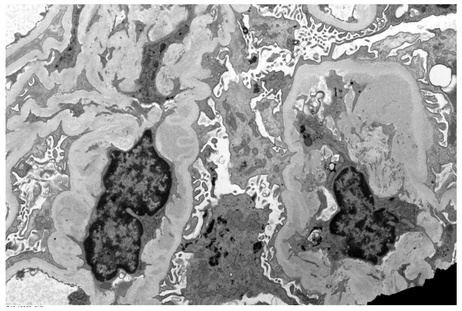
CLINICAL COURSE

- This patient is an 26 year old male with past medical history of significant for GERD on omeprazole presented with nausea, vomiting, abdominal pain, worsening fatigue and found to have renal failure. Patient was seen in the urgent care about 2 months ago for cough and sinus issues and was prescribed azithromycin. He went back to urgent care about a month later with nausea, vomiting, abdominal pain and diarrhea for 2 weeks. He also had epistaxis and sore throat for few days. He was diagnosed with possible gastroenteritis and esophagitis secondary to vomiting and was started on omeprazole. He went to urgent care after a week and half for change of taste in his mouth and was started on amoxicillin-clavulanic acid for sinusitis. The diarrhea resolved but patient continued to have nausea, vomiting and abdominal pain.
- He presented to the emergency department with nausea, vomiting, abdominal pain and worsening fatigue to the point where he has difficulty keeping up with his job. The laboratory work up showed BUN 260.6, creatinine 39.3, anion gap 43 and bicarbonate 6.3. He had normal renal function about 2 months prior to presentation. The patient was alert and oriented x4. CT of abdomen and pelvis did not show acute process. Upon questioning further, patient admit that he has subtle decrease in urine output and more frequent epistaxis. Patient was started on bicarbonate drip and transferred to our facility for higher level of care.
- The urinalysis showed leukocytes (100/uL), proteinuria (100/uL), glycosuria (100/uL), ketones, blood (150/uL), but nitrite negative with rare bacteria. The urine did not show casts and also negative for eosinophils. Urine osmolarity came back at 400. The FeNA was 1.4% which was consistent with intrinsic etiology. The lipase came back elevated which was thought to be due to severe renal failure. The renal ultrasound did not show any abnormalities. During hospitalization, he had adequate urine output. His labs improved minimally and patient was started on hemodialysis. There was suspicion for post-infectious glomerulonephritis, but Anti-streptomycin tiger (ASO) came back high normal (200 IU/mL). The hepatitis panel and HIV came back negative. All the serologies were normal. The renal biopsy (see images below) showed severe AIN thought to be secondary to omeprazole and/or amoxicillin, less likely azithromycin. No chronic changes or scarring was seen on biopsy. On the biopsy, there were findings suggestive of resolving post strep infectious glomerulonephritis. He was started on IV steroids and then transitioned to oral. The hemodialysis catheter was removed on the day of discharge as he showed some signs of renal recovery (improving creatinine) without dialysis for about a week. The patient was discharged with oral steroids and nephrology follow up with an anticipation at least partial renal recovery.
- The patient continued to follow with nephrology outpatient. His renal function continued to improve but did not gain full renal recovery even after a year. He has chronic kidney disease, stage 3, GFR 30-40s.

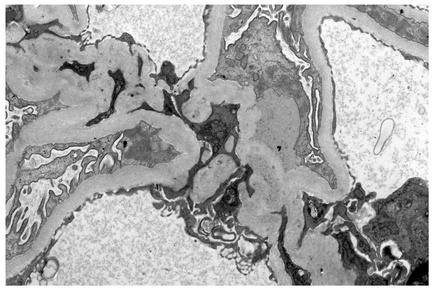
Renal biopsy microscopy



Renal cortex containing three glomeruli showing interstitial nephritis. One glomerulus is compressed artefactually, but none shows evidence of hypercellularity or sclerosis. Tubules are separated by an infiltrate of mononuclear inflammatory cells. Two tubules contain cellular debris. Jones stain, 100x



Electron micrograph showing adjacent glomerular capillaries, each enclosed by layers of basement membrane and endothelial cells. Both contain abundant mesangial/subendothelial electron-dense deposits. Print magnification: 7730x



Electron micrograph of a glomerulus showing segments of basement membrane with generally intact foot processes. A relatively large hump-like subepithelial deposit (center-right) is capped by a visceral epithelial cell. Less well-defined electron-dense deposit occupies the mesangium on the opposite side of the basement membrane. Print magnification: 11,400x.

DISCUSSION

This case demonstrates a very serious side effect of a commonly used medication in an otherwise healthy young patient.

Was the patient at an increased risk of drug induced AIN in the setting of resolving post-infectious glomerulonephritis and second exposure of omeprazole?

Renal biopsy is gold standard for diagnosis but is not necessary to make a definitive biopsy. Patient's suspected of having AIN should be considered for biopsy when

- Patients who have a characteristic urinalysis for AIN but are not being treated with a drug known to cause AIN.
- Patients who are being treated with a drug known to cause AIN but do not have a characteristic urinalysis.
- Patients who are being considered for treatment with glucocorticoids for AIN (usually drug induced). Among selected patients who decide night to undergo biopsy, glucocorticoids may be initiated in the absence of a biopsy. However, among such patients who do not improve after 5-7 days of steroid treatment, most should have a biopsy in order to exclude other diagnoses or the presence of severe interstitial fibrosis.
- Patients who present with advanced renal failure, providing the onset of renal failure is known to be relatively recent (ie, within three months).
- Patients with any features (such as high-grade proteinuria) that cause the diagnosis of AIN to be uncertain.

Clinical indicators of a decreased likelihood of recovery include prolonged kidney failure (greater than three weeks), AIN associated with nonsteroidal antiinflammatory drug (NSAID) use, and certain histologic findings (including interstitial granulomas, interstitial fibrosis, and tubular atrophy) on kidney biopsy.

CONCLUSION

Onset of drug induced AIN following drug exposure may range from 3-5 days (especially with second exposure of an offending agent) to many months. PPI and NSAIDS are less commonly associated with the classic triad of AIN compared to other medications.

There is ongoing research regarding association between PPI and AIN and increased risk of chronic kidney disease and progression to end stage renal disease.

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* Special thanks to Dr. Donald Houghton, pathologist at OHSU, for providing renal biopsy pathology images and description