



Brigham and Women's Hospital

Founding Member, Mass General Brigham

CHALLENGING CASE DISCUSSION: ALTERED MENTAL STATUS IN ESKD

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Disclosures

- Nothing to disclose

Learning Objectives

At the end of this presentation, learners will be able to:

- Identify causes of altered mental status in the setting of reduced kidney function
- Use appropriate tools for dosing medications in the setting of reduced kidney function

Case 1

A 27-year-old woman with ESKD since childhood and who has a longstanding history of depression refractory to usual medications is admitted to a psychiatric hospital for an acute exacerbation. She undergoes ECT and is trialed on a number of medications.

Past Medical History

- ESKD secondary to reflux nephropathy
 - Kidney transplant at age 18
 - Started back on dialysis at age 25
- Hypertension
- Secondary hyperparathyroidism

Case 1

Hospital Course

After about two months in the hospital, the renal fellow receives a call that the patient is to be discharged that day and will need outpatient hemodialysis the following day.

Medications upon discharge:

- Amlodipine 10 mg daily
- Calcitriol 0.5 ug daily
- Sertraline 100 mg daily
- Lorazepam 0.5 mg daily PRN anxiety
- EPO 5000 units three times weekly
- Amantadine 200 mg daily

Audience Feedback: Any concerns with her discharge regimen?

Case 1

Post-Hospital Course

The renal fellow calls the patient's outpatient nephrologist to let him know that the patient has been discharged on an inappropriate dose of amantadine. He replies, "I'll take care of it."

One week later the patient presents to the hospital with altered mental status and a movement disorder, best characterized as choreoathetosis.

Amantadine Dosing in CKD/ESKD

Altered kidney function: Oral:

Immediate release (Ref):

Note: Renally adjusted dose recommendations are based on a usual recommended dose of 100 mg twice daily.

CrCl >50 mL/minute: No dosage adjustment necessary.

CrCl 30 to 50 mL/minute: 200 mg on day 1, then 100 mg/day.

CrCl 15 to <30 mL/minute: 200 mg on day 1, then 100 mg every other day.

CrCl <15 mL/minute: 200 mg once every 7 days.

Emergent dialysis for amantadine neurotoxicity?

Hemodialysis, intermittent (thrice weekly): Oral: Not dialyzable (<5% of the dose removed by a 4-hour hemodialysis session) ([Ref](#)):

Extended release: Use is contraindicated.

Immediate release: Dose for CrCl <15 mL/minute.

Amantadine level



WE MEASURED HER AMANTADINE
LEVEL (SEND-OUT TEST).



HER LEVEL WAS 10000X
THERAPEUTIC.

Case 2

SS is a 45-year-old white man with a history of diabetes mellitus type 2 complicated by diabetic neuropathy. He was admitted to University Hospital with osteomyelitis of his left fifth toe. Creatinine on admission was 1.1 mg/dL. He underwent debridement and was placed on IV antibiotics. Cultures from the wound grew α -hemolytic streptococci, Group B streptococci, and coag-positive staph. He was discharged to home on the following medications:

Case 2- continued Discharge medications

- Vancomycin 1.75 g IV q 12 hours
 - Pentoxifylline 400 mg po tid
 - Gabapentin 1200 mg po tid
 - Metoclopramide 10 mg po qac and qhs
 - Omeprazole 20 mg po bid
 - Metformin 500 mg po bid
 - Methadone 40 mg po tid
- 70/30 Insulin
 - Atorvastatin 10 mg po q day
 - Amitriptyline 75 mg po q day
 - Fludrocortisone 0.8 mg po q day
 - Clonazepam 0.5 mg po qhs
 - Ticarcillin/clavulanate 12.4 g q day
 - Multivitamin

Case 2- continued

Patient was scheduled to receive four weeks of IV antibiotics. Three weeks into his treatment, the patient was noted to have a creatinine of 3 mg/dL. The next day, his creatinine was 5 mg/dL, and he was admitted to the hospital. At the time of admission, he was febrile to 101 degrees F. Physical examination was unremarkable. Laboratory studies on hospital day two were notable for BUN 59 mg/dL, creatinine 6.4 mg/dL, and K⁺ 5.8 mEq/L. Urine stain for eosinophils was 3+ positive. Because of hyperkalemia and oliguria, he required dialysis.

Questions-Case 2

Which of the following is the most likely explanation for this patient's acute renal failure?

- Post-infectious glomerulonephritis
- Acute interstitial nephritis
- Diabetic nephropathy
- RPGN

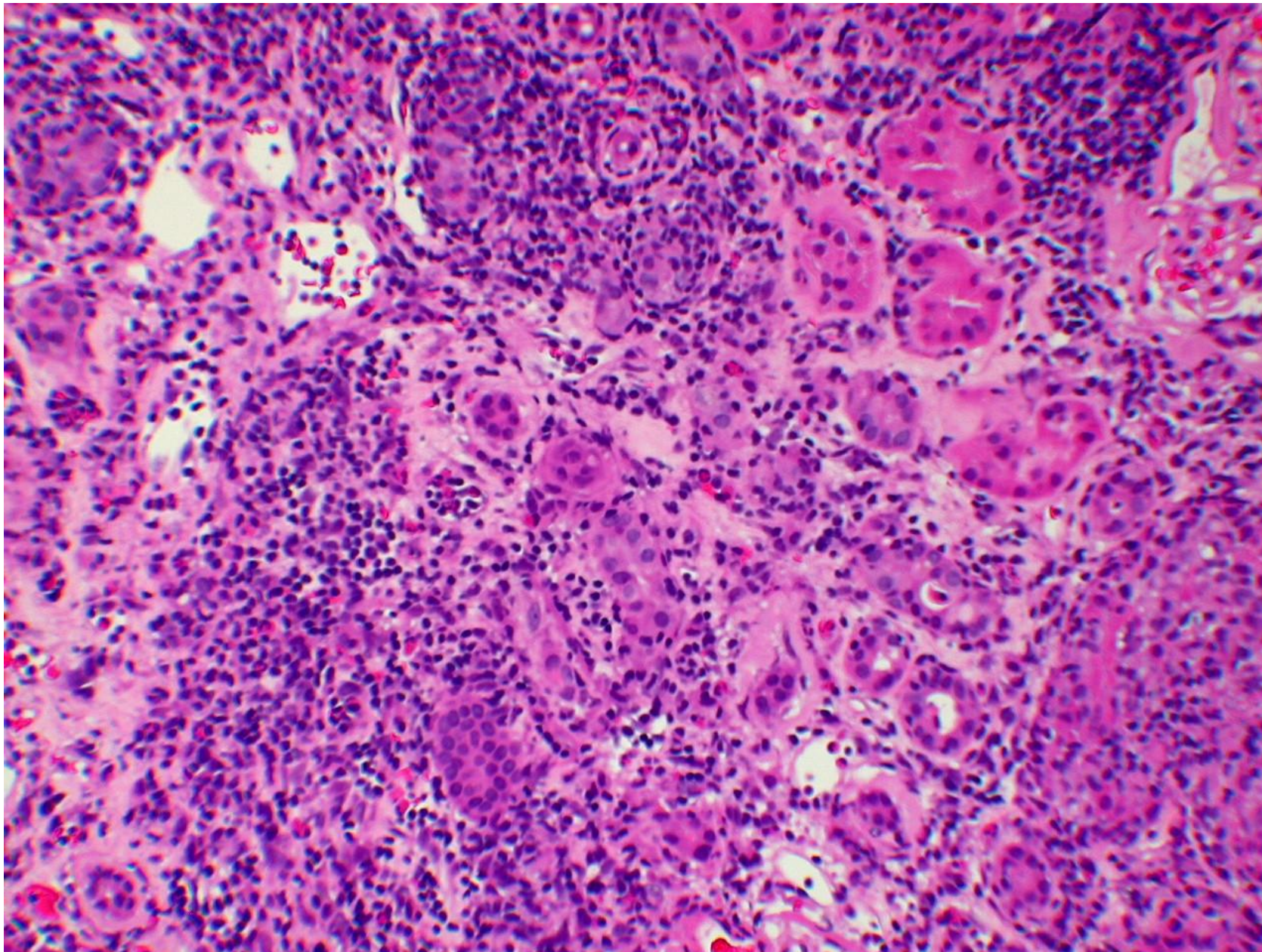
Questions-Case 2

Which of the following is the most likely explanation for this patient's acute renal failure?

- Post-infectious glomerulonephritis
- **Acute interstitial nephritis**
- Diabetic nephropathy
- RPGN

Explanation

Post-infectious GN and RPGN should both be considered in the differential diagnosis of this patient with a rapidly rising creatinine. The former might be associated with hypocomplementia, and both would be associated with glomerular hematuria. Diabetic nephropathy would not be expected to progress this rapidly. However, the development of acute renal failure associated with eosinophiluria in this patient recently treated with a penicillin makes acute interstitial nephritis the most likely diagnosis.



Courtesy of William J. Cook, M.D., Ph.D., UAB Department of Pathology

Hospital Course

- The patient's antibiotics are changed from ticarcillin/clavulanate to vancomycin and cefepime. He is started on intermittent hemodialysis and is given corticosteroids to treat the interstitial nephritis.
- Four days later, the patient is confused and delirious.
- The July intern says that the patient must be experiencing dialysis disequilibrium.

Audience Feedback: Any thoughts on this patient's new delirium?

Cefepime neurotoxicity

Risk factors:

- $\text{GFR} < 60 \text{ mL/min/1.73m}^2$
 - Sepsis
 - Prior CNS infection
 - Older age
-
- May occur even with appropriate dosing

Dialytic clearance of cefepime

Hemodialysis, intermittent (thrice weekly): Note: Achievement of cefepime pharmacodynamic targets is dependent on organism MIC, the absence or presence of residual kidney function, and interval between dialysis sessions (ie, 2- or 3-day interdialytic interval) ([Ref](#)). Factors such as severity of illness, location of infection, and patient weight should be considered when selecting between the higher and lower dosing regimens as well.

IV: Dialyzable (70% to 85% reduction in serum concentration from a 3.5- to 4-hour hemodialysis treatment with high flux filters ([Ref](#))).

Daily dosing (administer after hemodialysis on dialysis days): IV: Initial: 1 g (single dose) on day 1. Maintenance: 500 mg to 1 g every 24 hours ([Ref](#)). **Note:** If the usual recommended dose for normal renal function is 2 g every 8 hours or 1 g every 6 hours, utilize 1 g every 24 hours; use 500 mg every 24 hours for all other doses ([Ref](#)).

Case 3

A 44-year-old woman with ESKD is admitted to the hospital with pain in her right foot. She has wet gangrene of her right third toe and MRI shows underlying osteomyelitis. She is started on IV antibiotics. Surgery is consulted and plans to perform a toe amputation.

Past Medical History

- ESKD
- Hypertension
- Peripheral arterial disease
- Opioid use disorder

Case 3: Hospital course

The patient is given oral hydromorphone for pain control. While the pain in her foot is controlled, she develops back pain with spasms and requests increased dose of analgesics.

The hospitalist team is reluctant to give more opioids given her history of opioid use disorder and instead offers her a muscle relaxant.

Case 3: Hospital course: Escalation

Over the next two days, the patient becomes increasingly somnolent with periods of agitation and delirium.

The primary team accuses her of having family or friends bring in opioids from outside the hospital.

Security is called, and her room is searched with no opioids founds.

Audience Feedback: Any thoughts on why this patient has developed an altered mental status?



Baclofen in dialysis patients: Just say no!

July 16, 2014

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At our hospital, we started noticing a pattern of admissions among some of our maintenance dialysis patients. In one case, an elderly woman with DM, peripheral arterial disease, and ESRD on thrice weekly hemodialysis was sent to the emergency department from her nursing facility for altered mental status. She was normal three days prior to admission, but when her nurse found her confused and difficult to arouse, they sent her to our ED. We got consulted to continue maintenance dialysis, but we noticed that she had a fluent aphasia and marked perseveration. The rest of her exam and workup was

unremarkable. I immediately called the nursing facility and had them fax over her medication administration record. Lo and behold, three days prior she was started on baclofen 5mg three times daily for complaints of lower extremity leg pain (which was probably her claudication anyway). We diagnosed her with acute baclofen neurotoxicity.

Case 4

A 62-year-old man with ESKD secondary to scleroderma is admitted to the hospital with shortness of breath.

Past Medical History

- ESRD
- Scleroderma
- COPD
- Peripheral arterial disease
- Recurrent pleural effusion
- Malnutrition

Case 4

Hospital Course

- Diagnosed with pulmonary emboli → started on IV heparin
- Pneumonia treated with cefepime
- Ileus
- GI bleeding
- Sacral wound



Dermatology Consult

Dermatology Recommendations

- “Please start patient on IV acyclovir for HSV infection. Recommend touching base with pharmacy for appropriate dosing in HD patient”
- “Can transition to valacyclovir at discharge. Treatment duration will be until lesions heal”
- Patient started on acyclovir 5 mg/kg q 24 hours

Altered Mental Status

- Four days later patient develops altered mental status
- Sent for stat head CT
- Upon return from head CT, patient is anxious and confused and says, "I died down there."

Case 4 Question (Audience Response)

What is the most likely explanation for the patient's altered mental status?

- A) Inadequate dialysis
- B) Cefepime
- C) Acyclovir

Case 4 Question (Audience Response)

What is the most likely explanation for the patient's altered mental status?

- A) Inadequate dialysis
- B) Cefepime
- C) **Acyclovir**

Altered mental status in a dialysis patient

Always think about medications

- Acyclovir
- Cefepime
- Narcotics
- Gabapentin
- Amantadine
- Baclofen

Acyclovir neurotoxicity

DIAGNOSTIC DILEMMA

Aimee K. Zaas, MD

Thomas J. Marrie, MD, Section Editors



Death Delusions and Myoclonus: Acyclovir Toxicity

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Clinical features of acyclovir neurotoxicity

- Disturbances in consciousness
- Seizures
- Myoclonus
- Coma
- Death delusions
 - “Le delire de negation” or Cotard’s syndrome
 - A more specific neuropsychiatric symptom

Diagnosis and Management

- Diagnosis may be confirmed by measurement of metabolite 9-carboxymethoxymethylguanine
- Discontinuation of drug
- Hemodialysis

Take home messages

- When prescribing medications, particularly those not commonly used, to an ESKD patient, check the recommended dosing from a reputable source.
- Altered mental status in patients with ESKD is often due to a medication.
- Carefully review the medication list for medications that are contraindicated or require dose modification.