Case presentation

74 yo white male referred to VA from OSH for further management of back pain and compression fractures on 5/28/2015
HPI

- Started developing lower back pain about a month prior
- Evaluated at OSH by Neurosurgery, imaging notable for mild compression fracture T11-L1
- Treated with brace and opioid analgesics
- Also took Ibuprofen 400 mg q6 x 2 weeks
- Presented to PMD for worsening back pain
- Also with poor po intake due to inability to access water
- Referred to MVA for further Mx
HPI

At MVA, found with Cr of 1.6 (baseline 0.8), hence we were consulted
ROS

- Constitutional: *fatigue, weakness*, no weight loss, night sweats
- HEENT: No sore throat, URI
- Respiratory: *no shortness of breath, no cough*
- Cardiac: Negative for chest pain, orthopnea and palpitations
- GI: Negative for abdominal pain, change in bowel habits, nausea, vomiting +
- GU: Negative for dysuria, frequency, hematuria, frothy urine
- MSK: *severe back pain*
- Neurological: *no focal weakness*
History

PMH: HTN, HPL, BPH

PSH: Testicular cyst removal, Hernia repair

SH: several drinks per day, non smoker, no illicits

FH: Father with h/o renal Ca and sister with leukemia
Meds:

– Allopurinol 300 mg po d
– Tylenol-codeine 325/5 mg prn q 6
– Dexam 40 mg IB
– Heparin 5000 units Q8 SQ

NKDA
Physical Exam

- Vitals: afeb, BP 120/60, HR 60-90, RR 16, O2 sat 98% RA
  - Gen: thin man, mod discomfort, unable to move, mildly anxious, anox 3
  - HEENT: moist mm, no lymph nodes
  - Pulm: CTABL
  - CV: S1S2+, reg, no m/r/g
  - Abd: soft, non tender, non distended, BS+
  - Ext: no edema, wwp
  - Back: unable to move
  - Neuro: No focal deficits
Labs

**CBC**
- 6.6
- 38.1
- 12.7
- 205

**BMP**
- Ca\(^+\): 10.1
- Phos: 14.1
- Uric Acid: 12
- PTH: 19.2
- LDH 110

**Urine test**
- Urine UN: 694
- Urine Cr: 96
- Urine Na: 82
- Urine Osm: 480
- Urine protein: 1.6

**UA:** Clear
- Sp gravity – 1.013
- pH – 6
- Blood - Neg
- Portein – Neg
- LE / Nit - Neg

**Others**
- 129
- 98
- 27
- 5.1
- 28
- 1.6
- 83
Imaging

- Renal US: normal
- CXR: no acute cardio-pulmonary process
Differentials

- Pre-renal AKI from volume depletion
- AKI from hypercalcemia
- Cast nephropathy from multiple myeloma
- ? TLS
Additional Labs

UPEP: no monoclonal band
SIFE: monoclonal IgG K, alb 2.6, TP 12.5
IgG 9085, A 38, M < 21
β2 macroglobulin 5.2
FLC: K/L: 28.6/5.76, ratio 4.97
Hep B, Hep C – Neg
HIV – Neg
Hospital Course

- Treated with IV fluids, allopurinol

- Volume status improved, Cr down to 1.1, phos elevated, deproteinized sample 3.2

- Bone marrow biopsy c/w multiple myeloma (Monoclonal IgG k plasma cell, 11% in total)

- Chemotherapy started: VCD regimen (V 1.5 mg/m² (d1, 8), C 500 mg/m² (d1, 8, 15), D 40 mg)
Cast Nephropathy
Outline

- Multiple myeloma
- Formation of myeloma cells
- Different renal lesions
- Mechanisms for renal lesions: Ig dependent and independent
- Diagnosis
- Treatment
- Pseudohyperphosphatemia
Epidemiology of multiple myeloma

- Neoplastic plasma-cell disorder characterized by clonal proliferation of malignant plasma cells in the bone marrow microenvironment, monoclonal protein in the blood or urine, and associated organ dysfunction

- Accounts for ~ 1% of neoplastic diseases and 13% of hematologic cancers

- In Western countries, annual age-adjusted incidence is 5.6 cases per 100,000 persons

- The median age at diagnosis ~ 70 years
  - 37% pts < 65 years
  - 26% between 65 and 74 years
  - 37% > 75 years

Palumbo et al NEJM 2011
# Pathogenesis

<table>
<thead>
<tr>
<th>Multistep progressive disease</th>
<th>MGUS</th>
<th>Intramedullary multiple myeloma</th>
<th>Extramedullary multiple myeloma</th>
<th>Plasma-cell leukemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytogenetic abnormalities</td>
<td>Hyperdiploidy (50% of patients)</td>
<td>Secondary translocations</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Non-hyperdiploidy (50% of patients)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other molecular alterations</td>
<td>Increased expression of cyclin D1, D2, and D3</td>
<td>Oncogenic activation or mutation (RAS, FGFR3)</td>
<td>MYC dysregulation, TP53 mutation</td>
<td></td>
</tr>
</tbody>
</table>

Bone marrow microenvironment

Angiogenesis

Bone resorption
Interaction between plasma cells and MM

Figure 2. Interaction between Plasma Cells and Bone Marrow in Multiple Myeloma.
Renal Involvement

- The kidney is a major target organ in MM

- Up to 40% pts develop kidney impairment and 10% - 15% will require dialysis

- Incidence is highest in patients with advanced stage disease

- In a study of 1353 cases of newly diagnosed pts, renal failure present in 31% pts (Cr > 1.4 mg/dl), 49% by Cr clearance

Leung et al. Adv in CKD 2014
Renal Involvement

- Kidney impairment has a significant effect on the overall survival (OS) of patients.

- A study from Spain found that patients with AKI (Cr > 2 mg/dl) had a median OS of 8.6 months vs pts without AKI of 34.5 months (P 0.001)

- Median OS increased to 28.3 months in patients who recovered their kidney function (Cr < 1.5 gm/dl) vs 3.8 months in those who had irreversible kidney failure

- Similar results from the Nordic Myeloma SG, pts with normal Cr had a median OS of 36 months vs 18 months in pts with mod. kidney injury (SCr 1.48 mg/dL - < 2.27 mg/dL) and 13 months for those with severe kidney injury (SCr > 2.27 mg/dL)

Blade et al. JAMA 1998*
Causes of renal failure in multiple myeloma

- Ig dependent mechanisms
- Ig independent mechanisms

Heher et al CJASN 2013
Ig dependent mechanisms

- Cast nephropathy
- MIDD
- AL Amyloidosis
- Fanconi-like syndrome
- GN
- Tubulointerstitial nephritis
- Minimal change disease
- Membranous glomerulopathy
- Henoch–Scholein purpura/IgA nephropathy
- Immunotactoid glomerulopathy
- Intracapillary monoclonal deposits of IgM thrombi
- TMA
- Hyperviscosity syndrome

Heher et al CJASN 2013
Ig dependent mechanisms

- Volume depletion
- Sepsis
- Hypercalcemia
- TLS
- Medication toxicity
- Direct parenchymal invasion by plasma cells
- Pyelonephritis

Heher et al CJASN 2013
One disease: different patterns of renal injury

- Governed by structural peculiarities of monoclonal FLCs, esp of variable (V) domain
- Influenced by environmental factors viz pH, urea concentration or local tissue proteolysis
- Intrinsic host factors likely to have an imp role in determining both the type and severity of any renal response to a given FLC.

Heher et al CJASN 2013
Hutchison et al Nature Rev 2012
Lueng et al. Adv in CKD 2014
Peculiarities of the V domain seen in many types of renal disease induced by light chains

Myeloma-associated Fanconi syndrome
- PTC dysfunction 2/2 to FLC reabsorption and crystallization within the lysosomal compartment of PTCs
- FLCs nearly always of the Vκ1 subgroup, they display unique sequence peculiarities CDRs; replacement of polar residues by hydrophobic residues in the CDR can induce resistance of the Vκ domain to proteolysis and result in light chain crystallization
- Also proven in mouse model
One disease: different patterns of renal injury

MIDD:
- Results from sometimes fragmented or abnormally large light chains, generally of the k-type subtype 1, 3, or 4, which as a result of atypical glycosylation or amino acid patterns misfold, become insoluble and precipitate
- Vκ4 subgroup overexpressed
- FLCs have cationic isoelectric points, granular deposits from binding of cationic polypeptides to anionic BMs

Amyloid:
- Commonly a/w l-light chains, Vλ6 overexpressed
- LCs undergo endocytosis at the glomerulus and are delivered to lysosomes
- Isoelectric point of FLCs in AL amyloidosis is heterogeneous, amyloid b-pleated sheet forms as a result of electrostatic interactions between heparan sulfate proteoglycan, serum amyloid P, and permissive amino acids
One light chain renal disease per patient

Observations regd. light chain characteristics and clinical experience: only one type of renal disease is clinically manifest in the majority of patients.

In practice, pathologic findings of more than one type of disease are not uncommon.

In a series of 190 patients with multiple myeloma who underwent kidney biopsy, 12 patients had 2 distinct paraprotein-associated lesions.

One patient has been described to have developed cast nephropathy, AL amyloidosis and light chain deposition disease in the same kidney.

Cast nephropathy (Myeloma kidney)

- Most common renal lesion

- Autopsy studies found MCN in 32% to 48% of patients who died with a diagnosis of MM

- In a study of 34 patients with severe AKI, MCN was present in 86.6% of the 30 patients who had kidney histology

- Most cases occur in patients with a serum FLC > 100 mg/dL and high urine FLCs
Pathogenesis of FLCs

~ 500 mg of polyclonal FLCs produced daily by the normal lymphoid system and catabolized by the proximal tubule

Only about 1–10 mg of polyclonal FLCs normally excreted

FLC overproduction, hundreds of fold higher than normal in plasma cell dyscrasias

Overwhelms resorptive capacity of PTC, FLCs that appear in the urine are termed Bence Jones proteins

Mechanisms of injury

- Intratubular cast formation
- Direct tubular toxicity

Triggers for cast formation:
- Volume depletion, hyperCa, radio contrast media, NSAIDs

Lueng et al. Adv in CKD 2014
Pathogenesis of FLCs

- Light chains and THPs produce casts
- 5-10 mg/day FLCs in urine
- Potential triggers for cast formation:
  - Dehydration
  - Furosemide
  - Contrast agents
  - Infective agents

- 9 amino acid binding region of THP interacts with CDR3 domain of FLC

- Transcription of IL-6, IL-8, CCL2, TGF-β1
- NFκB + MAPK
- Redox pathways

- Progressive renal fibrosis
- Epithelial-mesenchymal transition

- Atrophy of tubule proximal to cast
- Leakage
- Inflammation
- Peritubular inflammatory cell infiltrate (lymphocytes, plasma cells and eosinophils) and migration into lumen

- Eventual interstitial fibrosis
Ig detection: SPEP

- Poor sensitivity for FLC
- Cannot always distinguish polyclonal from monoclonal light chain expansion
Ig detection: Immunofixation

- Greater sensitivity SPE, but is a qualitative test
- Limited usefulness in the monitoring of myeloma progression and Rx response
Ig detection: Free Light Chains

- Polyclonal Abs to k and \( \lambda \) can detect monomers and dimers of k and l at conc, 2–4 mg/L
- Increased diagnostic sensitivity: MIDD, amyloid, or nonsecretory myeloma, have abnormal serum k to l ratios
- Assess response to Rx and detect early relapse
- FLCs present in extremely high concentrations, the assay may result in paradoxically normal results, as the detecting Abs become saturated by the abnormal light chains
Biopsy
Management

- Elimination of the precipitating agents
  - correction of hypercalcemia and dehydration
  - increase of urine flow

Rapid reduction of serum FLC levels by
  - Chemotherapy
  - Extracorporeal removal

Lueng et al. Adv in CKD 2014
Removal of FLCs

- Two separate studies found a 50% reduction of serum FLC is the minimum required for kidney recovery.

- Timing is also essential because the kidney recovery rate decreased the longer it takes to achieve a 60% reduction in serum FLC levels.

- Kidney recovery decreases drastically after 21 days.

- HCO-Dialysis/Plasmapheresis/Chemo
**Background:** To assess the combination of chemotherapy and HCO-HD on serum FLC concentration and renal recovery in patients with cast nephropathy and dialysis-dependent acute renal failure.

### Table 2. Summary of the demographics and presenting features of study population

<table>
<thead>
<tr>
<th>Feature</th>
<th>Study group (n = 19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>60 (38 to 81)</td>
</tr>
<tr>
<td>Male gender, %</td>
<td>74%</td>
</tr>
<tr>
<td>Presenting creatinine, µmol/L</td>
<td>714 (427 to 1508)</td>
</tr>
<tr>
<td>Presenting eGFR</td>
<td>7 (3 to 13)</td>
</tr>
<tr>
<td>Patients with κ FLCs, %</td>
<td>50%</td>
</tr>
<tr>
<td>Presenting serum FLC concentration, g/L</td>
<td>2.6 (0.8 to 69)</td>
</tr>
</tbody>
</table>

*Hutchison et al CJASN 2009*
Design

27 Patients with dialysis dependent acute renal failure and multiple myeloma

Renal biopsy contraindicated:
1 patient urinary obstruction
2 patients lows platelet counts

24 patients underwent renal biopsy

22 patients with cast nephropathy on biopsy

1 patient with low platelet count received HCO dialysis

19 patients with cast nephropathy received HCO dialysis

13 patients completed FLC removal HD period. All became independent of dialysis

1 patient became independent of dialysis

Other pathologies:
1 patient acute interstitial nephritis
1 patient acute tubular necrosis

3 patients not suitable for further study
1 patient was demented
2 patients palliated

6 patients had chemotherapy withheld

1 patient with low platelet count received HCO dialysis

19 patients with cast nephropathy received HCO dialysis

13 patients completed FLC removal HD period. All became independent of dialysis

1 patient became independent of dialysis

5 patients remained dialysis dependent
Results

Comparison of reductions in serum FLC concentrations at 5, 12, and 21 d. Results presented as patients who completed FLC removal HD with (clear boxes, n 6) and without (shaded boxes, n 13) a break in their chemo.

Kaplan-Meier survival analysis of patients treated with chemo and FLC removal HD. Early interruption of chemo (solid line, n 6) vs uninterrupted chemo (broken line, n 13); P < 0.001..

Renal recovery rates of pts who received chemo and FLC removal HD. 14/ 19 pts who received FLC removal HD became independent of dialysis at a median of 28 d.
Role of plasmapheresis

- The evidence evaluating the effectiveness of plasmapheresis in patients with AKI due to myeloma is conflicting.

- 3 RCTs have evaluated the effectiveness of plasma exchange (PLEX).
Role of plasmapheresis: RCTs

Zucchelli et al. Int. 1988
- Randomized 29 pts with Scr > 5 mg/dl to HD and PLEX vs PD.
- 11 patients from each group required dialysis
- Renal function improved in 13/15 treated with PLEX vs only 2/14 with PD
- Limitation: 5 pts in PD group died within the first 2 months

Johnson et al. Arch Intern Med. 1990
- 21 patients
- Gp 1: forced diuresis and chemo (n=10) vs Gp 2: forced diuresis, chemotherapy and PLEX (n=11)
- No differences in the overall renal recovery rate (control 50% vs PLEX 64%, P=NS)
- Subgroup analysis of the dialysis patients, renal recovery occurred only in those who received PLEX
Objective: To assess the effect of 5 to 7 plasma exchanges on a composite outcome in patients with ARF at the onset of multiple myeloma.


Participants: 104 patients between 18 - 81 yrs with ARF at the onset of myeloma.

Intervention: Randomly assigned to conventional therapy + 5 to 7 PLEX for 10 days or conventional therapy alone.

Primary outcome: composite measure of death, dialysis dependence, or GFR < 30 mL/min per 1.73 m2.
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Control Group (n = 39)</th>
<th>Plasma Exchange Group (n = 58)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD) age, y</td>
<td>61.3 (11.0)</td>
<td>65.2 (11.5)</td>
</tr>
<tr>
<td>Men, n (%)</td>
<td>28 (71.8)</td>
<td>37 (63.8)</td>
</tr>
<tr>
<td>Mean (SD) serum calcium level</td>
<td></td>
<td></td>
</tr>
<tr>
<td>mmol/L</td>
<td>2.26 (0.29)</td>
<td>2.22 (0.35)</td>
</tr>
<tr>
<td>mg/dL</td>
<td>9.06 (1.16)</td>
<td>8.90 (1.40)</td>
</tr>
<tr>
<td>Mean (SD) serum albumin level, g/L</td>
<td>32.2 (8.2)</td>
<td>29.8 (7.1)</td>
</tr>
<tr>
<td>Mean (SD) urine protein level, g/L</td>
<td>7.25 (13.08)</td>
<td>4.70 (7.05)</td>
</tr>
<tr>
<td>Mean (SD) serum creatinine level†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>μmol/L</td>
<td>460.4 (187.6)</td>
<td>422.5 (213.6)</td>
</tr>
<tr>
<td>mg/dL</td>
<td>5.21 (2.12)</td>
<td>4.78 (2.42)</td>
</tr>
<tr>
<td>Mean (SD) GFR‡</td>
<td></td>
<td></td>
</tr>
<tr>
<td>mL·s⁻¹·m⁻²</td>
<td>0.13 (0.06)</td>
<td>0.14 (0.07)</td>
</tr>
<tr>
<td>mL/min per 1.73 m²</td>
<td>13.32 (6.16)</td>
<td>14.84 (7.53)</td>
</tr>
<tr>
<td>Durie–Salmon myeloma stage III, n (%)</td>
<td>17 (43.6)</td>
<td>24 (41.4)</td>
</tr>
<tr>
<td>Monoclonal Bence–Jones protein, n (%)</td>
<td>39 (100.0)</td>
<td>58 (100.0)</td>
</tr>
<tr>
<td>κ type, n (%)</td>
<td>21 (53.8)</td>
<td>22 (37.9)</td>
</tr>
<tr>
<td>λ type, n (%)</td>
<td>14 (35.9)</td>
<td>22 (37.9)</td>
</tr>
</tbody>
</table>
Results

- Primary outcome occurred in 69.2% pts in control group vs 57.9% patients in PLEX (difference between groups, 11.3% [95% CI, -8.3% to 29.1%])

- Cumulative survival similar for 2 groups; 33.3% in control gp and 32.8% patients in PLEX died by 6 months

- Conclusion: no statistically significant nor clinically meaningful difference in outcomes, although the wide confidence interval of the difference did not exclude the possibility of benefit or harm.
Limitations

- Number of patients small (though largest study) and was at risk for beta error.

- Composite outcome disadvantaged PLEX because patients who died with improved renal function were considered failures.

- Renal pathology was not verified due to the low biopsy rate.

- No method was employed to assess the adequacy of treatment.
Retrospective study to investigate the effectiveness of PLEX in the treatment of CN, diagnosis confirmed by renal biopsy and Rx guided by sFLC levels

42 pts met the inclusion criteria

28 (70%) patients underwent renal biopsy without any serious complications.
Results

- CN was identified in 18 (64.3%) patients.
- 14/18 pts had sFLC measured before and after PLEX.
- Renal response occurred in 77.8% (7/9) whose sFLC was reduced by 50% or more.
- None of the five patients with <50% reduction in sFLC had a renal response.

Figure 4 | Patient survival based on renal response. Median survival for renal responders was 31.8 months vs 11.0 months in non-responders; $P = 0.03$.

Figure 3 | Renal response by reduction of sFLCs. Of the six patients with $> 50\%$ reduction in sFLC without renal response, 3 had LCDD, 1 had diabetic nephropathy with acute tubular necrosis, 1 had cast nephropathy precipitated by intravenous contrast, and 1 had cast nephropathy with atypical tubulointerstitial nephritis and fibrosis. Three patients had $< 50\%$ reduction in sFLC and renal response. One had AL amyloidosis, 1 had ATN, and 1 was not biopsied.
Chemotherapy

- The sustained reduction of serum FLC levels requires effective chemotherapy

- Choice of chemo depends on: newly diagnosed diseased or relapsed

- In chemotherapy naïve patients, agents not renally cleared or metabolized preferred
  - bortezomib and thalidomide

- In relapsed MM
  - Pomalidomide and carfilzomib recently approved for use.
  - Neither undergoes significant kidney metabolism or clearance, experience in kidney failure patients is scant.

- High-dose steroids may have benefits in addition to its antimyeloma activity
Pseudohyperphosphatemia in Multiple Myeloma

- Hyperphosphatemia is rare in patients with MM, unless renal failure is present, esp GFR < 30

- Pseudohyperphosph: due to serum paraprotein in MM patients without impairment of renal function

- Phosphomolybdate UV assay most commonly used for measurement of serum P

- Relies on formation of a UV-absorbing complex between phosphate and molybdate. Pi reacts with ammonium molybdate in the presence of sulphuric acid to form an ammonium phosphomolybdate complex, absorbance measured at 340 nm.
Pseudohyperphosphatemia

- Serum of a patient with MM has falsely elevated absorbance because paraproteins react with ammonium molybdate to make the serum cloudy.

- Measure after ultracentrifuge with cut off < 10/25 KD or after addition of SSA to deproteinize the sample.

<table>
<thead>
<tr>
<th>Author</th>
<th>Year Published</th>
<th>No. of Patients</th>
<th>RCT</th>
<th>Intervention</th>
<th>Definition of Renal Failure</th>
<th>Histology Reported</th>
<th>Renal Recovery Rate of Non-Dialysis Dependent</th>
<th>Renal Recovery Rate of Dialysis Dependent</th>
<th>Rate of Independence of Dialysis Where Histology Reported as PTE Related</th>
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<tbody>
<tr>
<td>Zacchelli (11)</td>
<td>1988</td>
<td>29</td>
<td>Yes</td>
<td>PLEX</td>
<td>SC &gt; 5 mg/dl</td>
<td>Partial</td>
<td>Control 0% (0 of 3)</td>
<td>Control 18% (2 of 11)</td>
<td>—</td>
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<tr>
<td>Johnson (12)</td>
<td>1990</td>
<td>21</td>
<td>Yes</td>
<td>PLEX</td>
<td>Progressive renal failure</td>
<td>Yes</td>
<td>Control 63% (5 of 8)</td>
<td>Control 0% (0 of 2)</td>
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<td>Rayner (13)</td>
<td>1991</td>
<td>11</td>
<td>No</td>
<td>—</td>
<td>Dialysis dependent</td>
<td>No</td>
<td>—</td>
<td>36% (4 of 11)</td>
<td>—</td>
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<td>Torra (6)</td>
<td>1995</td>
<td>30</td>
<td>No</td>
<td>—</td>
<td>Dialysis dependent</td>
<td>No</td>
<td>—</td>
<td>5% (1 of 30)</td>
<td>3% (1 of 30)</td>
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<td>Irish (14)</td>
<td>1997</td>
<td>56</td>
<td>No</td>
<td>Acute</td>
<td>—</td>
<td>—</td>
<td>15% (7 of 47)</td>
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<td>Blacké (7)</td>
<td>1998</td>
<td>94</td>
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<td>Chemotherapy</td>
<td>SC &gt; 2 mg/dl</td>
<td>No</td>
<td>26% (24 of 91)</td>
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<td>Montgomery (3)</td>
<td>1998</td>
<td>118</td>
<td>No</td>
<td>—</td>
<td>Histology</td>
<td>Yes</td>
<td>11% (6 of 52)</td>
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<td>11% (6 of 52)</td>
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<td>Magee (5)</td>
<td>1998</td>
<td>34</td>
<td>No</td>
<td>Acute</td>
<td>—</td>
<td>Partial</td>
<td>3% (1 of 28)</td>
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<td>Knudsen (8)</td>
<td>2000</td>
<td>225</td>
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<td>—</td>
<td>SC &gt; 2.3 mg/dl</td>
<td>No</td>
<td>58% (130 of 225)</td>
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<td>Clark (15)</td>
<td>2005</td>
<td>97</td>
<td>Yes</td>
<td>PLEX</td>
<td>SC &gt; 2.3 mg/dl</td>
<td>No</td>
<td>—</td>
<td>Control 37% (7 of 19)</td>
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<td>Ludwig (16)</td>
<td>2007</td>
<td>8</td>
<td>No</td>
<td>Chemotherapy</td>
<td>eGFR &lt; 20 ml/min/1.73 m²</td>
<td>No</td>
<td>63% (5 of 8)</td>
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<td>Kastritis (17)</td>
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<td>No</td>
<td>Chemotherapy</td>
<td>SC &gt; 2 mg/dl</td>
<td>No</td>
<td>73% (30 of 41)</td>
<td>80% (8 of 10)</td>
<td>—</td>
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<tr>
<td>Chana-n-Khan (18)</td>
<td>2007</td>
<td>24</td>
<td>No</td>
<td>Chemotherapy</td>
<td>Dialysis dependent</td>
<td>No</td>
<td>—</td>
<td>17% (4 of 24)</td>
<td>—</td>
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<tr>
<td>Leung (19)</td>
<td>2008</td>
<td>40</td>
<td>No</td>
<td>PLEX</td>
<td>50% above baseline or SC &gt; 2 mg/dl</td>
<td>Yes</td>
<td>45% (18 of 40)</td>
<td>22% (2 of 9)</td>
<td>22% (2 of 9)</td>
</tr>
<tr>
<td>Current study</td>
<td>2008</td>
<td>19</td>
<td>No</td>
<td>HCO-HD</td>
<td>Dialysis dependent</td>
<td>Yes</td>
<td>74% (14 of 19)</td>
<td>74% (14 of 19)</td>
<td>—</td>
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