Disclosures

• SJMC Affiliations
  • Vice chair, Medicine
  • Pharmacy and Therapeutics co-chair
  • HAI physician champion
  • Medical director, dialysis and plasmapheresis services

• SoCal Kidney, partner
  • 15 physician nephrology group servicing North Orange Co

• Davita Medical Director
  • Davita Crossroads, Placentia
What’s onco-nephro?

Cancer and the Kidney: The frontier of nephrology and oncology (2 ed.)

Edited by Eric P. Cohen

Abstract
This resource covers the challenging overlap area of nephrology and oncology, both in terms of kidney problems in cancer patients, and cancer that affects kidney patients, including assessment of kidney function, to paraneoplastic disorders, acquired cysts and native kidney cancers, and all points inbetween.

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Acute renal failure

- Pre-renal
  - Volume depletion
    - Vomiting, diarrhea, sepsis
    - Meds: diuretics, NSAIDs, ACE, ARB, etc.
  - Hypercalcemia- natriuresis and vasoconstriction
    - PTH related protein production-promotes liberation of Ca from bone
      - SCC of lung, cervix, and esophagus, lymphomas, RCC, and adenocarcinoma of breast, prostate, ovary
    - Bone metastases- mobilize Ca and osteoclasts
      - Myeloma, breast and lung metastases
    - Expression of 1-alpha hydroxylase leading to conversion of 25-OH vit D to calcitriol
      - Hodgkin’s and Non-Hodgkin’s
    - Treatment- Volume, Bisphosphonates, Donosumab, rarely steroids
Acute renal failure

• Pre-renal (cont.)
  • Hepatic Sinusoidal Obstruction Syndrome
    • Complication of hematopoietic cell transplantation (HCT)
    • Acute radiochemotherapy induced damage to sinusoidal hepatocytes leading to thrombosis and portal hypertension
    • Similar physiology to hepato-renal but 70% will recover with supportive care
  • Calcineurin inhibitors
    • Used in prevention of GVHD, e.g. tacrolimus, cyclosporine
    • Can cause both dose dependent AKI and CKD
Acute renal failure

• Intrinsic
  • Glomerular (paraneoplastic syndromes)
    • Membranous GN (GVHD, solid tumor malignancy)
      • 5-25% related to malignancy
      • Can be idiopathic or malignancy associated, in 2009 Beck et al found circulating PLA2R Ab in those w idiopathic disease; 75% of those w idiopathic disease are +....remaining need age-appropriate cancer screening
    • Minimal Change Disease (hematologic malignancies)
    • IgA nephropathy (RCC)
    • FSGS, HSP, ANCA vasculitis, AA amyloid (more studies needed to illustrate relationship)
  • Lymphomatous infiltration of the kidney
Acute renal failure

• Intrinsic
  • Tubulointerstitial
    • Cast Nephropathy (15-40% of myeloma pts), requiring acute dialysis at diagnosis (10%)
      • Survival significantly shorter in those with renal failure
      • Clonal free light chains overwhelm the proximal tubule so they continue to the distal tubule where they bind to Tamm Horsefall protein and create tubular obstruction
    • Renal recovery appears to be time sensitive, prompt treatment key
TAMM-HORSFALL PROTEIN

- A glycoprotein secreted by thick part of ascending loop of henle and early distal convoluted tubules.

- Constitutes 1/3 of total urinary protein.

- Forms the matrix of all casts.

- The protein forms a meshwork of fibrils that can trap any elements present in the tubular filtrate including cells, cell fragments or granular material.
Plasmapheresis

Plasmapheresis at SJMC
Acute renal failure

• Intrinsic
  • Tumor lysis syndrome
    • Occurs after the treatment of large volume malignancies, usually hematologic, some solid tumor as well, occasionally even before treatment
    • Occurs when intracellular contents overwhelm excretion of the body
    • Hyperuricemia, hyperkalemia, hyperphosphatemia, hypocalcemia, hallmarks
    • Uric acid is the main concern causing injury that can prolong
    • Treatments include allopurinol, febuxostat and rasburicase
Acute renal failure

• Intrinsic
  • Thrombotic microangiopathy
    • Results from platelet activation and formation of thrombi with subsequent vessel wall swelling and necrosis
    • Forms include cancer-associated and hematopoietic cell transplantation-associated
Acute renal failure

- Post-renal
  - Obstruction - most common in bladder, uterine and prostate cancers
    - Tumor obstruction
    - Lymphatic obstruction
    - Retroperitoneal fibrosis (radiation-induced vs malignancy itself)
    - Treated with nephrostomy vs ureteral stent
<table>
<thead>
<tr>
<th>Drug</th>
<th>Kidney diseases</th>
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<tbody>
<tr>
<td>Glomeruli</td>
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<tr>
<td>Minimal-change disease</td>
<td>Interferon and pamidronate</td>
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<tr>
<td>Focal segmental glomerulosclerosis</td>
<td>Interferon, pamidronate and zoledronate</td>
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<td>Tubulointerstitium</td>
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<tr>
<td>Acute tubular necrosis</td>
<td>Platinums, zoledronate, ifosfamide, and mitramycin, pentostatin, imatinib, diaziquone and pemetrexed</td>
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<tr>
<td>Acute interstitial nephritis</td>
<td>Sorafenib and sunitinib</td>
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<td>Crystal nephropathy</td>
<td>Methotrexate</td>
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<td>Tubulopathies</td>
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<tr>
<td>Fanconi syndrome</td>
<td>Cisplatin, ifosfamide, azacitadine, diaziquone, imatinib and pemetrexed</td>
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<tr>
<td>Salt wasting</td>
<td>Cisplatin and azacitadine</td>
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<tr>
<td>Magnesium wasting</td>
<td>Cisplatin, cetuximab and panitumumab</td>
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<tr>
<td>Nephrogenic diabetes insipidus</td>
<td>Cisplatin, ifosfamide and pemetrexed</td>
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<td>Syndrome of inappropriate antidiuresis</td>
<td>Cyclophosphamide and vincristine</td>
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<td>Vasculature</td>
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<td>Hemodynamic acute kidney injury (capillary leak syndrome)</td>
<td>Interleukin-2 and demileukin difttox</td>
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<tr>
<td>Thrombotic microangiopathy</td>
<td>Bevacizumab, tyrosine kinase inhibitors, gemcitabine, cisplatin, mitomycin C and interferon</td>
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Chemotherapy in CKD

- Most chemo is renally excreted but data on renal/dialysis clearance is incomplete
- Excretion in general is of cytotoxic metabolites so delays in elimination can lead to toxicity/overdose
- Also chemo exacerbates chronic conditions like renal anemia, infection risks
- Glomerular filtration and hemodialysis play an important role in clearance of non-protein bound molecules (e.g. carboplatin, can be cleared in dialysis pts if timed well but after 24h, protein-binding increases leading to toxicity)
- Tyrosine kinase inhibitors generally safer as cleared by the liver but still a study on sorafenib saw far more bleeding events in dialysis patients due to more vulnerable vasculature
Cancer risk in CKD

- In CKD pts impaired immune system, decreased antioxidant defense, accumulation of carcinogens due to impaired clearance, chronic infection and inflammation all increase cancer risk.
- Uremic toxins also increase risk of viral mediated cancers.
- Chronic dialysis suppressed DNA repair activity of lymphocytes and also associated with glutathione peroxidase deficiency.
- Cystic kidney diseases increase the risk of kidney cancers.
- Thyroid cancers are higher during dialysis and after transplant.
- CKD pts treated with cyclophosphamide, azathioprine, other immunosuppressives, all increase risk.
- However, large retrospective studies have not necessarily isolated these differences in cancer rates in dialysis patients, possible due to reduced screening and high cardiovascular mortality.
Screening for cancer in ESRD

- Cost per unit of survival benefit may be 20x higher in dialysis patients
- A typical screening program may have a net gain in life expectancy of 5 days or less amongst a dialysis cohort
- Most societies recommend continuing screening in dialysis patients for those on a transplant waiting list but age cutoffs vary
- Renal cell carcinoma is not screened for in the general population but in those on dialysis 3 years or more aged 20 a 1.6 year survival benefit was suggested if screened every 3 years
### Table 2. Common cancers and recommendations for screening

<table>
<thead>
<tr>
<th>Cancer type</th>
<th>Recommendations for screening</th>
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<tbody>
<tr>
<td>Breast</td>
<td>Annual or biennial mammography for all women older than 50 years; for women between 40 and 49 years, no evidence for or against screening</td>
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<tr>
<td>Colorectal</td>
<td>Annual fecal occult blood testing and/or 5-year flexible sigmoidoscopy or colonoscopy for individuals &gt;50 years</td>
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<tr>
<td>Cervical</td>
<td>Annual pap and pelvic examination once sexually active</td>
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<tr>
<td>Prostate</td>
<td>Annual digital rectal examination and PSA in all males after age 50 years</td>
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<tr>
<td>Liver</td>
<td>α-Fetoprotein and liver ultrasound every 6 months in high-risk individuals, i.e., HBV or HCV infection, but no firm data</td>
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<tr>
<td>Skin</td>
<td>Monthly self-examination and total body skin examination every 6–12 months by an expert skin physician</td>
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<tr>
<td>Kidney</td>
<td>No firm recommendation, but some have suggested regular ultrasound of native kidneys</td>
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</tbody>
</table>

PSA, prostate-specific antigen. Adapted from reference 24.

References

- Cohen, E. Cancer and the kidney: The frontier of nephrology and oncology. 2nd Ed. November 2012