Proteinuria & cancer

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Onconephrology

CA:
A Cancer Journal for Clinicians

Review Article | Free Access

Onconephrology: The intersections between the kidney and cancer

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- Onconephrology is a new subspecialty of nephrology that recognizes the important intersections of kidney disease with cancer
  - Includes drug-induced nephrotoxicity
  - Electrolyte disorders
  - Paraneoplastic glomerulonephritis
  - Interactions of chronic kidney disease with cancer.

Paraneoplastic Diseases of the Glomerulus

- Glomerular diseases are associated with many solid and hematologic malignancies
- Exact pathogenesis is unclear

Pathophysiology of proteinuria

- Proteinuria is consequence of two mechanisms:
  1. Abnormal transglomerular passage
  2. Impaired reabsorption by the epithelial cells of the proximal tubuli.

Review > Kidney Int. 2003 Mar;63(3):809-25. doi: 10.1046/j.1523-1755.2003.00840.x.

Pathophysiology of proteinuria

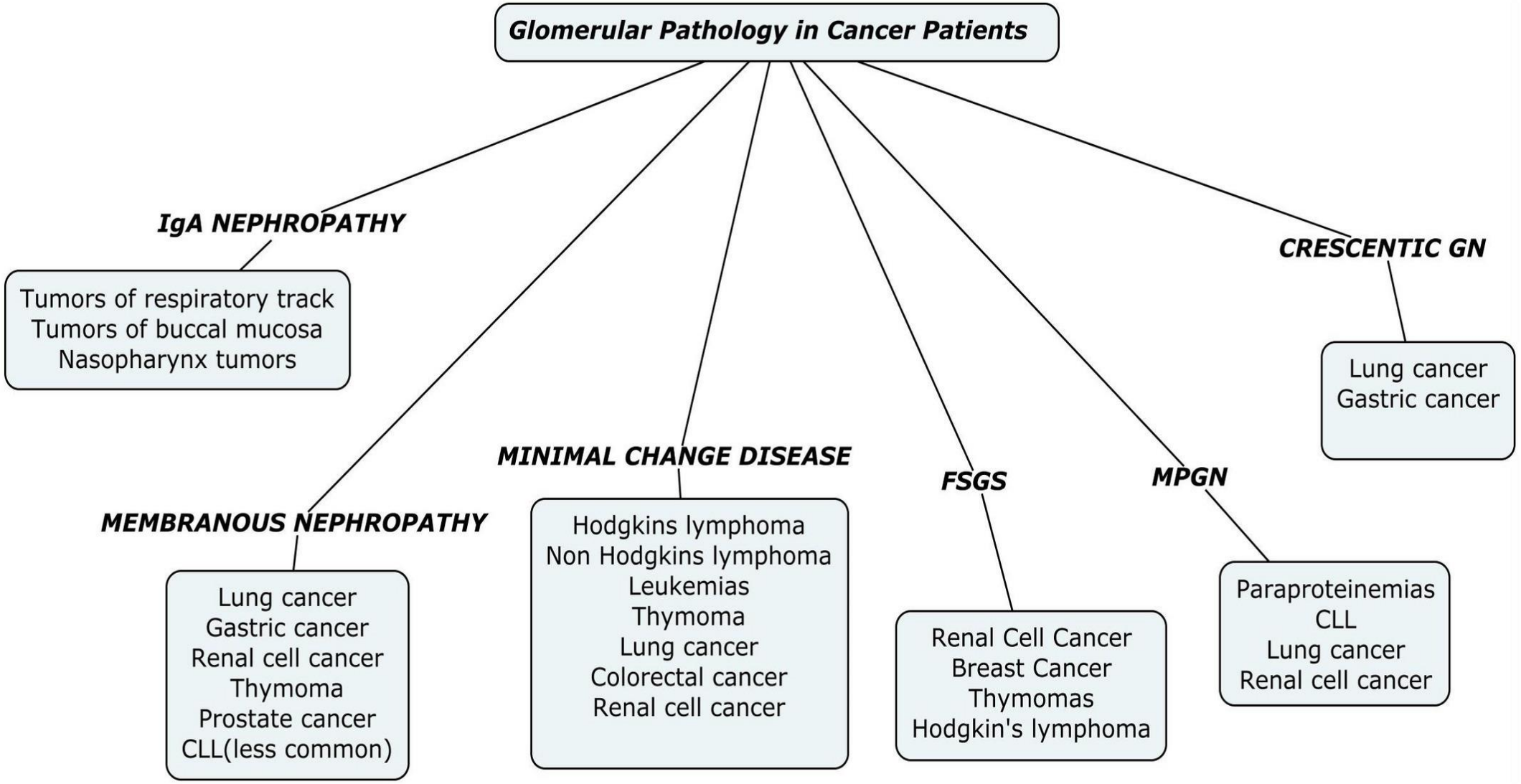
Giuseppe D'Amico [1], Claudio Bazzi

Affiliations + expand

PMID: 12631062 DOI: 10.1046/j.1523-1755.2003.00840.x

Free article

Onconephrology: The intersections between the kidney and cancer



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Membranous nephropathy

- MN is the most common glomerular pathology described in patients with solid tumors.
- In the largest systematic review of 240 patients with biopsy-proven MN, Lefaucheur et al reported a prevalence of malignancy of 10%

› Kidney Int. 2006 Oct;70(8):1510-7. doi: 10.1038/sj.ki.5001790. Epub 2006 Aug 30.

Membranous nephropathy and cancer: Epidemiologic evidence and determinants of high-risk cancer association

C Lefaucheur [1], B Stengel, D Nochy, P Martel, G S Hill, C Jacquot, J Rossert, GN-PROGRESS Study Group

Membranous nephropathy

- Only approximately one-half of these patients had symptoms related to cancer at the time of kidney biopsy
- The most common solid tumors (in order)

1. lung
2. Gastric cancers
3. RCC
4. Prostate
5. Thymoma

- Other cancers reported
  - Colorectal , pancreatic, esophageal, and hepatic carcinomas

Membranous nephropathy primary or scondry

- **Biomarkers in Primary Membranous Nephropathy, A Guide to Precision Medicine**

- M-type phospholipase A2 receptor (PLA2R)
- Thrombospondin type-1 domain-containing 7A (THSD7A)

- There are too many unanswered questions on the use of biomarkers in MN

Review > Iran J Kidney Dis. 2020 Sep;14(5):335-347.

Biomarkers in Primary Membranous Nephropathy, A Guide to Precision Medicine

Mohsen Nafar, Nooshin Dalili, Shiva Samavat [1]

Other glomerular diseases in solid tumors

- MCD
  - lung cancer, colorectal cancer, RCC, and thymoma and ……..
- IgA nephropathy:
  - RCC and solid tumors of the respiratory tract, buccal mucosa, and nasopharynx.
- Crescentic GN
  - RCC, gastric cancer, and lung cancer.

Glomerular diseases consistent with a paraneoplastic process

GLOMERULAR DISEASE PATHOLOGY	CLINICAL AND PATHOLOGY CLUES
Membranous nephropathy	Age >65 y, smoking history, negative anti-PLA2R in the serum, negative staining on kidney biopsy for anti-PLA2R, presence of >8 inflammatory cells in the glomeruli, absence of IgG4 deposits, presence of THSD7A staining, clinically resistant to several cytotoxic agents (cyclophosphamide, rituximab, calcineurin inhibitors)
Minimal change disease	Age >65 y; no other secondary cause found, such as medications or infections, clinically resistant to several cytotoxic agents (steroids, cyclophosphamide, rituximab, calcineurin inhibitors)
Focal segmental glomerulosclerosis	No secondary cause obviously found, clinically resistant to several cytotoxic agents (steroids, cyclophosphamide, rituximab, calcineurin inhibitors)
IgA nephropathy	New diagnosis at age >65 y
Membranoproliferative glomerulonephritis	Monoclonal on immunofluorescence, electron microscopy shows immunotactoid or cyroglobulin-like features, no autoimmune cause found—important to screen for certain hematology malignancies, such as CLL, CML, WM, and plasma cell dyscrasias
ANCA vasculitis	Clinically resistant to several cytotoxic agents (steroids, cyclophosphamide, rituximab, calcineurin inhibitors) and plasmapheresis, and no drug-induced cause found

Glomerular diseases consistent with a paraneoplastic process

- Membranous nephropathy
  - Age >65 y
  - Smoking history
  - Negative anti-PLA2R in the serum
  - Negative staining on kidney biopsy for anti-PLA2R
  - Presence of >8 inflammatory cells in the glomeruli
  - Absence of IgG4 deposits
  - Presence of THSD7A staining
  - Resistant to several cytotoxic agents (cyclophosphamide, rituximab …….)

Glomerular diseases consistent with a paraneoplastic process

- Minimal change disease
  - Age >65 y
  - No other secondary cause found
  - Resistant to several cytotoxic agents (steroids, cyclophosphamide, rituximab, calcineurin inhibitors)

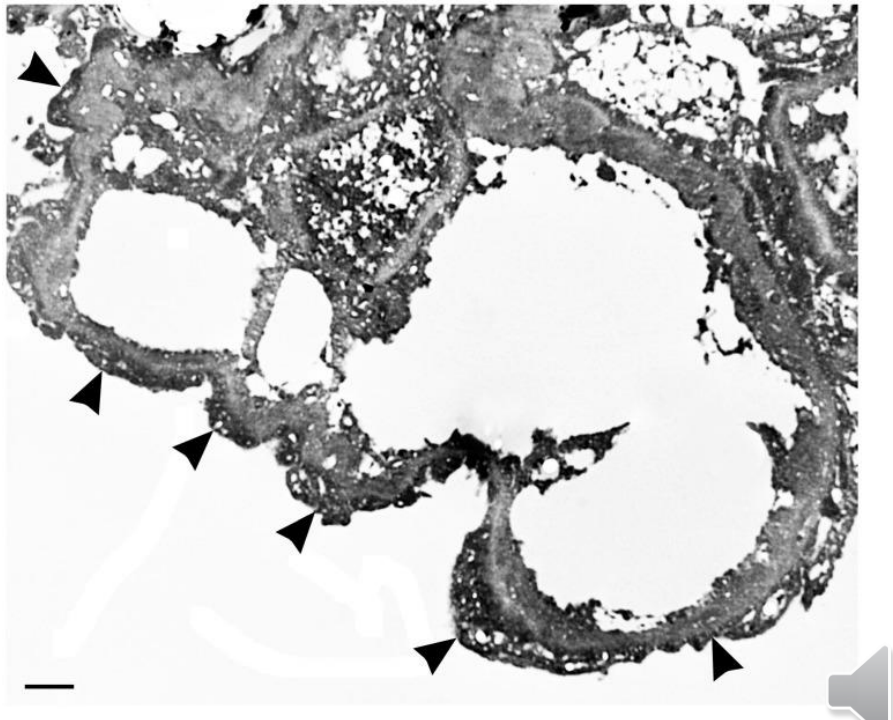
Glomerular diseases consistent with a paraneoplastic process

- Focal segmental
  - No secondary cause obviously found, clinically resistant to several cytotoxic agents
- IgA nephropathy
  - New diagnosis at age >65 y

Anticancer Agents & porteinuria

Nephrotoxicity Associated with Novel Anticancer Agents (Aflibercept, Dasatinib, Nivolumab

- Cancer patients have an incidence of about 60% kidney disease
- Renal adverse effects may range from asymptomatic proteinuria to renal failure



International Journal of Molecular Sciences

MDPI

Int J Mol Sci. 2020 Jul; 21(14): 4878.
Published online 2020 Jul 10. doi: 10.3390/ijms21144878

PMCID: PMC7402330
PMID: 32664269

Nephrotoxicity Associated with Novel Anticancer Agents (Aflibercept, Dasatinib, Nivolumab): Case Series and Nephrological Considerations

Luca Piscitani,[1] Vittorio Sirolli,[1] Lorenzo Di Liberato,[1] Manrico Morroni,[2] and Mario Bonomini[1,*]

> Gan To Kagaku Ryoho. 2019 Feb;46(2):245-249.

[Proteinuria in Patients with Gastric Cancer Treated with Ramucirumab]

[Article in Japanese]
Yutaka Kimura [1], Jota Mikami, Yoichi Makari, Chika Fujii, Yoko Hiraki, Motohiro Imano, Junya Fujita, Takushi Yasuda

- Ramucirumab, an antiangiogenic agent
  - Frequency of proteinuria was 43.5%
    - Grade 1: 26.1%
    - Grade 2: 8.7%
    - Grade 3: 8.7%)
- **Conclusions:** In patients with gastric cancer, treated with ramucirumab, the protein/creatinine ratio should be examined in cases of 2+, 3+ or 4+ via a qualitative examination.

SCIENTIFIC REPORTS
nature research

Sci Rep. 2020; 10: 2011.
Published online 2020 Feb 6. doi: 10.1038/s41598-020-58994-5

PMCID: PMC7005043
PMID: 32029849

Predictive factors for the development of proteinuria in cancer patients treated with bevacizumab, ramucirumab, and aflibercept: a single-institution retrospective analysis

Yuko Kanbayashi,[1,2,3] Takeshi Ishikawa,[1,4] Yusuke Tabuchi,[5] Koichi Sakaguchi,[3] Yoshimi Ouchi,[3] Eigo Otsuji,[6] Koichi Takayama,[7] and Tetsuya Taguchi[1,3]

- The development of proteinuria restrict …….
- Significant factors for development of proteinuria
  - SBP
  - Number of cycles
  - Calcium channel blocker use
- There was no difference among the three anti-angiogenic agents or among cancer types.

Review > J Am Soc Nephrol. 2010 Aug;21(8):1381-9. doi: 10.1681/ASN.2010020167. Epub 2010 Jun 10.

Bevacizumab increases risk for severe proteinuria in cancer patients

Shenhong Wu [1], Christi Kim, Lea Baer, Xiaolei Zhu

- Humanized mAb that neutralizes vascular endothelial growth factor
- Analyzed data from 16 studies comprising 12,268 patients with a variety of tumors.

Categories	No. of Studies	Bevacizumab (Events/Sample Size)	Control (Events/Sample Size)	Incidence (%; 95% CI)	RR (95% CI)
Overall	16	186/6482	24/5786	2.2 (1.2 to 4.3)	4.79 (2.71 to 8.46)

- In conclusion, the addition of bevacizumab to chemotherapy significantly increases the risk for high-grade proteinuria and nephrotic syndrome.

J Endocrinol Invest. 2021 Jan;44(1):95-103. doi: 10.1007/s40618-020-01272-y. Epub 2020 May 3.

Proteinuria is a late-onset adverse event in patients treated with cabozantinib

V Cappagli [1], D Moriconi [2], A G Bonadio [3], D Giannese [2], Gaetano La Manna [4], M Francesca Egidi [2], G Comai [4], G Vischini [5], V Bottici [1], R Elisei [6], D Viola [1]

- Tyrosine kinase inhibitors (TKIs)
  - Proteinuria was observed in 4/18 patients (22.2%)
  - Associated with previous chemotherapy (p = 0.005)
  - Treatment with other TKIs (p = 0.04),
  - Prolonged use of cabozantinib (p = 0.0004)

We should Be aware

Cancer and its treatment can induced proteinuria in multiple different way

THANKS FOR YOUR ATTENTION