Title: *IgA Nephropathy in cancer patients: either tumor-related or immunotherapy induced immune dysregulation*

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Introduction: IgA nephropathy (IgAN) is the most common primary glomerulonephritis worldwide and usually follows a slow, chronic course. In cancer patients, it arises in two distinct scenarios: paraneoplastic (secondary) IgAN, and IgAN induced by cancer therapies, particularly immune checkpoint inhibitors (ICIs). Paraneoplastic IgAN may precede, coincide with, or follow the cancer diagnosis, and malignant relapse can trigger glomerulonephritis recurrence; treatment targets the underlying tumor. ICI-induced IgAN is far rarer than acute tubulointerstitial nephritis. We report two cases: one paraneoplastic and one ICI-induced.

Case 1: A 48-year-old woman with metastatic peritoneal mesothelioma, having failed multiple chemotherapy lines since 2018, began atezolizumab and bevacizumab for disease progression. After two months, she developed nephrotic-range proteinuria (4.7g), prompting nephrology referral. Biopsy performed to distinguish ICI-nephritis from antiangiogenic induced renal limited thrombotic microangiopathy revealed secondary IgAN due to ICI (M0E1S1, NOS) with moderate arteriosclerosis and mild arteriolosclerosis. Immunotherapy was held and losartan replaced with sparsentan.

Case 2: A 66-year-old man with papillary thyroid cancer (diagnosed 2015, thyroidectomy 2016) was treated with sunitinib, then lenvatinib, stopped after 15 months for proteinuria and hypertension despite normal kidney function. Biopsy showed IgAN (M0E1S). For persistent disease, therapy was switched to dabrafenib and trametinib, with good response. Cancer response was accompanied by reduced proteinuria, and this parallel improvement supports a paraneoplastic etiology for the IgAN.

Conclusion: These cases underscore the value of kidney biopsy in cancer patients with proteinuria. ICIs rarely induce secondary IgAN as an immune-related adverse event, typically presenting with hematuria, proteinuria, and sometimes acute kidney injury. Our ICI case was unusual in lacking both hematuria and acute kidney injury. The paraneoplastic patient's proteinuria improved alongside cancer response to therapy.

Table:

Case	Age	Male/ female	Cancer	Chemo at presentation	Months on treatment before proteinuria	Urine/protein creatinine at presentation	Initial blood pressure	Urine/protein creatinine at follow up	Follow up blood pressure (mm Hg)	Kidney Biopsy
1	48y	F	Metastatic peritoneal mesothelioma	Atezolizumab Bevacizumab	2	4.7g	156/68	0.6g	124/68	IgAM0E1S1;mild arteriosclerosis
2	66y	M	Thyroid papillary cancer	Sunitinib Lenvatinib	15	9g	144/84	1.3g	138/81	IgA(M0E1S1); Diabetic nephropathy;mild arteriosclerosis