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GUEST EDITORIAL

Onconephrology: The Growth of Cancer–Kidney Connection, Part 2

Check for updates

In Part 1 of "Advances in Onconephrology" (volume 28, number 5) we discussed acute kidney injury; conventional, immunotherapy, and targeted therapy–induced kidney adverse events; tumor lysis syndrome; pediatric onconephrology; cancer survivorship; and screening, among other topics. In the second installment we will discuss other important aspects in onconephrology in our cutting-edge review articles covering this rapidly evolving sub-specialty.

This issue starts with a state-of-the-art review by Sy-Go and colleagues, "Monoclonal Gammopathy–Related Kidney Diseases" (pp 86-102), which provides a comprehensive overview of this complex topic. Paraproteinemia encompasses a broad range of clonal B lymphocyte or plasma cell disorders producing either whole or truncated immunoglobulin molecules.[1] This can affect virtually any compartment of the nephron, leading to a wide spectrum of clinical and morphological presentations—podocytopathy, glomerulonephritis, tubulopathies, interstitial or vascular involvement, and each may culminate in a progressive loss of kidney function. Electron microscopy and mass spectroscopy has revolutionized the diagnosis of these disorders. The authors describe the most common cause of acute kidney injury (AKI) in patients with myeloma, cast nephropathy, but also cover a wide array of disorders such as glomerular and tubular disorders that are associated with paraproteinemia.

Hematogenic stem cell transplant (HSCT) has improved our ability to treat several benign and malignant hematologic disorders. The spectrum of kidney disease that may occur after HSCT includes AKI (incidence 12% to 73%), chronic kidney disease (CKD), thrombotic microangiopathy (TMA), nephrotic syndrome, and calcineurin inhibitor toxicity.[2] Dialysis requirement post HSCT is associated with mortality exceeding 80%. In "Kidney Disease Following Hematopoietic Stem Cell Transplantation" (pp 103–115), Abudayyeh and Wanchoo review the risk factors, pathogenesis, and management of these disorders. Given the high morbidity and mortality related to development kidney disease after HSCT, nephrologists need to be aware of the various causes of kidney damage and the best treatment options.

Paraneoplastic glomerular diseases are secondary glomerular lesions caused by hormones, cytokines, or tumor antigens secreted by the tumor and can be the presenting symptom of both hematologic and solid-organ cancers.[3] After the first description of nephrotic syndrome in Hodgkin's disease in 1922 by Galloway,[4] our understanding of these enigmatic lesions has undergone a paradigm shift with the unraveling of newer tumor antigens, especially in the setting of membranous nephropathy. Jeyabalan and Trivedi cover the various pathological entities in "Paraneoplastic Glomerular Diseases" (pp 116-126). This is an evolving field, and our understanding is sure to grow as newer glomerular targets are identified.

Thrombotic microangiopathy (TMA) can occur in patients with cancer as a downstream effect of disordered coagulation and complement dysregulation characterized by macroangiopathic hemolytic anemia and end-organ dysfunction; its cause may be the cancer itself or its treatment.[5] TMA is not a disease in itself, but a pattern of injury resulting from a systemic disorder. Hanna and colleagues discuss the pathophysiology and approach to various TMA syndromes in "Thrombotic Microangiopathy Syndromes—Common Ground and Distinct Frontiers" (pp 149-160). TMA syndromes share a mechanistic link with rheumatological diseases (systemic lupus erythematosus, scleroderma renal crisis, etc), preeclampsia, and solid-organ transplant (antibody-mediated rejection, calcineurin inhibitor toxicity, etc), and a wide spectrum of other diseases metabolic disease (cobalamin deficiency, medication-induced TMA). The authors appropriately conclude that more work needs to be done to understand the genetics and molecular basis of this disease spectrum

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to unravel the mystery of this disease process and to identify potential therapeutic strategies.

Hematologic malignancies can commonly involve the kidney. Manifestations encompass a broad spectrum of disease: prerenal AKI, acute tubular necrosis, renovascular disease, parenchymal infiltration with cancer cells, obstruction, glomerulopathies, and electrolyte and acid-base abnormalities. Abramson and Mehdi elaborate about the kidney manifestations in patients with leukemia, lymphoma, and myeloma in "Hematological Malignancies and the Kidney" (pp 127-140). AKI most frequently occurs in patients with multiple myeloma (31.8%), followed by those with leukemia (27.5%) or lymphoma (18.8%).[6,7] Kidney disease adversely affects the survival of patients with hematological malignancies through multiple factors: ie, reduced remission rates, increased relapse rates, and increased likelihood of refractory disease.

Nephrologists often are consulted to assess kidney health in patients with sickle cell disease. Sickle cell nephropathy includes defects in urine concentration, impaired electrolytes and acid base handling, albuminuria, AKI, and CKD.[8] Glomerular hyperfiltration, endothelial damage from repeated sickling and vaso-occlusive episodes, and iron-induced pro-inflammatory changes in the glomerular mesangium and tubule-interstitium are some of the mechanisms of kidney damage. Amarapurkar and colleagues walk us through the various manifestations, their diagnosis, and management, in "Sickle Cell Disease and Kidney" (pp 141-148). The authors emphasize screening and nephrology referral, novel urinary biomarkers, iron chelation therapies, and kidney replacement therapy including kidney transplantation for patients with sickle cell disease.

AKI is also a common and important complication of cancer surgeries, associated with increased health care expenditure, risk of incident or progressive CKD, and mortality. The pathogenesis of AKI is multifactorial and determined by patient and cancer-specific factors. Zafar and colleagues provide an excellent overview of the above-mentioned aspects in "Oncosurgery-Related Acute Kidney Injury" (pp 161-170). AKI is most common after surgical management of genitourinary cancers and is mostly related to the nephron loss. To date, there has never been a study demonstrating the role of early nephrology consult to reduce the risk of AKI among patients undergoing oncosurgery, but this can be an important area of further investigation.

In the part 1 of this Onconephrology series in ACKD (volume 28, number 5), Rosner and colleagues discussed disorders of divalent ions.[9] In the current issue, Ratanasrimetha and colleagues provide a case-based approach in "Sodium and Potassium Dysregulation in the Patient with Cancer" (pp 171-179). Hyponatremia is the most common electrolyte abnormality seen in patients with cancer.[10] Hypokalemia, hyperkalemia, and pseudohyperkalemia are also common. Understanding the variety of mechanisms driving common electrolyte abnormalities in patients with cancer is important to ensure prompt and effective management.

Anemia can be a feature of both cancer and advanced chronic kidney disease. In "Anemia Management in the Cancer Patient With CKD and End-Stage Kidney Disease" (pp 180-187), Rashidi and colleagues elaborate the nuances of evaluation and management of anemia in the setting of cancer and CKD. Anemia can occur from true or functional iron deficiency, chronic inflammation, drug-induced bone marrow suppression, hemolysis, marrow infiltration, etc.[11] The authors highlight the use of iron therapy, hypoxia inducible factor agents, erythrocyte stimulating agents, and blood transfusions in this unique population.

Recent advances in cancer therapies have dramatically improved survival outcomes; however, patients with kidney transplant face unique challenges of immunosuppression management, cancer screening, and recurrence of cancer post-transplant. Murakami and colleagues discuss salient topics for the kidney transplant population in "Transplant Onconephrology in Patients With Kidney Transplants" (pp 188-200). These include current recommendations for how long kidney transplant should be delayed in patients with prior cancer history, cancer screening after kidney transplant, the risk of posttransplant lymphoproliferative disorder, strategies for kidney transplantation in patients with multiple myeloma, and the unique risk of cancer immunotherapy in the kidney transplant population. The authors emphasize the importance of a multidisciplinary approach involving the general and transplant nephrologist, oncologist, and the patient and their family to ensure patient-centered goals are achieved.

Kidney palliative care is a growing discipline within nephrology. It specifically addresses the stress and burden of advanced kidney disease through the provision of expert symptom management, caregiver support, and advance care planning with the goal of optimizing quality of life for patients and families. Corona and colleagues elaborate on key aspects of symptom management and end of life care in "Palliative Care for Patients with Cancer and Kidney Disease" (pp 201-207). End-of-life care brings special considerations for patients living with cancer and kidney disease, particularly for those on kidney replacement therapy. The authors provide an excellent framework regarding prognosis and goals of care discussion.

Because of exclusion of patients with significant kidney disease from the cancer clinical trials, there is paucity of data pertaining to dosing guidelines of anti-cancer drugs in CKD. In "Cancer Drug Dosing in Chronic Kidney Disease and Dialysis" (pp 208-216), Shirali and Sprangers provide a comprehensive overview of glomerular filtration rate estimation and pharmacokinetic and dynamic considerations in patients with CKD. The authors lead us into discussion of the specifics of conventional chemotherapy, targeted therapies, and immunotherapy management in patients with advanced kidney disease.

There have been tremendous advances in the field of oncology and onconephrology since the last special issue of *Advances in Chronic Kidney Disease* was focused on Onconephrology in 2014. We are thankful to the authors and reviewers of this two-part update on Onconephrology

and to Dr Charuhas V. Thakar, Editor-in-Chief, for inviting us to edit this issue. We are also thankful of the visual abstract team led by Drs Matthew Sparks, Mythri Shankar, and Brian Rifkin for supporting each manuscript with incredible visual abstracts. We sincerely hope these 2 issues improve the delivery of care and inform future research in patients with cancer and kidney disease.

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