

Nephrology issues in Oncology- Our Observations

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Introduction

A complex relationship exists between Kidney and cancer. Onco-nephrology is a subspecialty that focuses on all aspects of kidney disease in cancer patients.¹ Nephrological manifestations in cancer patients may be a) Acute Kidney Injury, b) Electrolyte Imbalance, c) Paraneoplastic Renal manifestations like Proteinuria, d) Chronic Kidney disease, e) Contrast induced Nephropathy, f) Obstructive Nephropathy to mention the common forms. Neoplasia in patients undergoing treatment for Chronic Kidney Disease and post-transplantation malignancies are the Oncology issues faced by patients who are already under Nephro-care. Hence a close association and healthy interaction is needed between the Nephrologist and Oncologist so as to deliver the best health care to these patients.

Our Institution is a Government Multispecialty Hospital wherein there are Medical, Surgical and Radiation Oncology as well as Nephrology Departments. We undertook a pilot study to analyze the renal manifestations requiring referral to Nephrology Department in patients with malignancy in our hospital.

Material and Methods

The data of patients referred to Nephrology Department of the hospital during the period August 2016 to January 2017 from the Oncology Departments (Medical, Surgical and Radiation), such as name, age, gender, co morbidities, primary malignancy and treatment given with purpose of referral were analyzed and the renal syndrome associated was observed.

Demography and basic data: 74 patients were studied. There were 34 females among them. There was only one patient below 20 years of age, 5 patients between 20 to 40 years, 34 each in the age groups 40 to 60 years and more than 60 years. Table I and Table II represents the various renal syndromes and primary malignancies respectively and the number of individuals in each condition considered for the study. Multifactorial AKI in the study is due to various combinations of Drugs, obstructive Nephropathy, contrast exposure and prerenal factors. The Figure 1 and 2 are pie charts giving the comparison of distribution of various renal syndromes and primary malignancies.

Table 1: Renal syndromes and their distributions

Syndrome	No. of patients
Prerenal azotemia	23
Drug induced AKI	15
Multifactorial AKI	8
Obstructive nephropathy	9
CKD with malignancy	8
Sepsis / AKI	2
Hypokalemia	2
RCC causing renal insufficiency	1
Myeloma Kidney	1
HT/AKI	1
Contrast induced Nephropathy	1
Proteinuria	1
Lymphomatous infiltration AKI	1
AKI – Unknown cause	1

Table 2: Primary malignancies and their distributions

Syndrome	No. of patients	Syndrome	No. of patients
Gastrointestinal	8	Testicular	1
Skin	5	Phaeochromocytoma	1
Lymphoproliferative	2	Bladder	3
Breast	7	RCC	3

Laryngopharyngeal	6	Maxilla	2
Pulmonary	4	Myeloma	1
Sarcoma	2	Hepatocellular Ca	2
CNS	5	CML	1
Ca cervix	10	Thyroid	2
Ca endometrium	4	Prostate	1
Ovarian Ca	4	TM JT	1
		Unknown primary	1

Some patients had malignancy in more than one site.

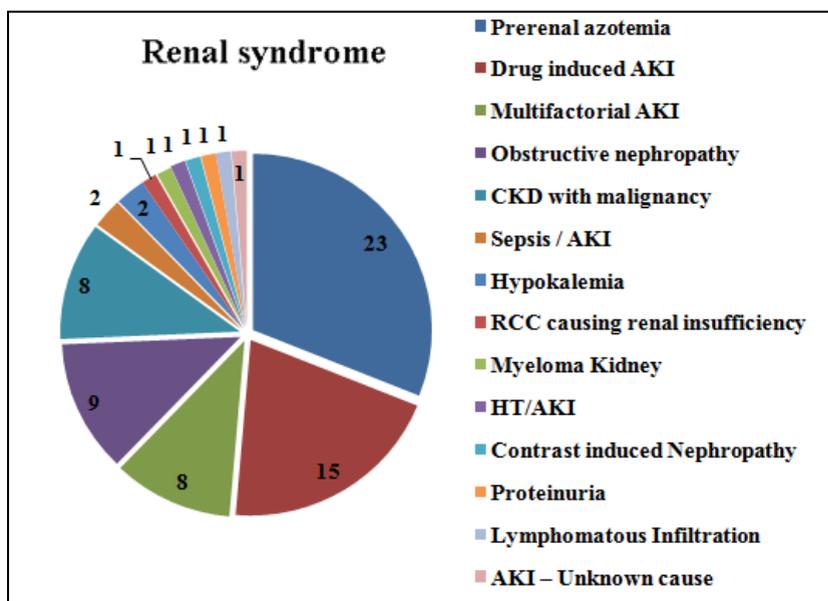


Fig. 1: Comparison of the distribution of various renal syndromes considered in the study

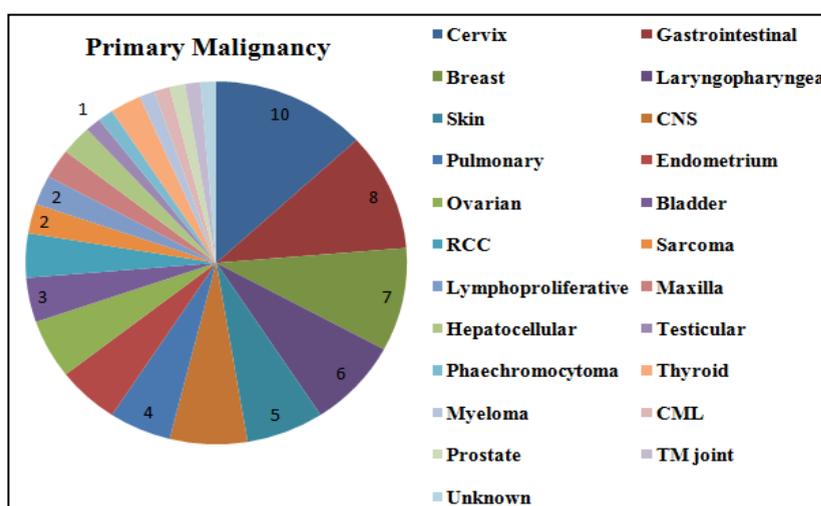


Fig. 2: Comparison of the distribution of various Primary malignancies considered in the study

Discussion

Acute Kidney Injury: In Our study there were a significant number of pre-renal azotemia cases which were due to malignancy of Upper GI or Upper respiratory tract precluding food intake. Some of them had undergone radiotherapy resulting in hypovolemia

due to vomiting and dehydration. Renal failure in these patients recovered following adequate volume replacement. Drug induced AKI was seen in 15 patients, the drugs implicated being, chemotherapeutic drug Cisplatin and NSAIDs taken for pain. Drug induced AKI was moderate in severity and recovered as

the drugs were withheld. There were 8 cases of Multifactorial AKI due to various combinations of Drugs, obstructive Nephropathy, contrast exposure and prerenal factors. Majority of contrast exposures were associated with multiple factors causing AKI. 2 patients had Sepsis contributing to AKI. Sick patients especially those with sepsis had a poor prognosis. In various studies the risk factors for AKI in cancer patients have been found to be Elderly age, Nephrotoxic anticancer drugs and radiotherapy. In a study by Howlander et al., it was found that Elderly people have higher cancer incidence rates² and USRDS data states that the elderly had 10 fold higher AKI rates when compared to the non-elderly population.³ Coming to drugs Cisplatin Nephrotoxicity had been well documented. Wide array of kidney functional disturbances such as hypertension, Dyselectrolytemias, Proteinuria, Acute interstitial nephritis have been observed with targeted agents.⁴ We had one patient of AKI due to Lymphomatous infiltration of the Kidneys who succumbed to the illness and we had a patient of Hepatocellular carcinoma with AKI of unknown cause. As the patient was very sick, we could not proceed with Renal Biopsy.

Chronic Kidney Disease: 8 patients in our study were noted to have Chronic Kidney Disease. CKD-Cancer relationship can be explained as being circular since, CKD can be a risk factor for Cancer as well as CKD can result from Cancer or its treatment. In a study done by Vacher V. et al.⁵ it was found that CKD is quite prevalent in cancer patient. A high incidence of lymphoma and skin cancers have been observed in graft recipients from the beginning of transplantation. With improvement in graft and patient survival, the incidence of various other types of cancers have also increased.⁶

Dyselectrolytemia: Hypomagnesaemia due to chemotherapy with Cisplatin can cause hypokalemia. It was also found that Small Cell Lung Cancer releases ACTH which can result in increased levels of Aldosterone resulting in Hypokalemia.⁷ In Myeloma, Renal tubular injury due to Myeloma Proteins can cause hypokalemia due to Potassium wasting. Urinary magnesium loss due to Chemotherapeutic agents can cause hypokalemia.⁸ Low Potassium levels have been found to occur in patients with vomiting also. In our Observational study, we found that 2 patients had hypokalemia. One patient with Ca Endometrium developed hypokalemia due to vomiting following chemotherapy and another patient with CKD/Ca Breast had diuretic induced hypokalemia. Both patients responded to potassium supplementation.

Renal Cell Carcinoma: RCC is known to cause renal insufficiency due to loss of renal mass. In Danish study it was found that 1 year risk of AKI was 17.5% with a 5 year risk of 27%. Radical Nephrectomy done for RCC is found to be associated with 33.7% risk of AKI and predicts future development of CKD. We had 3 cases of Renal Cell Carcinoma. 1 patient presented with renal insufficiency due to RCC and one patient had mild AKI

due to Gemcitabine which showed improvement on stopping the drug. The third patient had Ca Cervix as well as RCC and the presentation was with Obstructive Nephropathy.

Sepsis: In a study done by Rosolem et al., the most frequent sites of infection in cancer patients were the lung, abdomen and the Urinary tract. 91% of the patients had severe sepsis and septic shock. Failure of Respiratory, Renal and Cardiovascular systems were associated with increased mortality.⁹ In our study, we had 2 patients with Sepsis /AKI, one with Ca Stomach and one with Ca Oropharynx.

Obstructive Nephropathy: There were 9 patients with Obstructive Nephropathy. 5 patients had cancer cervix and one each had Non Hodgkin's Lymphoma, Ca Prostate, Ca Colon and Ca Endometrium. All the patients underwent urological evaluation and had bladder catheterisation to relieve the obstruction. 2 patients with Ca Cervix underwent Per Cutaneous Nephrostomy. In a study done by Alzira et al., 49.4% of patients having Cervical Cancer and AKI were found to have Postrenal AKI, of whom 68.7% were treated with Per Cutaneous Nephrostomy.¹⁰

Contrast Induced Nephropathy: We had one patient with Contrast nephropathy, a patient with Testicular malignancy, who recovered with conservative management. In a study done by Cicin et al., the incidence of CIN after CT in hospitalized oncological patients was 20 %. CIN was found to be 4.5-times more frequent in patients with cancer who had undergone recent chemotherapy. Hypertension and the combination of bevacizumab/irinotecan were found additional risk factors for CIN development.¹¹

Multiple Myeloma: We had one patient with Multiple Myeloma and Renal failure who was referred for Chemotherapy. The patient had mild renal failure not requiring dialysis. He was not willing for Renal Biopsy and therefore we could not establish the cause of renal involvement. With Chemotherapy the patient had good response and his renal function remained stable. The factors that can contribute to the development of AKI in Multiple Myeloma are dehydration, hypercalcaemia, and the ingestion of Nephrotoxic drugs. One should also think about concomitant amyloid or another renal pathology unrelated to Multiple Myeloma. All these factors can result in the development of cast nephropathy, which is the commonest cause of severe AKI which has a poor prognosis if not treated early.¹² In an Observation by Dimopoulos et al, it was found that 50% of Multiple Myeloma patients had AKI of variable degree of whom 1/5th have severe AKI needing immediate renal Replacement Therapy.¹³

Proteinuria is seen in solid tumours of Lung, Gastric, Breast, Prostate, Kidneys and Colon as well as in Hematological malignancies. Membranous nephropathy is in general the most commonly reported paraneoplastic glomerulonephritis; MCD, membranoproliferative glomerulonephritis, RPGN and

IgA nephropathy have been reported less frequently.¹⁴ We had one patient with mild proteinuria in a patient with treated Ca Breast, due to Diabetic Nephropathy.

Hypertension: There was one patient with Hypertension due to Pituitary Adenoma who presented with accelerated Hypertension and Acute on CKD which improved subsequently with Hypertension Control. She is on regular follow up with us and maintains a stable serum creatinine with good control of Hypertension. In a study done by Vinicius Barbosa de Souza et al, it was found that there was a high co prevalence of hypertension and cancer as they share same risk factors such as smoking, obesity, and unhealthy diet. It was also found that there was an association of hypertension with the use of angiogenesis inhibitors (bevacizumab, sorafenib and sunitinib), corticosteroids, erythropoietin and non-steroidal anti-inflammatory drugs.¹⁵

Tumor lysis syndrome (TLS) is characterized by a massive tumor cell death leading to the development of metabolic derangements and target organ dysfunction. Tumor lysis syndrome TLS can occur spontaneously or as a result of cancer treatment. Hematological malignancies constitute the vast majority of Tumor lysis syndrome cases because of the sensitivity to therapy and rapid division rates. Solid cancers rarely cause Tumor lysis syndrome and are usually advanced by then. There were no cases of tumour lysis syndrome in this observational study.¹⁶

Conclusion

Almost all types of Renal Syndromes have been encountered in Various Cancers. Almost all the patients with mild renal failure recovered. Drug induced AKI was moderate in severity and recovered as the drugs were withheld. Only the very sick patients and those with sepsis had a poor prognosis. Majority of contrast exposures were associated with multiple factors causing AKI. With the increasing therapeutic armamentarium for cancer patients wherein new drugs especially Biologicals are used, the Nephrologists have to equip themselves to deal with elderly cancer patients and drug induced renal issues.

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