The nephrologist's role in the oncology – haematology ward

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Abstract

Cancer patients require care by a multidisciplinary medical team. Although nephrology usually is not the "core" speciality in such a multidisciplinary team, nonetheless it may substantially improve the quality of care. This paper reviews nephrologist's role in the management of the cancer patient.

Key words: cancer, multidisciplinary care, nephrologist.

Introduction

Cancer patients require care by a multidisciplinary medical team. Although nephrology is usually not the "core" speciality in such a multidisciplinary team, nonetheless it may substantially improve the quality of care.

Malignancy and its treatment modalities may be associated with a variety of renal and metabolic abnormalities. Nephrologist is usually called in when one of the following problems is encountered:

- Kidney insufficiency either preexisting or developing in the course of disease
- Glomerular injury presenting as nephritic or nephrotic syndromes
- Obstructive nephropathy causing kidney failure
- Tubulointerstitial disease
- Tumor invasion of the kidney
- Fluid and electrolyte disorders
- Decision regarding renal replacement therapies.

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These may be either the result of the presence of malignancy (local or remote effects) or be associated with treatment or diagnostic procedures.

Acute renal failure (ARF)

May arise as a consequence of the most disorders described in this presentation including acute tubular necrosis, glomerular disease, tubulointerstitial disease, abnormalities of intrarenal blood vessels. Particular attention should be paid to the nephrotoxicity of drugs used in the treatment of cancer patients (*Tab. 3*). In the management of ARF in the setting of oncology-hematology department meticulous attention should be paid to the prevention of ARF. Dialysis may be necessary in more severe cases.

In cancer patients decrease in effective circulating blood volume leading to renal hypoperfusion with consequent decrease in GFR, may be induced by several mechanisms. Most common causes of hypovolemia include vomiting, diarrhoea, edema, hepatorenal syndrome and treatment with interleukin-2 (which induces alterations in vascular permeability, leading to a capillary leak syndrome). Management of prerenal failure is directed towards the correction of the underlying cause and, restoration of extracellular fluid volume to optimal.

Chronic renal failure (CRF)

May be the consequence of most of the disorders described in this presentation including glomerular disease, tubulointerstitial abnormalities, renovascular disease, and chronic obstructive uropathy

Glomerular disease

Glomerular disease is a recognised complication of malignancy. Its true incidence is unknown although it is probably not as frequent as generally thought and does not warrant an extensive workup in search for malignancy. Most frequent glomerulopathies seen in the association with malignancy are membranous nephropathy, minimal change disease, membranoproliferative GN, RPGN, focal segmental glomerulosclerosis

Table 1. **Most common causes of chronic renal failure in cancer patients**

Clinical syndrome	Type of disease
Glomerular disease	Glomerulonephritis Amyloidosis Primary renal cancer Chemotherapeutic drugs
Tubulointerstitial abnormalities	Monoclonal immunoglobulin deposition disease Light chains deposition disease Infiltration by tumor cells Radiation nephropathy Chemotherapeutic drugs
Renovascular disease	Thrombotic microangiopathy (HUS, TTP) Hypertension Renal vein thrombosis
Chronic obstruction	Ureteral obstruction Unilateral obstruction in the case of a single functioning kidney Retroperitoneal fibrosis (irradiation, drugs, carcinoid tumors, reactions to metastases obstruction of the urethra)

and amyloidosis. They were described usually in the setting of Hodgkin lymphoma; other lymphoproliferative disorders; squamous cell carcinoma; adenocarcinomas of the lung, kidney, thyroid, cervix, and gastrointestinal tract [1-5]. This topic is described in more detail elsewhere in this issue of the journal.

Tubulointerstitial disease

Most common forms of tubulointerstitial disease observed in cancer patients are listed in *Tab. 2*.

Obstructive uropathy

May be caused by bilateral ureteral obstruction (or unilateral obstruction in the case of a single functioning kidney) by tumors growing in the vicinity of the urinary tract, or develop as a result of blood clots or stones induced by therapy. Most common tumors causing urinary tract obstruction include:

- bladder tumors and tumors of the collecting systems
- uterine tumors, especially carcinoma of the cervix
- retroperitoneal tumors (rare)
- primary renal tumors (rare).

Other rare causes include: retroperitoneal fibrosis (irradiation, drugs (busulfan), carcinoid tumors, reactions to metastases), or obstruction of the urethra.

Diagnosis is usually made by ultrasonography although it should be remembered that normal-appearing collecting system does not exclude the diagnosis. Treatment is directed toward relieving obstruction by urological procedures or chemotherapy in order to decrease tumor mass [6].

Tumor invasion of the kidney

It is needless to say that primary renal tumors (like renal cell carcinoma) invade renal parenchyma, but usually do not require nephrological consultation. Kidney failure develops only when there is extensive bilateral renal involvement. More commonly kidney insufficiency results from surgery, and consultation may

Table 2. **Tubulointerstitial disease in cancer patients**

Cause	Symptoms
Products or metabolites of cancer cells	
Lysozyme	Hypokalemia Fanconi's syndrome
Immunoglobulin light chains	Renal tubular acidosis Fanconi's syndrome
Hypercalcemia	Polyuria, polydypsia
Amyloid deposits in collecting ducts	Nephrogenic diabetes insipidus
Cast nephropathy in multiple myeloma	Nephrogenic diabetes insipidus
Drugs	
Cisplatin	Hypomagnesemia
Cyclophosphamide	SIADH
Ifosfamide	Fanconi's syndrome
Streptozotocin	Renal tubular acidosis Hypophosphatemia Fanconi's syndrome
Vincristine	SIADH
Change in hormones	
↑ PTH-like	Hypercalcemia Hypophosphatemia
↑ ADH	Hyponatremia (SIADH)
↓ ADH	Hypernatremia (central diabetes insipidus)
Adrenocortical excess	Hypokalemia
Adrenocortical insufficiency	Hyperkalemia

Table 3. **Drugs used in oncology associated with kidney damage**

Syndrome	Drug
Nephrotic syndrome	Mitomycin C Gemcitabine Interferon-2
Acute tubular necrosis	Antibiotics – aminoglycosides, amphotericin, pentamidine, cephalosporin (rare), vancomycin (rare), acyclovir, gancyclovir, foscarnet Chemotherapeutics – methotrexate, cisplatin, carboplatin, streptozocin, semustine, carmustine, ifosfamide, interferon-A, mithramycin
Acute interstitial nephritis	Penicillins, cephalosporins, sulfonamides, thiazide diuretics, loop diuretics, antituberculous drugs, NSAIDs
Chronic renal failure	Cisplatin, semustine, carmustine, streptozotocin, cyclosporine, gemcitabine, and deoxycoformycin
Hemolytic-uremic syndrome	Mitomycin (potentiated by tamoxifen), bleomycin + cisplatin, radiation + high dose cyclophosphamide
Tubular interstitial fibrosis	Cisplatin, carboplatin, cyclosporine, FK-506, ifosfamide
Fanconi's syndrome	Ifosfamide

be asked by surgeon to aid in management plan after tumor removal [7].

Many tumors metastasise to kidneys but usually late in the course of the disease and rarely require nephrological intervention.

Most often kidneys are involved in lymphoproliferative malignancies (acute lymphoblastic leukemia and lymphomas). The spread of malignancy to kidneys is usually manifested by proteinuria, hematuria, increased kidney size in imaging studies and impaired renal function. Treatment includes chemotherapy and local irradiation.

Involvement of kidney in hematological malignancies

Kidney failure is present in up to 20-40% of patients with multiple myeloma at the time of presentation [8-10]. A variety of renal disease is associated with multiple myeloma and might present either as acute or chronic renal failure. Most common pathomechanism is due to the overproduction of immunoglobulin light chains. These include myeloma kidney (which refers to renal failure resulting from filtration of light chains, that lead to a formation of intratubular casts and are toxic to tubular cells), light chain deposition disease, primary amyloidosis, and tubulopathies.

Other renal problems observed in multiple myeloma are hypercalcemia, radiocontrast nephropathy, acute urate nephropathy, direct invasion of the kidneys by neoplastic cells and cryoglobulinemia [10].

This topics is the subject of a separate presentation during present symposium and therefore will not be covered in detail.

Drugs used in cancer patients

Both chemotherapeutics used to treat malignancy and other drugs commonly used to treat complications may induce renal damage. *Tab. 3* shows typical clinical syndromes seen with different drugs

Tumor lysis syndrome

Is characterized by electrolyte abnormalities and frequently acute renal failure. It usually occurs in patients with lymphoproliferative malignancies, most often after initiation of treatment, when massive lysis of tumor cell generates large amounts of uric acid, potassium, and phosphate. Tubular obstruction by uric acid and calcium phosphate crystals may cause acute renal failure. Treatment includes intravenous hydration; alkalinization of urine; use of allopurinol or recombinant urate oxidase; lowering serum potassium levels; and dialysis if necessary [11].

Radiation nephritis

Usually develops 6 to 12 months after kidneys receive dosesgreater than 2000cGy most often in patients receiving whole abdominal radiation therapy or in the bone marrow transplantation setting [12,13]. It manifests with impaired renal function, hypertension, and often with hematuria, oliguria, fatigue, and renal atrophy. Chronic radiation nephropathy develops 10 to 15 years after radiation treatments, and present as chronic interstitial nephritis. Urinary sediment is usually bland. Treatment of radiation nephropathy is limited to the control of elevated blood pressure [13].

Renovascular disease

Thrombotic microangiopathies (TTP and HUS) are closely related disorders presenting as a triad of ARF, thrombocytopenia and hemolytic anemia. In patient with malignancy they may be caused by some types of tumors or by drugs used in chemotherapy [14]. Treatment is directed to the removal of culprit and occasionally plasmapheresis is necessary [14].

Renal venous thrombosis in a cancer patient may be a consequence of tumor growth, hypercoagulability, nephritic syndrome or massive hyperleukocytosis [15,16].

Fluid and electrolyte abnormalities

Most common fluid and electrolyte abnormalities include hyponatremia, hyperkalemia, hypercalcemia and polyuria but almost any electrolyte abnormality may be encountered in cancer patient. Electrolyte abnormalities may be associated with hormonal changes induced by neoplasia (*Tab. 2*), tumor lysis syndrome, treatment (*Tab. 3*) or spread of cancer to bones.

Bone marrow transplantation

Occasionally nephrologist might be called to consult a bone marrow transplant (BMT) recipient. The spectrum of renal involvement in such a patient encompasses most of the aforementioned diseases. Most frequent are ARF, CRF, thrombotic microangiopathies (TTP, HUS) and hepatic veno-oclusive disease (VOD).

Acute deterioration in renal function (defined as doubling serum creatinine) develops in about 50% of the patients after successful BMT, usually as results of sepsis, urinary tract infection, nephrotoxic drugs or in association with VOD [17,18]. VOD usually develops 2 to 3 weeks after BMT and its clinical picture resembles that of hepato-renal syndrome.

Similarly to recipients of solid organs, BMT patients may develop nephrotoxicity associated with calcineurin inhibitors therapy (cyclosporine, tacrolimus), although chronic calcineurin inhibitors nephrotoxicity is less frequent, because these drugs are given in full doses to stable patients for shorter periods of time, than in solid organ recipients. This does not hold true for cases when graft-versus-host disease develops. Late-onset renal failure occurs in up to 20% of survivors of BMT as a consequence of the so-called bone marrow transplant nephropathy [12].

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