# 8 Acute Kidney Injury and Cancer: Incidence, Pathophysiology, Prevention/Treatment, and Outcomes

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## 8.1 Introduction

Acute kidney injury (AKI) is an important complication of cancer and its treatment [1] [1–3].

Although AKI in the cancer patient is often multifactorial, it is useful to consider the causes of AKI in the traditional categories of prerenal, intrarenal, and postrenal [1]. These are summarized in Table 8.1. Risk factors which predispose to AKI in the cancer patient include advanced age, pre-existing renal disease, hypovolemia, intrinsic nephrotoxicity of a given chemotherapy drug, the cumulative dose received of that drug, and exposure to other nephrotoxins such as non-steroidal anti-inflammatory drugs (NSAIDs). Not only does AKI complicate the general management of the cancer patient, but it can delay or prevent administration of optimal anticancer therapy. As in many areas of medical practice, the development of AKI is generally associated with a poorer overall prognosis.

## 8.2 Prerenal AKI

Hypovolemia is a common complication of cancer. Fluid intake may be inadequate due to anorexia from the underlying disease or from the chemotherapy. Cancers involving the abdomen and pelvis—particularly when advanced—can cause small bowel obstruction (an example being ovarian cancer with peritoneal metastases). The chemotherapy may directly cause vomiting and diarrhea. Hypercalcemia of malignancy can exacerbate volume depletion.

Anticancer drugs can cause renal hypoperfusion and prerenal AKI by other mechanisms. High-dose interleukin-2 can cause a capillary leak syndrome (and nausea + vomiting), leading to reduced effective circulatory volume. Cancer patients are at increased risk of NSAID-induced prerenal syndromes because (a) NSAIDs are often prescribed to treat cancer pain and (b) hypovolemia is common in these patients. The topic of NSAID-induced AKI is discussed in more detail in Chap. 9.

### 8.2.1 Hepatorenal Syndrome

Hepatorenal syndrome can be a rare complication of massive liver infiltration by tumor cells. Occasional cases occur because of severe drug-induced hepatitis, e.g., with erlotinib, a tyrosine kinase inhibitor. Hepatorenal syndrome is most

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**Table 8.1** Causes of AKI in the cancer patient

| |
|---|
| **Prerenal** |
| Hypovolemia (poor fluid intake, vomiting, diarrhea, capillary leak syndrome with IL2) |
| NSAIDs |
| Hypercalcemia |
| Hepatorenal syndrome (after HCT, massive infiltration by cancer cells) |
| **Intrarenal** |
| *Glomerular* |
| Rapidly progressive glomerulonephritis syndromes (rare) |
| Collapsing glomerulopathy (IV bisphosphonates, interferon) |
| *Tubulointerstitial* |
| ATN due to septic or hypovolemic shock |
| ATN due to IV contrast |
| ATN due to drugs (cisplatin, ifosfamide, zoledronate) |
| Acute cast nephropathy (myeloma)[a] |
| Tumor lysis syndrome (uric acid and calcium-phosphate deposition)[a] |
| High-dose methotrexate[a] |
| Interstitial nephritis (immune checkpoint inhibitors such as ipilimumab, nivolumab, and pembrolizumab) |
| Lysozymuria |
| *Vascular* |
| HUS (gemcitabine, mitomycin C, and other drugs; conditioning regimen for allogeneic HCT)<br>Anti-VEGF inhibitors and tyrosine kinase inhibitors |
| **Postrenal** |
| Obstruction of both urinary tracts by urological and non-urological cancers |
| Retroperitoneal fibrosis |
| **Other** |
| Bilateral nephrectomy (renal cancer) |
| Massive infiltration of kidneys by lymphoma<br>Partial or total nephrectomy for renal cell carcinoma |

This list is not exhaustive
*ATN* acute tubular necrosis, *HCT* hematopoietic cell transplantation
[a]Associated with both tubular injury and tubular obstruction

commonly seen after myeloablative hematopoietic cell transplantation.

### 8.2.2 Hypercalcemia

Hypercalcemia is a relatively common complication of malignancy and indeed may be its presenting feature [2, 4]. Most cases of cancer-associated hypercalcemia are due to release of parathyroid hormone-related peptide (PTHrp) or local bone breakdown (mediated by cytokines)—see Table 8.2. Rarely, hypercalcemia is due to ectopic production of 1,25-dihydroxyvitamin D (calcitriol) in patients with lymphoma. AKI associated with hypercalcemia is predominantly due to renal vasoconstriction and hypovolemia. Treatment typically involves large volumes of normal saline (followed later by loop diuretics), high-dose bisphosphonates, steroids (where the tumor is presumed to be steroid sensitive, e.g., myeloma or lymphoma), and treatment of the underlying disease. Occasionally, oliguric AKI associated with severe hypercalcemia is treated with hemodialysis with a low calcium dialysate. In general, the renal prognosis is good because the hypercalcemia is usually reversible. The overall prognosis is frequently poor, however.

**Table 8.2** Causes of hypercalcemia in the cancer patient

| Type | Approximate % of total cases | Typical cancers | Bone metastases | Mediators |
|---|---|---|---|---|
| Humoral hypercalcemia of malignancy | 80 | Squamous cell cancers (of the lung, head + neck, uterine cervix), ovarian cancer, renal cancer | Minimal | PTH-related protein (PTHrP) |
| Local bone breakdown | 20 | Multiple myeloma, breast cancer, lymphoma | Extensive | Cytokines, chemokines |
| Excess 1,25 vitamin D3 | <1 | Lymphomas | Variable | 1,25 vitamin D3 |
| Ectopic PTH | <1 | Various | Variable | PTH |

## 8.3 Intrarenal AKI

Cancer and its treatment are associated with multiple intrarenal causes of AKI which can be subdivided into glomerular, tubulointerstitial, and vascular—see Table 8.1.

### 8.3.1 Glomerular Diseases

In general, cancer-associated glomerular disease tends to present with proteinuric syndromes and/or subacute deterioration in renal function (rather than AKI; see "angiogenesis inhibitors" below). Well-described—but rare—examples of such presentations are tumor-associated membranous nephropathy and minimal change disease. Light chain deposition disease and amyloidosis are well-known complications of myeloma and other forms of monoclonal gammopathy. Again, "pure" AKI with these conditions is rare.

Other glomerular diseases (membranoproliferative glomerulonephritis, ANCA-associated vasculitis) have been reported in patients with cancer, although the association overall is not strong. In patients with membranoproliferative glomerulonephritis, however, an underlying monoclonal gammopathy should always be excluded.

One glomerular disease that has been described almost exclusively in cancer patients is bisphosphonate-induced collapsing focal segmental glomerulosclerosis (FSGS). This form of FSGS is thought to be a direct toxic effect of high doses of intravenous bisphosphonates, particularly pamidronate (historically, cancer patients tended to receive higher doses of bisphosphonates than other non-cancer patients). Patients with this form of kidney damage typically present with nephrotic syndrome and renal failure [3, 5]. Stopping the bisphosphonate may improve renal function somewhat, but many patients have residual CKD. This complication can be minimized by avoiding very high-dose bisphosphonate regimens (especially in patients with pre-existing renal disease), administering the drug slowly and with IV fluids, and monitoring the patient's plasma creatinine and urinalysis. Another clue to bisphosphonate "overdose" is the development of hypocalcemia. Fortunately, bisphosphonate nephrotoxicity appears to be less common because of greater awareness of this significant adverse effect.

### 8.3.2 Tubulointerstitial Diseases

Acute tubular necrosis may occur (just as in any patient) after inadequate renal perfusion associated with the shock syndromes (hypovolemic, septic, or cardiogenic shock). Again, cancer patients are more at risk of hypovolemic and septic shock due to their underlying diagnosis and the toxic effects of chemotherapy (neutropenia, mucositis, etc.). The management of AKI from ATN in this setting is broadly similar to that of the non-cancer patient. Acute tubular injury/necrosis may also have more "cancer-specific" causes—typically nephrotoxic effects of a chemotherapy drug or of a toxic substance released by the tumor cells. General measures to prevent chemotherapy nephrotoxicity are summarized in Table 8.3.

**Table 8.3** General strategies to minimize the nephrotoxicity of chemotherapy

| |
|---|
| Avoid supra-therapeutic doses |
| Adjust dose for lower GFR |
| Administer high volumes of NS or other solution to maintain high urine output before/during/after infusion of drug |
| Monitor patient for rising creatinine and proteinuria; consider switching or postponing therapy if these occur |
| Avoid other nephrotoxins such as NSAIDs |

*NS* normal saline

AKI due to acute interstitial nephritis has recently been associated with a new class of drug called immune checkpoint inhibitors. These drugs function—at least in part—by unblocking checkpoints in the patient's immune response. Not surprisingly, severe inflammatory reactions have been reported in a number of organs including the kidneys, lungs, and GI tract [3, 6].

### 8.3.3 Cisplatin

Cisplatin, commonly used in the treatment of solid organ cancer, is associated with dose-related nephrotoxicity [4, 7]. Its nephrotoxic effects include AKI, CKD, Fanconi-like syndrome, and magnesium wasting. Hemolytic uremic syndrome (HUS) has been reported when cisplatin is combined with gemcitabine or bleomycin.

Typically, the patient presents with non-oliguric AKI after repeated exposure to cisplatin. Hypomagnesemia is common. There may be other evidence of tubular injury such as glycosuria and hypophosphatemia. Prevention involves adequate hydration at the time of administration and monitoring plasma creatinine. Worsening renal function may prompt a switch to a less nephrotoxic alternative such as carboplatin. Some degree of renal dysfunction and electrolyte wasting may persist for years, even after stopping the offending agent.

### 8.3.4 Ifosfamide

Ifosfamide can also cause severe tubular injury again resulting in AKI, CKD, and electrolyte wasting [4–8]. Nephrotoxicity is associated with higher cumulative doses. Preventive strategies are as described above for cisplatin.

### 8.3.5 Bisphosphonates

High doses of intravenous bisphosphonates, particularly zoledronate, can cause acute tubular necrosis, as opposed to the collapsing glomerulopathy described above [6, 9]. Prevention of this form of AKI is similar to that proposed for the glomerular lesion.

### 8.3.6 Acute (Myeloma) Cast Nephropathy

The term "cast nephropathy" is preferable to the less specific "myeloma kidney." The AKI in acute cast nephropathy is due to a combination of tubular injury and tubular obstruction (by casts containing light chains) [2].

In the healthy person, small amounts of light chains are filtered across the glomerular barrier and resorbed in the proximal tubule. In the setting of massive production of a pathological light chain (i.e., multiple myeloma), the normal kidney resorptive mechanisms are overwhelmed, and the light chains cause direct tubular injury and—when combined with Tamm-Horsfall protein—intratubular obstruction. Risk factors for acute cast nephropathy (in addition to production of a nephrotoxic light chain) include hypovolemia, hypercalcemia, and NSAIDs.

AKI in the setting of myeloma (or presumed myeloma) is a medical emergency. A high index of suspicion for acute cast nephropathy should be entertained in any elderly patient presenting with AKI especially if bone pain, hypercalcemia, anemia, or high plasma globulins are present. Urgent serum electrophoresis, urine electrophoresis (or serum free light chain assay), and bone marrow biopsy should be performed. Immediate treatment includes large volumes of intravenous fluids and treatment of exacerbating factors (hypercalcemia, sepsis, etc.). Where the index of suspicion for acute cast nephropathy is high and results are

pending, dexamethasone therapy should be started immediately. Renal biopsy is sometimes useful in making the diagnosis of cast nephropathy but may not be required where the diagnosis of myeloma is very likely or already known.

Once the diagnosis is established, definitive chemotherapy can be given. The goal of such chemotherapy is *to reduce light chain production as quickly as possible*. Current regimens in this setting usually incorporate the proteasome inhibitor, bortezomib, plus dexamethasone. In theory, extracorporeal removal of light chains might hasten renal recovery. Early small trials of plasmapheresis were somewhat encouraging in this regard, but the most recent randomized controlled trial showed little benefit [7, 10]. Similarly, high cutoff dialysis showed promise in preliminary studies, but a benefit has not yet been shown in larger randomized controlled trials. It should be noted that plasmapheresis *is* useful in the rare cases of AKI due to hyperviscosity syndrome.

In summary, the management of presumed or confirmed acute cast nephropathy involves a high index of suspicion, rapid diagnosis, IV fluids, and early aggressive chemotherapy to rapidly reduce light chain production. Other causes of AKI in the myeloma patient are summarized in Table 8.4.

### 8.3.7 Tumor Lysis Syndrome

TLS is a metabolic syndrome that can complicate cancer treatment but can occasionally arise de novo, in the setting of rapid cell turnover [2].

It is most commonly associated with lymphomas and leukemias but can complicate any rapidly proliferating malignancy, particularly if highly sensitive to chemotherapy. The metabolic abnormalities that occur in TLS result from massive cell death with the release of intracellular contents—see Fig. 8.1. The pathogenesis of the AKI is twofold. Firstly, uric acid crystals are deposited within the renal tubules, causing direct tubular toxicity and intratubular obstruction. Such deposition will be favored by a low ambient pH. Secondly, calcium-phosphate crystals precipitate in the renal parenchyma—this is exacerbated by a high ambient pH.

**Table 8.4** Causes of AKI in the myeloma patient

| |
|---|
| Hypercalcemia |
| NSAIDs |
| Hyperviscosity syndrome |
| Acute cast nephropathy |
| ATN |
| High-dose bisphosphonates |

The typical onset of TLS is within 24–72 h of starting cancer treatment. TLS is characterized by hyperkalemia, hyperphosphatemia, hyperuricemia, hypocalcemia, and AKI. Plasma lactate dehydrogenase (LDH) is also elevated. With appropriate measures TLS is preventable—see also Table 8.5:

(a) Identify those at high risk of developing TLS, e.g., patients with pre-existing renal impairment or hypovolemia and high tumor load with a rapid cell turnover.
(b) Administer large volumes of IV fluids to ensure a high urine output. Typically, normal saline is used because of concerns that sodium bicarbonate solutions might worsen calcium-phosphate deposition (see above). Overuse of bicarbonate solutions might also cause significant hypocalcemia. Intravenous normal saline at >200 mL/h should commence *prior* to starting cancer treatment.
(c) Allopurinol or rasburicase (recombinant uricase) should be started prior to chemotherapy to treat or prevent hyperuricemia. Allopurinol is the less costly option. Note that these drugs do not prevent calcium-phosphate deposition.

Established TLS is a medical emergency. Treatment involves high-volume normal saline to maintain a high urine output and high-dose allopurinol or rasburicase (usually the latter). The metabolic derangements, such as hyperkalemia, should be aggressively treated. In advanced or severe cases, renal replacement therapy should be started early. *High-dose* hemodialysis or CRRT (preferably the former) is required to remove the large amounts of potassium being liberated; high-dose dialysis will also tend to rapidly normalize uric acid, calcium, and phosphate concentrations, thus treating the underlying

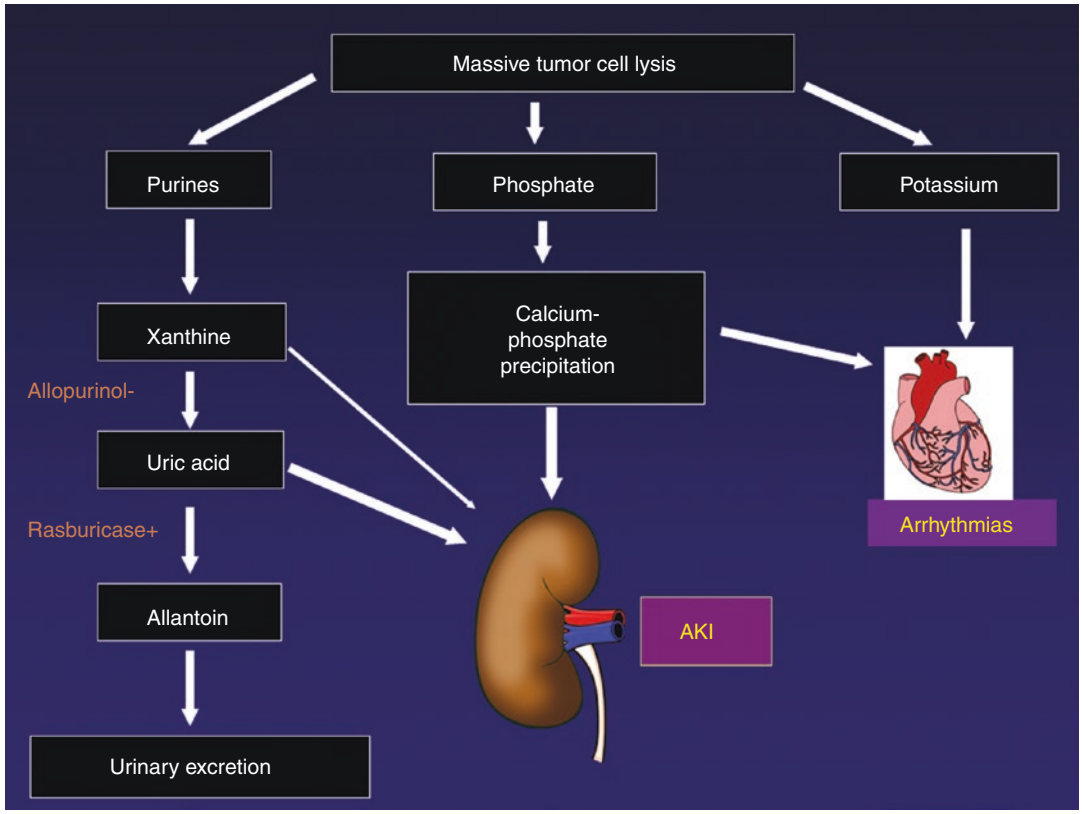


**Fig. 8.1** Pathophysiology of tumor lysis syndrome. The mechanisms by which allopurinol and rasburicase prevent uric acid deposition in the kidneys are also illustrated

**Table 8.5** Prevention of tumor lysis syndrome in the high-risk patient

| Therapy | Comment |
|---|---|
| Large volumes of IV fluids | Aim to keep urine output >150 mL/h |
| Allopurinol | High doses needed. Safe and moderately effective; not expensive |
| Rasburicase | Recombinant form of uricase. Rapid acting, safe, and very effective but expensive. Can be used to treat established cases |

causes of AKI and hastening renal recovery. In general, the renal prognosis with TLS is good, assuming the patient survives the acute event.

### 8.3.8 Methotrexate

High-dose IV methotrexate followed by folinic acid rescue is used in the treatment of certain leukemias, lymphomas, and solid organ cancers. High-dose protocols can cause severe AKI [3].

Nephrotoxicity is not a concern with low or standard dose methotrexate, but at high doses the drug and its metabolites can crystallize in the tubular lumina (causing obstruction and direct tubular damage). Precipitation of the drug is exacerbated by a lower urine pH. The resultant fall in GFR reduces the elimination of methotrexate—potentially exposing the patient to severe toxic effects such as myelosuppression and hepatitis.

Risk factors for methotrexate nephrotoxicity include pre-existing renal impairment, hypovolemia, and a high drug concentration at 72 h post-infusion. As urinary alkalinization reduces the intrarenal precipitation of methotrexate, a bicarbonate-based hydration regimen is recommended for the prevention of nephrotoxicity. This solution should be commenced

*prior* to therapy and continued for 24–48 h after the infusion, aiming to achieve a urinary pH of >7.0.

An acute rise in plasma creatinine during or immediately after methotrexate infusion is usually the first marker of AKI. Established cases are treated with ongoing urinary alkalinization and additional folinic acid. Glucarpidase (a rescue agent, which cleaves methotrexate into nontoxic metabolites) is used in severe cases [8, 11]. Although methotrexate is not readily dialyzable and a rebound in levels occurs after cessation of dialysis, dialysis is sometimes prescribed in severe, established cases of MTX-induced AKI, pending administration of glucarpidase. Early recognition and treatment of this complication is essential.

### 8.3.9 Vascular Diseases

The most common vascular cause of AKI in patients with cancer is hemolytic uremic syndrome (HUS). HUS is a well-described complication of both cancer and its treatment. In some cases, an underlying adenocarcinoma of the stomach, pancreas, or prostate is directly responsible. However, most cases arise in the setting of cancer *plus* chemotherapy. The most frequently implicated chemotherapy drugs are gemcitabine, mitomycin C, and the combination of cisplatin + bleomycin. HUS can also complicate hematopoietic cell transplantation (HCT), particularly if the conditioning regimen includes irradiation and high-dose cyclophosphamide. Other causes of AKI in the patient with HCT are summarized in Table 8.6.

The renal dysfunction in cancer-associated HUS may be acute or subacute and is often associated with severe hypertension. Other clues to the diagnosis are the laboratory features of thrombotic microangiopathy (raised plasma LDH, schistocytes on blood film, falling hemoglobin, falling platelets, low haptoglobin), but these abnormalities can be subtle. The AKI may not manifest until several months after initial exposure to the offending drug (median time to diagnosis in our gemcitabine series was 8 months) [9, 12]. Patients who are receiving the above drugs should have regular monitoring of blood pressure, platelet count, renal function, and LDH. New or exacerbated hypertension is often the first sign of an evolving HUS. Further tests such as serum haptoglobin and blood films can be done when clinical suspicion for HUS is high. Urinalysis typically shows blood and protein. Renal biopsy is occasionally performed when the diagnosis is not apparent. Management involves cessation of the offending agent, control of hypertension, and supportive care. Data to support the use of plasma exchange is lacking, but some centers use it in severe cases. The overall prognosis in cancer patients who develop HUS is often guarded.

**Table 8.6** Types of hematopoietic cell transplant (HCT) and associated AKI

| | Allogeneic myeloablative | Autologous myeloablative | Allogeneic nonmyeloablative |
|---|---|---|---|
| Cancers treated | Many leukemias, lymphomas, myelodysplastic syndromes | Lymphomas, multiple myeloma | As for allogeneic myeloablative |
| Intensity of conditioning regimen | High | High | Low |
| AKI after HCT | Common; sometimes severe | Rare | Common; rarely severe |
| Causes of AKI (usually first 3 months) | HRS, shock syndromes, nephrotoxic drugs[a], CNIs, sirolimus | Shock syndromes, nephrotoxic drugs, occasionally HRS | CNIs |

This list is not exhaustive
*HRS* hepatorenal syndrome, *CNI* calcineurin inhibitor
[a]Aminoglycosides, amphotericin

### 8.3.10 Angiogenesis Inhibitors

Both vascular endothelial growth factor (VEGF) inhibitors (bevacizumab, aflibercept) and tyrosine kinase inhibitors (imatinib and dasatinib) have been reported to cause proteinuria and hypertension. Less commonly, AKI may occur. The predominant histological findings have been renal thrombotic microangiopathy [4] [2, 7].

## 8.4 Postrenal AKI

Postrenal causes of AKI are common and should always be considered in the differential diagnosis of causes of AKI in the cancer patient. Conversely, malignancy should be considered in any patient who presents with bilateral urinary tract obstruction. Obstruction can be intrarenal (intratubular) or extrarenal—only the latter will be associated with hydronephrosis on imaging.

Intratubular obstruction can be caused by light chain casts, uric acid crystals (in tumor lysis syndrome), or crystallization of certain drugs (such as high-dose methotrexate). Acute cast nephropathy, tumor lysis syndrome, and methotrexate nephrotoxicity are discussed above. Maintaining a high urine output in "at-risk" patients is the best way to avoid intratubular precipitation and AKI.

Extrarenal obstruction typically occurs at the level of the ureters or bladder (urethral obstruction is rare). Of course, both urinary tracts must be obstructed for severe AKI to occur, unless the patient has, at baseline, a solitary functioning kidney. Bilateral ureteric obstruction can be caused by a wide range of cancers, most commonly gynecological, gastrointestinal, or urological; its presence usually indicates metastatic (and advanced) disease. Pelvic irradiation and certain malignancies such as lymphomas and sarcoma can cause retroperitoneal fibrosis and ureteric obstruction; here there may be minimal or no hydronephrosis/hydroureter.

The clinical presentation of postrenal failure depends to some extent on the degree, the acuity, and the site of the obstruction. Severe, acute cases may present with oliguria and suprapubic or flank pain. Examination may show an enlarged bladder and/or flank tenderness. There may be other symptoms and signs (such as bone pain) suggesting a diagnosis of cancer. Ultrasound is the initial imaging modality of choice because it is inexpensive, is readily available, involves no IV contrast, and is a sensitive test for hydronephrosis—see Fig. 8.2. It does not, however, provide good visualization of the distal ureters. CT or MRI are often used to define the level of obstruction and to stage the underlying malignancy. Initial treatment involves relief of the obstruction (see Fig. 8.2) and treatment of the underlying malignancy. Nephrostomies and ureteric stenting often result in reasonable recovery of renal function—assuming renal parenchyma is reasonably well preserved at the time of presentation. Unfortunately, the overall prognosis is often guarded because the obstruction is usually due to extensive tumor. The prognosis can be better, however, with lymphoma-induced obstruction; indeed effective treatment of the lymphoma can dramatically reduce tumor and lymph node bulk in the retroperitoneum, allowing safe removal of nephrostomies/stents.

In summary, the general management of postrenal AKI involves:

(a) Making the diagnosis based on history, examination, and basic tests (e.g., ultrasound showing bilateral hydronephrosis)
(b) Where appropriate, excluding prerenal and intrarenal causes
(c) Rapid relief of the obstruction and treatment of its underlying cause

### 8.4.1 Miscellaneous Conditions

#### 8.4.1.1 Bilateral or Unilateral Nephrectomy

Von Hippel-Lindau (VHL) disease is an autosomal dominant condition manifested by a variety of benign and malignant tumors, including clear cell carcinoma of the kidney. Renal cancers may be bilateral—see Fig. 8.3. Bilateral renal call cancers may also occur in the absence of VHL. Although partial nephrectomy and other nephron-sparing treatments are now widely used in such cases, some patients ultimately require

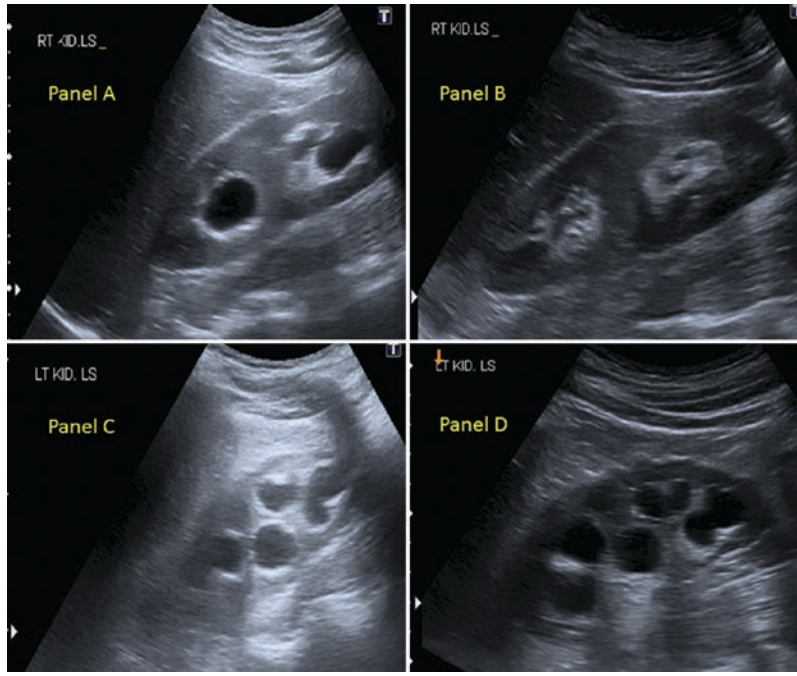


**Fig. 8.2** Ultrasound images of a 70-year-old male who presented with suprapubic discomfort and oliguria and was ultimately diagnosed with prostate adenocarcinoma. Examination showed a palpable suprapubic mass (bladder). Plasma creatinine was 4.3 mg/dL. Insertion of a bladder catheter improved urine output, and creatinine fell, but not to normal. Panels (**a**) and (**b**) show the right kidney before and after insertion of a bladder catheter (resolution of the hydronephrosis). Panels (**c**) and (**d**) show the left kidney before and after insertion of the bladder catheter (persistent hydronephrosis). Further imaging showed obstruction of the left ureter by enlarged lymph nodes. Note the left kidney is also somewhat atrophic

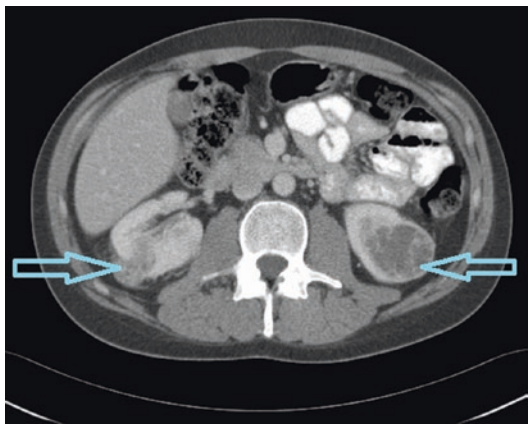

**Fig. 8.3** CT of a 27-year-old male recently diagnosed with intracranial hemangioblastoma. Arrows show complex cysts/masses in both kidneys. The patient ultimately needed bilateral nephrectomy

single and then double nephrectomy. This obviously precipitates the need for dialysis.

Unilateral or partial nephrectomy is often required for the optimal treatment of renal cell carcinoma. Such surgery can precipitate AKI, particularly in the patient with risk factors for renal disease [2, 13].

#### 8.4.1.2 Tumor Infiltration

Metastases to the kidney are not uncommon, particularly on autopsy. However, involvement severe enough to cause AKI requires that both kidneys are extensively involved—this happens occasionally with rapidly growing hematologic malignancies, such as lymphoma or acute leukemia. Affected patients usually present with AKI, a bland urinalysis, and enlarged kidneys. The presence of large kidneys on imaging in a patient with known lymphoma or leukemia is suggestive of tumor infiltration. When large kidneys and AKI are observed in a patient with no known malignancy, the diagnosis can be established by renal biopsy. The renal prognosis depends on the responsiveness of the tumor to therapy. A rapid reduction in kidney size and improvement in renal function may be seen within days if the

tumor responds rapidly to therapy. Appropriate prophylaxis to prevent tumor lysis syndrome is important.

### 8.4.2 AKI after Hematopoietic Cell Transplantation

The general purpose of HCT is to allow administration of otherwise lethal (and ideally curative) doses of chemoradiotherapy, followed by engraftment of stem or progenitor cells for marrow recovery. Most commonly, HCT is used to treat hematologic cancers, but other indications now include certain nonhematologic cancers, severe genetic disorders (such as immunodeficiencies), and severe autoimmune diseases. The three main types of HCT are summarized in Table 8.6. Of note, calcineurin inhibitors are commonly prescribed after forms of allogeneic HCT, to prevent graft-versus-host disease.

AKI is common after HCT, but its incidence and severity depend on the type of HCT (and on the definition of AKI used in reported series) [10, 14]. It is most common after myeloablative allogeneic HCT, reflecting the propensity of this regimen to cause profound immunosuppression (with associated risk of severe sepsis) and liver damage (with associated risk of hepatorenal syndrome); furthermore, CNIs are routinely prescribed for the first 100 days after transplantation. Severe AKI is least common after nonmyeloablative HCT—even though patients are older and sometimes sicker—reflecting the shorter period of pancytopenia and the rarity of severe posttransplant liver disease [10, 14]. The principal cause of AKI in this setting is probably CNI toxicity; severe AKI necessitating dialysis is relatively rare. Myeloablative autologous HCT has an intermediate incidence of AKI. If dialysis is required for severe AKI, the overall prognosis is usually very poor, whatever the type of HCT. Fortunately, rates of AKI appear to be decreasing—probably related to multiple improvements in peritransplant care [11, 15].

Hepatic sinusoidal obstructive syndrome (SOS), also known as veno-occlusive disease of the liver, is one of the most common causes of severe AKI after myeloablative HCT, particularly allogeneic myeloablative HCT. The pathophysiology is thought to involve radiotherapy—and chemotherapy-induced damage to the hepatic venules. Clinically, SOS is manifested as a form of hepatorenal syndrome and usually appears in the first 30 days. In mild to moderate cases, sodium and fluid restriction, diuresis, and analgesia may be required, and the syndrome eventually resolves. Severe SOS complicated by liver and renal failure (and frequently respiratory failure) carries a very high mortality >80% [12, 16]. Treatment involves supportive care (sodium and fluid restriction, avoidance of all hepatotoxins, etc.) and, in severe cases, defibrotide [13, 17]. Hemodialysis or CRRT may be required; the latter has the potential advantages of minimizing changes in intracranial pressure and more easily controlling the large daily obligate fluid intake.

**Conclusion**

AKI is an important complication of cancer and its treatment. As new therapies are constantly being introduced into oncology, physicians need to be aware of the possibility of new nephrotoxic drugs and "new" renal syndromes. Common sense strategies such as identifying the high-risk patient in advance (allowing close monitoring of renal function), minimizing unnecessary exposure to nephrotoxins, and avoiding hypovolemia can prevent some cases of AKI. Early diagnosis and treatment of AKI is important—this is most likely to happen when there is close collaboration between oncologists and nephrologists.

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