organ toxicity of chemotherapeutics

haematological toxicity

Toxic Effect	Anticancer Agents	Diagnostic Findings	Treatments
Anemia	Methotrexate, 5-FU, cytarabine℞, 6-mercaptopurine	Macrocytic anemia with normal levels of vitamin B_{12} and folate	Erythropoietin, blood transfusion
Thrombocytopenia	Nitrosoureas	Onset 4 to 6 weeks after chemotherapy	Transfusions
Marrow hypoplasia	Nitrosoureas, anthracyclines, busulfan ℞	Anemia, thrombocytopenia, leukoneutropenia; nadir between 6 and 15 days after chemotherapy	Transfusions, erythropoietin, growth factors (G-CSF), stem cell reinjection
Thrombotic microangiopathy	Gemcitabine, mitomycin ℞	Mechanical hemolysis (anemia, profound haptoglobin decrease, negative Coombs' test, schizocytes), high levels of LDH and free bilirubin, thrombocytopenia, renal failure	VIP transfusion, plasmapheresis, glucocorticoids, aspirin℞, dialysis
Hemostasis disorders	L-Asparaginase	Decreased PT, increased APTT; decreased fibrinogen, AT III, and plasminogen	Symptomatic: VIP transfusion, injection of AT III
Induced leukemia	Alkylating agents, nitrosoureas, etoposide℞, methotrexate, anthracyclines	AML 2 to 10 years after initial chemotherapy; complex karyotype abnormalities	-
Impaired cell-mediated immunity	2-CdA (cladribine℞, Leustatin), fludarabine (Fludara), pentostatin℞ (Nipent), anti-CD52 (alemtuzumab℞, Campath)	Lymphopenia, opportunistic infections	Prophylaxis for *Pneumocystis carinii* infection

AML, acute myeloid leukemia; APTT, activated partial thromboplastin time; AT III, antithrombin III; 5-FU, 5-fluorouracil; G-CSF, granulocyte colony-stimulating factor; LDH, lactate dehydrogenase; PT, prothrombin time; VIP: virus-inactivated plasma.

neurological toxicity

Toxic Effect	Drugs	Diagnostic Findings	Treatments
Encephalopathies (headache, confusion, seizures)	BiCNU, cisplatin℞, cytarabine℞, 5-FU, ifosfamide℞, asparaginase℞, methotrexate, procarbazine	-	-
Cerebellar syndrome	Cytarabine℞, 5-FU	Clinical, imaging studies	-
Myelopathy (paraplegia, cauda equina syndrome)	Intrathecal methotrexate, cytarabine℞, thiotepa℞	-	-
Peripheral neuropathy	Vincristine, cisplatin℞, and taxanes	Clinical, electrophysiologic testing	Prevention: glutathione, amifostine℞ for cisplatin; pain control
Stroke and cerebral vein thrombosis	Asparaginase℞, high dose methotrexate, BiCNU or cisplatin℞ by intracarotid injection	Clinical, imaging (CT, MRI)	-
Ototoxicity	Cisplatin℞	Audiogram	Amifostine℞, glutathione
SIADH	Vincristine	Low serum sodium	-
Cranial nerve involvement	Vincristine (nerves IV, V, and VI), ifosfamide℞	-	-
Aseptic meningitis	Intrathecal methotrexate and cytarabine℞	Spinal tap	-
Leukoencephalitis	Methotrexate	MRI	Hydration, folinic acid rescue therapy
Ophthalmologic involvement	Cisplatin℞, vincristine	Transient cortical blindness, retrobulbar optic neuropathy, retinal involvement, extraocular nerve palsy	Glutathione IV, amifostine℞

BiCNU, carmustine; CT, computed tomography; 5-FU, 5-fluorouracil; MRI, magnetic resonance imaging; SIADH, syndrome of inappropriate secretion of antidiuretic hormone.

metabolic toxicity

- Metabolic disorders in patients receiving cancer chemotherapy fall into two groups:
(i) disorders related directly to the tumor (e.g., urinary tract compression, spontaneous lysis, syndrome of inappropriate secretion of antidiuretic hormone [SIADH]) and
(ii) disorders related to anticancer agents (e.g., drug-induced tumor lysis, electrolyte disturbances)

- Spindle poisons (eg vincristine, vinblastine) can cause SIADH, often with concomitant peripheral neuropathy and intestinal ileus.
- Alkylating agents such as cyclophosphamide (lymphomas and solid tumors) or melphalan (myelomas) and, more rarely, chlorambucil and thiotepa can induce SIADH.
- Cisplatin (used to treat cancer of the lung, ovary, or testis and relapsing lymphoma) is associated with hyponatremia related to SIADH or tubular wasting in 4% to 10% of patients.

pulmonary toxicity

Diagnostic strategy should follow the rules that apply to all drug-induced lung disorders:
1. Rule out pulmonary edema due to congestive heart failure.
2. Rule out lung infection due to an opportunistic or nonopportunistic organism
3. Rule out lung infiltration by the cancer cells.
4. Check that the time from chemotherapy administration to respiratory symptom onset matches cases reported in the literature and determine whether the respiratory symptoms recur with each chemotherapy course (rechallenge).
5. Check that the clinical manifestations and laboratory test abnormalities are consistent with lung toxicity induced by the suspected drug (intrinsic evidence of causality).
6. Determine whether the symptoms resolve after the drug is stopped and glucocorticoids are given if needed

Bleomycin
- Bleomycin toxicity occurs in 3% to 40% of patients, the lung being the main target.
- Pneumonitis with diffuse infiltrates and fibrosis is the most typical manifestation, and it has a fatal outcome in 1% to 15% of cases
- Established risk factors include:
(i) higher cumulative bleomycin dose
(ii) renal failure.
(iii) age older than 70 years,
(iv) tobacco use,
(v) concomitant radiation therapy to the chest,
(vi) use of high fractional concentrations of inspired oxygen (often during surgery), and
(vii) concomitant use of G-CSF or of other cancer chemotherapy agents exhibiting lung toxicity

Methotrexate:
- Methotrexate causes acute or subacute pneumonitis simulating an infection, usually with interstitial involvement, in 1% to 7% of patients.

Other drugs:
- With fludarabine, lung toxicity occurs in 8% of patients.
- Gemcitabine use causes pulmonary toxicity in 5% of patients.
- Within 8 days after cytarabine, respiratory distress of variable severity develops in 13% to 28% of patients.
- Cyclophosphamide leads to clinical lung toxicity in almost 1% of patients.

cardiac toxicity

- Anthracyclines (doxorubicin, daunorubicin, epirubicin, idarubicin, and mitoxantrone) are the main culprit of cardiac toxicity.
- Drugs of the taxane class, most notably paclitaxel , given in combination with anthracyclines, lead to cardiotoxicity which occurs in more than 20% of patients treated with this combination.

- Two clinical presentations can be distinguished based on the timing of symptoms relative to anthracycline therapy-acute cardiotoxicity and chronic cardiotoxicity, which may be early (subacute) or delayed.

- Acute cardiotoxicity manifests as a rapid deterioration in cardiac function during or within 1 week after the administration of anthracycline therapy, usually with reversal of the abnormalities after discontinuation of the drug (occurs in fewer than 1% of patients).

- Chronic cardiotoxicity is far more common.
- The subacute form is characterized by irreversible dilated cardiomyopathy within 1 year after anthracycline discontinuation; the delayed form develops insidiously after more than 1 year and runs a slowly progressive course.

renal & urological toxicity

Toxic Effect	Drugs	Diagnostic Findings	Treatments
Chronic renal failure (cumulative dose)	Carmustine℞, semustine, streptozocin℞, platin derivatives, ifosfamide℞, pentostatin℞	Renal biopsy	Discontinuation of the anticancer agent
Acute renal failure	Methotrexate	-	Prevention: appropriate hydration, urine alkalinization
Glomerular disease	Carmustine℞, semustine, streptozocin℞	-	-
Tubular disease	Streptozocin℞, cisplatin℞, carboplatin℞, ifosfamide℞, cytarabine℞	Hypophosphatemia, hypokalemia, hypomagnesemia, hypouricemia, metabolic acidosis, glucosuria, aminoaciduria	Hyperhydration and forced diuresis for platin derivatives; amifostine; thiosulfate sodium
Hemorrhagic cystitis	Ifosfamide℞, cyclophosphamide℞	-	Hyperhydration, mesna ℞
Dysuria, hematuria	Methotrexate, pentostatin ℞	-	Appropriate hydration