**General Oncology Issues**

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1. A 14-year-old boy of Middle Eastern descent presents with a history of fever, abdominal distension, and decreased urine output. His serum creatinine is 1.5 mg/dL, serum uric acid is 13 mg/dL, and serum LDH is 900 U/L. You suspect Burkitt lymphoma and would like to request computed tomography of his abdomen with intravenous contrast. However, his renal function precludes obtaining the study. You institute intravenous hydration and plan to administer rasburicase to rapidly bring down his serum uric acid.

Before administering rasburicase, which of the following is it imperative that you obtain?

A. Thiopurine s-methyltransferase status

B. Pyruvate kinase status

C. Uridine diphosphate glucuronosyltransferase 1 isoform A1 status

D. Glucose-6-phosphate dehydrogenase status

E. Adenosine deaminase status

**Explanation**

Rasburicase is contraindicated in patients with known G6PD deficiency because it can cause severe hemolytic anemia.

2. A 2-month-old baby girl is found to have a small, hard mass on her scalp. The mass grows in size over the next 4 weeks, after which a biopsy is performed that confirms a diagnosis of embryonal rhabdomyosarcoma. You would like to start the patient on chemotherapy with vincristine, dactinomycin, and cyclophosphamide.

What is the most appropriate dosage of vincristine to administer?

A. Full dosage based on body surface area

B. Half dosage based on body surface area

C. Half dosage based on weight

D. Three-fourths dosage based on weight

E. Full dosage based on weight

**Explanation**

Infants have a proportionately larger body surface area, and chemotherapy dosages are based on body weight. Vincristine is metabolized in the liver, and newborns have hepatic immaturity. Therefore, vincristine is dosed at 50% of the calculated dosage based on body weight.

3. A 5-year-old boy with history of stage III favorable Wilms tumor of the left kidney treated with vincristine, dactinomycin, and doxorubicin for 24 weeks and left flank radiation relapses in both lungs 9 months after completion of primary treatment. You plan to treat his relapse with ifosfamide, carboplatin, and etoposide chemotherapy. His measured glomerular filtration rate is 65 mL/min/1.73 m2.

What is the most appropriate measure to prevent prolonged thrombocytopenia?

A. Target area under the concentration-time curve (AUC) for carboplatin dosage.

B. Premedicate with dexamethasone and ranitidine before etoposide.

C. Administer ifosfamide as a continuous infusion.

D. Divide carboplatin over 3 days.

E. Reduce ifosfamide dosage by 25%.

**Explanation**

Carboplatin is cleared primarily by the kidneys, and myelotoxicity is dose limiting. Thrombocytopenia is directly proportional to carboplatin drug exposure as measured by the AUC.

4. A 4-year-old child being treated for acute lymphoblastic leukemia is found to be heterozygous deficient for the enzyme thiopurine methyl transferase (TPMT). Based on this finding, what would be the best dosing guidance for administration of mercaptopurine?

A. Administer no more than 10% of the usual dosage and observe closely for myelosuppression.

B. Administer 50% of the standard mercaptopurine dosage and observe closely for myelosuppression.

C. Monitor red blood cell thioguanine nucleotides to avoid toxic concentrations.

D. Consider a small dosage reduction of mercaptopurine and modify dosing based on peripheral blood counts.

E. Switch to thioguanine in place of mercaptopurine.

**Explanation**

Only patients who are homozygous-deficient for TPMT need major dosage reductions; usually no more than 10% of the usual dosage of mercaptopurine is then administered. Although tolerance to mercaptopurine is diminished in heterozygotes, overall the drug remains reasonably well tolerated and can be managed based on the peripheral blood counts.

5. A 15-month-old child is diagnosed with standard-risk acute lymphoblastic leukemia. On what should the dosage of intrathecal chemotherapy that this patient receives be based?

A. Age

B. Body surface area

C. Weight

D. Body mass index

E. Head circumference

**Explanation**

Cerebrospinal fluid volume has been shown to correlate with patient age and not size and remains fairly constant above 3 years of age. Therefore, intrathecal dosing is age-based.

6. A 15-year-old girl is being treated for localized osteosarcoma of the left distal femur and received high-dose methotrexate. Her serum creatinine increased three times over baseline 24 hours after methotrexate administration, and her serum methotrexate level at 24 hours was 100 µmol/L.

What is the most effective way to rapidly decrease serum methotrexate level?

A. Double the leucovorin dosage for rescue.

B. Increase the frequency of leucovorin rescue from every 6 hours to every 3 hours.

C. Order hemodialysis.

D. Administer glucarpidase.

E. Increase IV hydration and give bicarbonate bolus infusion.

**Explanation**

Glucarpidase is a carboxypeptidase enzyme indicated for the treatment of toxic plasma methotrexate concentrations (more than 1 µmol per liter) in patients with delayed methotrexate clearance due to impaired renal function and is administered as a single intravenous injection of 50 U/kg. It is a recombinant bacterial enzyme that hydrolyzes the carboxyl-terminal glutamate residue from folic acid and classic antifolates such as methotrexate. Glucarpidase converts methotrexate to its inactive metabolites 4-deoxy-4-amino-N10-methylpteroic acid and glutamate. It provides an alternative nonrenal pathway for methotrexate elimination in patients with renal dysfunction during high-dose methotrexate treatment. Leucovorin rescue should be continued even when glucarpidase is administered but should not be given within a 2-hour time period before and after glucarpidase because it is a competing substrate.

7. A 16-year-old girl with relapsed rhabdomyosarcoma received vincristine, irinotecan, and temozolomide. She developed grade 3 abdominal pain and diarrhea that resolved with loperamide therapy after a period of 1 week. When she is due for her next course of chemotherapy, she is started on cefixime to decrease the risk of gastrointestinal toxicity.

What is the rationale for using cefixime?

A. Cefixime decreases the conversion of irinotecan to its active metabolite, SN-38, which causes diarrhea.

B. Cefixime decreases the excretion of SN-38 in the bile, thus decreasing the incidence of diarrhea.

C. Cefixime decreases intestinal bacteria that are responsible for deconjugating SN-38 glucuronide.

D. Cefixime promotes healing of the small intestinal brush border that is damaged by SN-38.

E. Cefixime increases the transit of SN-38 through the gut, resulting in decreased diarrhea.

**Explanation**

Irinotecan is a prodrug that is converted by carboxylesterases in the liver and intestinal tract to the active metabolite SN-38. SN-38 is conjugated to SN-38 glucuronide (SN-38G) by hepatic uridine diphosphate glucuronosyltransferase 1A1 and excreted in the bile. Intestinal bacteria produce β-glucuronidase, which deconjugates SN-38G to SN-38, which may be responsible for the delayed diarrhea from irinotecan.

8. An 18-year-old man with localized osteosarcoma of the tibia is due to receive week 10 of chemotherapy with high-dose methotrexate.

Which of the following is an absolute contraindication to proceeding with high-dose methotrexate therapy?

A. Serum AST and ALT that are 10 times upper limit of normal

B. Serum creatinine of 2.2 g/dL

C. Platelet count of 60,000/mm3

D. Grade 1 mucositis

E. History of transient hemiparesis associated with previous dose of high-dose methotrexate

**Explanation**

Methotrexate is excreted primarily through the kidneys. Delayed methotrexate excretion due to impaired renal function can result in severe methotrexate toxicity.

9. A 12-year-old patient with Ewing sarcoma of the chest wall is due to receive chemotherapy with vincristine, doxorubicin, and cyclophosphamide (VDC). The patient has been receiving local radiation therapy Monday through Friday and has 5 more treatment sessions to complete radiation. The patient’s peripheral blood counts are adequate to receive chemotherapy.

How should chemotherapy be administered?

A. Proceed with VDC chemotherapy unmodified.

B. Delay chemotherapy until radiation is completed and then proceed with VDC chemotherapy.

C. Administer VDC chemotherapy with dexrazoxane before doxorubicin infusion.

D. Omit doxorubicin and proceed with vincristine and cyclophosphamide.

E. Replace doxorubicin with dactinomycin.

**Explanation**

Doxorubicin should not be administered during radiation therapy or soon after radiation therapy because of the risk of radiation recall injury. Dactinomycin can also cause radiation recall injury.

10. A 17-year-old patient with metastatic osteosarcoma is being treated with cisplatin, doxorubicin, high-dose methotrexate, ifosfamide, and etoposide. The pain at his primary site rapidly resolves after initiation of chemotherapy. However, after tumor resection he was found to be a poor histological responder despite multiagent chemotherapy. You suspect cross-resistance as a cause.

Which drug is *least* likely to be involved with cross-resistance?

A. Cisplatin

B. Doxorubicin

C. Methotrexate

D. Ifosfamide

E. Etoposide

**Explanation**

Cisplatin and ifosfamide are alkylating agents and are subject to enhanced DNA repair and increased detoxification. Increased multidrug resistance (MDR) expression or MDR gene amplification can result in increased efflux of both doxorubicin and etoposide from tumor cells. Mechanisms of methotrexate resistance are unique and are due to decreased expression of folate transporter, decreased folylpolyglutamyl synthetase, and amplified dihydrofolate reductase.

11. A 13-year-old boy completed treatment for parameningeal alveolar rhabdomyosarcoma with vincristine, dactinomycin, and cyclophosphamide. He presented 3 years later with fatigue, pallor, and easy bruising. CBC reveals pancytopenia. You suspect acute myeloid leukemia secondary to cyclophosphamide.

What cytogenetic abnormality is most likely to be detected in the leukemic blasts?

A. 11q23 translocation

B. Monosomy 7

C. PAX3/FOXO1 fusion

D. Trisomy 8

E. Trisomy 21

**Explanation**

Secondary leukemia induced by alkylating agents such as cyclophosphamide commonly is associated with monosomy 7 and deletion of 5q. Topoisomerase 2 inhibition by etoposide can lead to double-strand DNA breaks that result in translocations involving 11q23.

12. A 9-year-old girl with standard-risk acute lymphoblastic leukemia is due to receive day 8 delayed intensification chemotherapy with vincristine and doxorubicin. The nurse places a peripheral IV catheter and administers doxorubicin as a short infusion over 15 minutes. During the infusion, the girl complains of severe pain at the catheter insertion site. The nurse notes significant swelling and redness distal to the catheter tip and stops the infusion immediately.

What is the appropriate management for this patient?

A. Remove the IV catheter and discharge the patient with instructions to take ibuprofen for pain and call if there are further skin changes.

B. Place ice immediately over the affected area and request a surgical consult for debridement.

C. Administer dexrazoxane IV once daily for 3 days.

D. Inject dimethylsulfoxide (DMSO) locally around the extravasation site.

**Explanation**

Severe skin necrosis is a serious complication of extravasation of certain chemotherapy agents such as anthracyclines, vinca alkaloids, and taxanes. The incidence of chemotherapy extravasation has decreased significantly after the routine use of central venous catheters for chemotherapy administration. Dexrazoxane has been approved for the treatment of extravasation injury due to anthracyclines and prevents significant skin necrosis necessitating surgical debridement in more than 90% of cases by acting as a free radical scavenger and speeding up removal of the extravasated drug from the tissues. It is usually administered at a dosage of 1,000 mg/m2 intravenously on days 1 and 2 and 500 mg/m2 on day 3. Using ice packs is generally discouraged because it decreases blood flow to the region; warm packs may be beneficial. Topical dimethyl sulfoxide (DMSO) is used in nonspecific treatment of chemotherapy extravasation burns.

13. A hematology/oncology fellow is designing a clinical trial for the treatment of high-risk non-Hodgkin lymphoma and is advised to design a 6-week therapy window with two blocks of multiagent chemotherapy (vincristine, doxorubicin, etoposide, cisplatin, and cyclophosphamide) administered 3 weeks apart.

Which of the following is the most rational design?

A. Vincristine/doxorubicin; cisplatin/cyclophosphamide

B. Doxorubicin/etoposide; vincristine/cisplatin

C. Cisplatin/doxorubicin; etoposide/cyclophosphamide

D. Vincristine/etoposide; cyclophosphamide/doxorubicin

**Explanation**

A principle of multiagent chemotherapy is to administer drugs with different mechanisms of action and avoid cross-resistance to maximize cell kill. The most rational choice of regimens above is cisplatin/doxorubicin; etoposide/cyclophosphamide because it combines a topoisomerase inhibitor with an alkylating agent. One of the most important mechanisms of multidrug resistance is overexpression of the MDR-1 gene, which encodes for P-170 membrane glycoprotein, which promotes the efflux of vinca alkaloids, anthracyclines, taxanes, actinomycin D, epipodophyllotoxins, and other natural products from cancer cells. On the other hand, alkylating agents may share cross-resistance related to enhanced DNA repair mediated by nucleotide excision repair enzymes.

14. A 9-year-old girl with Ewing sarcoma who is undernourished is hospitalized to receive a 5-day course of ifosfamide and etoposide and to begin hyperalimentation. She becomes agitated and confused on the second day of chemotherapy and also has some myoclonic jerks.

Which of the following is the most appropriate treatment for these new symptoms?

A. Vitamin B12

B. Methylene blue infusion

C. Activated charcoal

D. Flumazenil

E. Disulfiram

**Explanation**

The patient’s symptoms are likely caused by ifosfamide neurotoxicity. These encephalopathic symptoms are more likely to occur in patients with poor nutrition and decreased renal function and are related to the accumulation of chloroacetaldehyde, which disrupts the mitochondrial respiratory chain, leading to accumulation of NADH. Methylene blue can reverse these symptoms by disrupting the formation of chloroacetaldehyde.

15. A 15-year-old boy with localized osteosarcoma of the right distal femur is being treated with cisplatin, doxorubicin, and high-dose methotrexate chemotherapy. His father reports that the night before he is admitted to the hospital for chemotherapy, his son complains of nausea and vomits several times on his way to the hospital for admission.

Which of the following pharmacotherapeutic agents is most likely to help his symptoms?

A. Ondansetron

B. Aprepitant

C. Dexamethasone

D. Lorazepam

E. Diphenhydramine

**Explanation**

The patient has anticipatory nausea and vomiting due to chemotherapy. There is modest evidence to suggest that benzodiazepines benefit both adult and pediatric patients with anticipatory nausea and vomiting due to chemotherapy. Lorazepam is preferred over alprazolam and diazepam and is recommended at a dosage of 0.04 to 0.08 mg/kg/dose (maximum dose 2 mg), given at bedtime the night before and on the morning of chemotherapy. The dosage may be titrated to minimize sedation and maximize efficacy.

16. A 3-year-old girl presents with a cough and shortness of breath. On physical examination, she has tachypnea and labored respiration, with peripheral oxygen saturations of 94% on room air. A chest X ray reveals whiteout of the left lung field, with a mediastinal shift to the left. A CT scan of the chest shows a solid heterogenous mass occupying most of the left chest, with collapse of the left lung. A CT-guided biopsy reveals a small round blue cell and spindle cell neoplasm with focal areas of rhabdomyoblastic differentiation. The patient has a strong family history of thyroid disease and an older sister who had an ovarian Steroli-Leydig tumor.

You inform the patient’s parents that the patient and her sister have a cancer predisposition secondary to an inherited germline mutation in which of the following genes?

A. TP53

B. NF1

C. SMARCB1

D. DICER1

E. ALK

**Explanation**

Patients with DICER1 germline mutations are at increased risk for malignant and benign tumors that arise in the lungs, kidney, ovary, and thyroid gland. These tumors commonly arise in childhood and are rare in adults and include pleuropulmonary blastoma, cystic nephroma, Steroli-Leydig tumor of the ovary, and multinodular goiter. The DICER1 gene encodes micro-RNA that regulates protein expression.

17. A newborn infant has a birth weight of 4 kilograms and has a large protruding tongue, umbilical hernia, and right-sided hemihypertrophy.

While counseling the child’s parents, you inform them that their child is at risk of the following pediatric malignancies except which one?

A. Hepatoblastoma

B. Wilms tumor

C. Medulloblastoma

D. Rhabdomyosarcoma

E. Neuroblastoma

**Explanation**

The clinical features of the infant are diagnostic of Beckwith-Wiedemann syndrome, which is an overgrowth disorder caused by mutations in the short arm of chromosome 11 (11p15) that leads to overactivity of the IGF2 gene or no active copy of CDKN1C. Causes include paternal uniparental disomy, loss of heterozygosity, maternal gene rearrangement, and DNA methylation. Patients with Beckwith-Wiedemann syndrome are at increased risk of Wilms tumor and several other childhood cancers but not medulloblastoma.

18. A 16-year-old patient with history of high risk B precursor acute lymphoblastic leukemia presents with headache, vomiting, and an upper motor neuron facial nerve palsy. His CBC count is normal, and CSF cytology reveals 300 WBCs/mm3, with 85% blasts that are Tdt positive. Bone marrow aspirate reveals a normocellular marrow with no morphological evidence of leukemia. However, an abnormal B cell population consistent with minimal residual disease of leukemia was detected by flow cytometry. After reinduction chemotherapy, the patient has persistent lymphoblasts in the CSF. The patient is referred to radiation oncology for craniospinal irradiation (CSI).

To ensure coverage of the thecal sac during CSI, the inferior border is best placed at approximately which of the following locations?

A. L3

B. L5

C. S3

D. Coccyx

**Explanation**

For an individual patient, the thecal sac is best determined by the sagittal T2 MRI. At a population level, the mean position is at approximately S2. For coverage with a margin, the most appropriate level to cover is approximately S3. L3 is below the inferior extent of the spinal cord (not the thecal sac).

19. An 8-year-old boy with a newly diagnosed infratemporal parameningeal alveolar rhabdomyosarcoma is referred to radiation oncology for local tumor control. The radiation oncologist recommends proton beam radiation therapy over intensity-modulated radiation therapy with photons.

Which of the following statements is not true regarding proton beam radiation therapy?

A. Protons have a larger mass, resulting in less scatter.

B. Protons are more effective than photons in killing rhabdomyosarcoma cells.

C. Tissue surrounding the tumor receives less radiation, such that there are fewer acute and long-term effects.

D. The radiation dosage is maximum at the Bragg peak.

**Explanation**

Protons are charged particles that are used in external beam radiation to target tumor tissue by using a particle accelerator. Protons are heavier than photons and do not have significant scatter, thereby sparing surrounding normal tissue. The penetration range of protons is controlled by a given energy and is maximum at the Bragg peak. Different energies have different Bragg peaks, and the total radiation dosage with protons is called the spread-out Bragg peak. Proton beam radiation is used for children with brain tumors and many sarcomas to avoid acute and late toxicity caused by damage to surrounding tissue. The effective dosage delivered to the tumor is not different from that of intensity-modulated radiotherapy with photons.

20. A 14-year-old boy presents with cough, shortness of breath, and difficulty lying down. His face and neck swell when his arms are raised. Chest X ray reveals a large mediastinal mass. A tissue diagnosis is desired. A biopsy is performed with local anesthesia because the anesthesiologist thinks that the patient has a very high general anesthesia risk.

Which of the following findings does *not* make general anesthesia unsafe?

A. Tumor diameter greater than 45% of transthoracic diameter

B. Tracheal cross-sectional area less than 50% of predicted

C. Peak expiratory flow rate less than 50% of predicted

D. A malignancy of hematopoietic origin

E. A large pericardial effusion

**Explanation**

There are no standard criteria to predict the severity of superior vena cava syndrome (SVCS). Several studies have evaluated anesthesia complication risks. Great vessel and tracheal compression with increasing respiratory symptoms and signs are predictive of anesthesia complications. SVCS results most often from an anterior mediastinal mass that can be caused by Hodgkin or non-Hodgkin lymphoma, T cell lymphoblastic leukemia, sarcomas, and germ cell tumors. It is usually not caused by neuroblastoma, which can present as a posterior mediastinal mass.

21. An 18-month-old boy is brought in by his parents with a history of vomiting and lethargy. The child is found to be irritable on clinical exam. A CT scan of the brain reveals hydrocephalus with a mass in the right lateral ventricle. The patient undergoes an emergency ventriculostomy, and the mass is biopsied endoscopically. The pathology is consistent with a choroid plexus carcinoma.

Germline testing on this patient is likely to reveal a mutation in which of the following genes?

A. RB1

B. BRCA

C. MSH2

D. TP53

E. NF1

**Explanation**

Li-Fraumeni syndrome (LFS) is characterized by an increased risk of several cancers, particularly in children and young adults. It is caused by a germline mutation in the TP53 gene and is inherited in an autosomal dominant pattern. Classic LFS is diagnosed when all of the following criteria are fulfilled: a sarcoma diagnosed before age 45 years, a first-degree relative with any cancer before age 45, and a second-degree relative being diagnosed with a sarcoma at any age or any cancer before age 45. Chompret criteria for the clinical diagnosis of LFS and indications to test for TP53 germline mutation include any of the following criteria: a tumor belonging to the LFS spectrum (soft tissue sarcoma, osteosarcoma, premenopausal breast cancer, brain tumor, adrenocortical carcinoma, leukemia, or lung bronchoalveolar cancer) before age 46 years *and* at least one first-degree or second-degree relative with an LFS-related tumor (except breast cancer if proband has breast cancer) before age 56 years or with multiple tumors; proband with multiple tumors (except multiple breast tumors), two of which belong to the LFS tumor spectrum and the first of which occurred before age 46 years; or patient with adrenocortical carcinoma or choroid plexus tumor irrespective of family history.

22. A 9-year-old boy is being treated for standard-risk acute lymphoblastic leukemia. His treatment protocol calls for administration of intravenous methotrexate and intramuscular L-asparaginase during interim maintenance chemotherapy.

What is the most appropriate sequence of drug administration?

A. Administer L-asparaginase during the methotrexate infusion.

B. Administer L-asparaginase immediately after the methotrexate infusion

C. Administer both drugs at the same time to maximize synergistic activity.

D. Administer methotrexate 24 hours after the asparaginase.

E. Administer the L-asparaginase 24 hours after the methotrexate.

**Explanation**

L-asparaginase can prevent methotrexate toxicity, probably by interfering with the formation of methotrexate polyglutamates intracellularly. Therefore, L-asparaginase is administered 24 hours after methotrexate and is the rationale behind the Capizzi I regimen. The reverse sequence (L-asparaginase followed by methotrexate) or concomitant administration of both drugs can abrogate the anticancer effect of methotrexate.

23. A 14-year-old Hispanic girl weighing 52 kilograms with localized Ewing sarcoma develops 2+ glucosuria during her fifth course of etoposide and ifosfamide. Her serum glucose at the same time was 160 mg/dL.

What is the most likely cause of the glucosuria?

A. 10% dextrose that is being administered with her IV hydration

B. Dexamethasone that is being administered as an antiemetic

C. Secondary Fanconi syndrome

D. False positive on the urine dipstick

E. Hispanic ethnicity

**Explanation**

The normal tubular maximum for glucose is 180 mg/dL. Ifosfamide can cause a proximal tubular defect that causes wasting of bicarbonate, certain electrolytes such as phosphorus and potassium, and glucose in the urine that usually gets worse with further ifosfamide exposure.

24. Purine analogs and pyrimidine analogs exert their cytotoxic action by being incorporated into DNA during which of the following phases of the cell cycle?

A. G0 phase

B. G1 phase

C. S phase

D. G2 phase

E. M phase

**Explanation**

Antimetabolites interfere directly with DNA synthesis and are therefore cell cycle and S-phase specific. More prolonged drug exposure that results from administering these agents by continuous infusion or by chronic daily dosing increases the chance of exposing a higher proportion of the tumor cell population to drugs during active DNA replication.

25. A 2-year-old boy is being treated for stage III favorable histology Wilms tumor with adjuvant vincristine, dactinomycin, and doxorubicin. He is brought into the emergency department with seizures and lethargy. Serum electrolytes reveal serum sodium of 122 mEq/L.

What is the most likely cause of hyponatremia?

A. Vincristine

B. Dactinomycin

C. Doxorubicin

D. Radiation damage to remaining kidney

E. Hyperperfusion injury to remaining kidney

**Explanation**

The most likely cause is syndrome of inappropriate ADH secretion, which is a known side effect of vincristine.