**Sarcoma**

**David Walterhouse, MD**

**Only using first 15 questions for 2019 R.C.**

1. The pathologist calls you after reviewing a biopsy taken from a lesion in the femur of a 12-year-old girl. The pathologist is confident it is an osteosarcoma based on a specific finding. Which of the following is pathognomonic for osteosarcoma?

A. Small round blue cells

B. Tumor osteoid

C. Patchy CD99 staining

D. Lytic bone lesion

E. Sunburst pattern

**Explanation**

The best answer is B. Tumor osteoid is generally considered pathognomonic for osteosarcoma. Osteosarcoma or Ewing sarcoma may have small round blue cells and on imaging may be lytic bone lesions, although this is more typical of Ewing sarcoma, or have a sunburst pattern, indicating extension of tumor through the periosteum. Diffuse membranous CD99 staining is seen in the majority of Ewing sarcomas, but other tumors may show patchy CD99 staining.

2. A 15-year-old boy presents with a paratesticular mass. A surgeon already has completed an inguinal orchiectomy with removal of the mass, and pathology confirms embryonal rhabdomyosarcoma. Scrotal skin was not involved with the tumor. You order a CT of the chest, abdomen, and pelvis and a PET scan. No other abnormalities are seen.

Which of the following is the most appropriate next step?

A. Begin chemotherapy

B. Surgical assessment of retroperitoneal lymph nodes

C. Surgical assessment of inguinal lymph nodes

D. Bone marrow aspirate

E. Bone scan

**Explanation**

The best answer is B. Approximately 20% of boys 10 years of age or older with paratesticular rhabdomyosarcoma will have pathologic involvement of retroperitoneal lymph nodes even if nodes are not enlarged. Nodal involvement affects therapy and event-free survival. It is recommended that all boys aged 10 years or older undergo retroperitoneal nodal assessment, so answer A is not correct. Paratesticular rhabdomyosarcoma rarely involves inguinal lymph nodes unless scrotal skin is involved. Bone marrow aspirate and bone scan are very rarely positive in T1 embryonal rhabdomyosarcoma. The role of PET scan in assessing involved nodes remains uncertain.

3. You are completing a staging evaluation on a patient with what appeared to be a malignant bone tumor in the left ileum, based on plain film. A biopsy showed fusion-positive Ewing sarcoma. You ordered an MRI of the pelvis, a PET scan, and a chest CT. You find three other lesions in the left ileum on MRI and PET and a 2-mm pulmonary nodule in the right lung on CT scan.

Based on this evaluation, which of the following is most correct?

A. Neither the pulmonary lesion nor the pelvic skip lesions should be considered metastatic disease.

B. The pulmonary lesion but not the pelvic skip lesions should be classified as metastatic disease.

C. The pelvic lesions but not the pulmonary lesion should be classified as metastatic disease.

D. Both the pulmonary lesion and pelvic lesions should be considered metastatic disease.

**Explanation**

The best answer is A. This question addresses the concept of skip lesions and definitions of pulmonary metastases. A skip lesion occurs in the same bone as the primary tumor. For bone sarcomas these generally are not considered distant metastases, but they must be resected or irradiated at the time of local control to the primary tumor. Therefore, the lesions in the ileum are considered skip lesions. Definitions of pulmonary metastases remain arbitrary, and management of small nonspecific lesions in the lungs remains a challenge. Biopsy when possible may be important. Typically, solitary pulmonary nodules greater than 5 mm or multiple nodules greater than 3 mm are considered metastatic disease for bone sarcomas.

4. You are completing staging for a patient with a cheek mass that has been completely resected. Staging studies show no evidence of metastatic disease. The pathologist tells you this is alveolar rhabdomyosarcoma, given small round blue cell morphology and diffuse myogenin staining, but neither the PAX3-FOXO1 nor PAX7-FOXO1 fusion is present.

When discussing this case with the pathologist, what would you conclude:

A. This should be characterized as an undifferentiated sarcoma because the tumor stained for myogenin.

B. This is an embryonal rhabdomyosarcoma, given the morphology and immunostaining pattern in addition to the fact that it is fusion negative.

C. This is an alveolar rhabdomyosarcoma, but fusion testing must be repeated to confirm the diagnosis.

D. This is a fusion-negative alveolar rhabdomyosarcoma, which may be associated with a more favorable outcome.

**Explanation**

The best answer is D. Fusion-negative alveolar rhabdomyosarcoma (ARMS) accounts for up to 20% of cases considered alveolar by morphology and immunostains. These cases may be associated with a more favorable prognosis than cases of fusion-positive alveolar rhabdomyosarcoma. A is not correct because undifferentiated sarcoma is a tumor that is too undifferentiated to place in a specific category. Given the myogenin staining, this is a rhabdomyosarcoma. Embryonal rhabdomyosarcoma is typically a spindle cell tumor with patchy myogenin staining, which rules out B. Alveolar versus embryonal rhabdomyosarcoma are distinguished by morphology and immunohistochemical stains, and to some extent, this is independent of fusion status, which rules out C. The alveolar form is typically a small round cell tumor with diffuse myogenin staining.

5. A patient has been referred to you with a 7-cm high-grade alveolar soft part sarcoma of the posterior thigh. Staging evaluation does not show evidence of metastatic disease. You are considering therapeutic modalities. With which of the following should this patient be treated?

A. Radiotherapy, chemotherapy

B. Surgery, radiotherapy, chemotherapy

C. Radiotherapy

D. Surgery, chemotherapy

E. Surgery, radiotherapy

**Explanation**

Alveolar soft part sarcoma is generally categorized as a nonrhabdomyosarcoma soft tissue sarcoma that is not sensitive to chemotherapy including doxorubicin and ifosfamide. Synovial sarcoma and undifferentiated sarcoma are nonrhabdomyosarcoma soft tissue sarcomas that are considered sensitive to doxorubicin and ifosfamide. The best answer is E. Surgical resection of nonrhabdomyosarcoma soft tissue sarcomas is a critical part of treatment. Radiotherapy is generally used after surgery if margins are positive or for patients with certain risk factors at diagnosis, such as large size (more than 5 cm at the time of presentation) or high grade. A combination of therapy that includes surgery and radiotherapy may be as good as it gets for this case. The role of pazopanib, a tyrosine kinase inhibitor, in nonrhabdomyosarcoma soft tissue sarcoma is under investigation.

6. A 7-year-old presents to a surgeon with a left lower extremity soft tissue mass. The surgeon completely resects the tumor. Pathology shows embryonal rhabdomyosarcoma. The surgeon refers the patient to you for further management. You tell the surgeon that left-sided inguinal lymph nodes should be sampled even though they are not enlarged on imaging or on examination. Pathology shows nodal involvement with tumor.

Which of the following statements is most correct regarding radiotherapy for this patient?

A. The patient does not need radiotherapy.

B. The patient needs radiotherapy to the primary site only.

C. The patient needs radiotherapy to the nodal chain only.

D. The patient needs radiotherapy to the primary site and the nodal chain.

**Explanation**

The best answer is C. Regional node sampling is generally recommended for rhabdomyosarcoma of the extremity. Radiotherapy for rhabdomyosarcoma is usually based on group assignment. The correct group in this case is IIB; the primary tumor has been completely resected, but there is evidence for regional lymph node involvement without remaining gross disease. For group IIB, the nodal chain needs radiotherapy. Answer A is true for group I, which cannot have nodal involvement. Answer B is true for group IIA or III if there is no evidence of nodal involvement. Answer D is true for group IIC or III if there is evidence of nodal involvement.

7. A 14-year-old girl presents to you with left shoulder pain. You treated her 10 years ago for stage 3, group III fusion-positive alveolar rhabdomyosarcoma of the proximal left upper extremity with chemotherapy and radiotherapy. Imaging now shows a tumor with bone and soft tissue components involving the left scapula.

Which of the following is most likely?

A. A recurrence of her alveolar rhabdomyosarcoma

B. A secondary alveolar rhabdomyosarcoma caused by radiotherapy that she received for her original rhabdomyosarcoma

C. An osteosarcoma, indicating that she has Li-Fraumeni familial cancer syndrome

D. An osteosarcoma caused by radiotherapy that she received for her rhabdomyosarcoma

**Explanation**

The best answer is D. Given that the initial histology was fusion-positive alveolar rhabdomyosarcoma, her previous treatment included radiotherapy, and the tumor now involves bone and occurred 10 years later, this is probably a radiation-induced secondary osteosarcoma. Answer A is unlikely because it would be unusual for rhabdomyosarcoma to recur 10 years later. Answer B is unlikely because radiation-induced secondary alveolar rhabdomyosarcoma would be unusual. Answer C is unlikely because rhabdomyosarcoma associated with the Li-Fraumeni familial cancer syndrome is typically embryonal histology with anaplasia.

8. A 5-year-old presents with unilateral proptosis. Imaging shows a tumor confined to the orbit, and biopsy demonstrates embryonal rhabdomyosarcoma. An ophthalmologist asks you for guidance regarding the role of tumor resection.

Which of the following recommendations is most appropriate?

A. Complete resection is associated with a better prognosis, and therefore every effort should be made to completely resect an orbital rhabdomyosarcoma at the time of diagnosis.

B. A surgical approach that does not affect function or cosmesis is preferred for patients with rhabdomyosarcoma, and therefore most orbit rhabdomyosarcomas are not resected.

C. Debulking the tumor at the time of diagnosis, even leaving gross residual disease, will be beneficial because the radiation field will be reduced and will lessen late effects.

D. Neoadjuvant chemotherapy should be given, and after the tumor shrinks it should be resected to eliminate the need for radiotherapy.

**Explanation**

The best answer is B. This question addresses the role of surgery for rhabdomyosarcoma. Generally, surgery that affects function or cosmesis is not recommended. Instead local control is achieved with radiotherapy. These principles also apply to rhabdomyosarcoma of the orbit. Complete resection of most orbit rhabdomyosarcomas at the time of diagnosis, as in answer A, would require orbit exenteration, which affects function and cosmesis. In general, there is not a role for debulking rhabdomyosarcoma, as in answer C. Delayed surgical resection after neoadjuvant chemotherapy is sometimes done for rhabdomyosarcoma, as in answer D, but generally does not eliminate the need for radiotherapy.

9. A 15-year-old has a diagnosis of osteosarcoma of the right distal femur. A CT scan of the chest demonstrates several 1-cm pulmonary nodules, some with calcification. You initiate chemotherapy and tell the patient that surgical resection of the primary tumor will be necessary.

Which of the following is most correct concerning resection of the pulmonary nodules?

A. Surgical resection of remaining pulmonary nodules will be done sometime after the primary has been resected.

B. Radiotherapy will be used to treat the pulmonary nodules after the primary has been resected.

C. If all pulmonary nodules have not resolved at the time that the primary tumor is resected, chemotherapy will be modified.

D. You will obtain a PET scan after several cycles of chemotherapy to determine whether remaining pulmonary nodules require further therapy.

**Explanation**

The best answer is A. This question addresses the role of surgery for metastatic osteosarcoma. In general, therapy with curative intent requires surgical resection of all sites of disease and chemotherapy. Osteosarcoma is quite radiation resistant, and the role for radiotherapy, as in answer B, is limited. Modification of chemotherapy for osteosarcoma based on extent of response, as in answer C, has not been shown to impact outcome. Some pulmonary nodules seen on CT scan may be too small to evaluate with PET scan, as in answer D, which can limit its role. Pulmonary nodules with calcification generally require resection.

10. A 23-year-old patient presents with pain and a 3.5-cm lytic lesion in the talus. Biopsy shows Ewing sarcoma with an EWS-ERG fusion. Staging studies show no evidence of metastatic disease. Which of the following is the most *unfavorable* prognostic feature for this patient?

A. Tumor size

B. Age

C. Bone involvement

D. Stage

E. Fusion-protein

**Explanation**

The correct answer is B. This question addresses prognostic features in Ewing sarcoma. The most important unfavorable prognostic feature for this patient is age greater than 18 years. Tumor size, as in answer A, is a prognostic feature, with tumors larger than 8 cm generally considered unfavorable. Whether a localized Ewing sarcoma arises in bone or soft tissue, as in answer C, has not been clearly shown to affect prognosis. Patients with localized tumors, as in answer D, have a more favorable prognosis than those with metastatic disease. Whether a tumor has a EWS-FLI1 or EWS-ERG fusion, as in answer E, has not been clearly shown to affect prognosis.

11. A mass on the left arm of a 14-year-old girl has been biopsied. The pathologist tells you that the immunostain for desmin is positive but wants to do an additional immunostain to confirm the diagnosis. Which of the following stains would be most helpful to establish the diagnosis?

A. CD99

B. Vimentin

C. Synaptophysin

D. Keratin

E. Myogenin

**Explanation**

The best answer is E. Desmin is positive in tumors with myoblastic components such as rhabdomyosarcoma, myofibroma/myofibromatosis, or inflammatory myofibroblastic tumor. Rhabdomyosarcoma can generally be distinguished from these by morphology. Rhabdomyosarcoma can be distinguished from other spindle cell and small round blue cell tumors of childhood by desmin and myogenin or myoD. Generally, staining for myogenin confirms the diagnosis of rhabdomyosarcoma. CD99 and vimentin are markers for Ewing sarcoma/primitive neuroectodermal tumor (PNET). Keratin can be positive in synovial sarcoma. Synaptophysin may be positive in PNET or neuroblastoma.

12. A 13-year-old was referred to you with a chest mass. After biopsy of the mass, the pathologist tells you that this is a small, round, blue cell tumor and that immunostains are positive for neuron-specific enolase, synaptophysin, and vimentin.

Which of the following findings is most likely to be present in the tumor cells?

A. t(2;13)(q35;q14)

B. t(11;22)(q24;q12)

C. Ring chromosome

D. N-MYC amplification

E. t(X;18)(p11;q11)

**Explanation**

The correct answer is B. The immunohistochemistry results suggest primitive neuroectodermal tumor (PNET). The chromosomal translocation that is characteristic of Ewing family tumors, including PNET, is t(11;22)(q24;q12). The t(2;13)(q35;q14) is characteristic of alveolar rhabdomyosarcoma; the t(X;18)(p11;q11) is characteristic of synovial sarcoma. Ring chromosome is characteristic of a few low-grade mesenchymal tumors, such as parosteal osteosarcoma, and N-MYC amplification is characteristic of neuroblastoma, which would not stain for vimentin.

13. You are reviewing the MRI of a patient with a tumor of the distal femur. The radiologist tells you that the tumor is on the surface of the bone and does not invade the medullary cavity. The radiologist suspects osteosarcoma.

Which of the following do you expect the MRI will suggest?

A. This is not an osteosarcoma, based on the location on the surface of the bone.

B. This is a low-grade osteosarcoma that can be treated with resection alone.

C. This is a high-grade osteosarcoma that can be treated with resection alone.

D. This is an osteosarcoma, and all osteosarcomas require chemotherapy.

**Explanation**

The best answer is B. A surface osteosarcoma that does not invade the medullary cavity suggests the possibility of a low-grade parosteal osteosarcoma, especially in the distal femur. Parosteal osteosarcoma can be treated with resection alone.

14. A 3-month-old infant presents with paraspinal infantile fibrosarcoma. Molecular studies show the presence of a characteristic chromosomal translocation. Based on cytogenetic analysis, this tumor seems to share a genetic origin with which of the following tumors?

A. Mesoblastic nephroma

B. Desmoid tumor

C. Infantile hemangiopericytoma

D. Inflammatory myofibroblastic tumor

E. Malignant rhabdoid tumor

**Explanation**

The correct answer is A. Infantile fibrosarcoma has a t(12;15)(p13;q25). The translocation causes a fusion of the ETV6 transcription factor with the NTRK3 growth factor receptor tyrosine kinase. This leads to constitutive activation of the NTRK3 receptor signaling pathway. Larotrectinib is an inhibitor of NTRK receptors and currently is undergoing investigation for treatment of infantile fibrosarcoma. This translocation also is found in congenital mesoblastic nephroma and secretory breast carcinoma, suggesting a shared genetic origin for these tumors.

15. You are taking care of a 4-year-old child with a stage 3, group III embryonal rhabdomyosarcoma of the bladder. After 12 weeks of therapy with vincristine, dactinomycin, and cyclophosphamide (VAC), you obtain an MRI, and the radiologist tells you that the tumor has not changed in size.

Which of the following treatment approaches should you recommend?

A. Continue with the current chemotherapy regimen, which also calls for local radiotherapy to begin shortly.

B. Change to an alternative chemotherapy regimen and reassess in another 12 weeks.

C. Proceed to exenterative surgery followed by an alternative chemotherapy regimen.

D. Change to an alternative chemotherapy regimen and initiate local radiotherapy.

E. Biopsy the mass and base further decisions on the viability of the tumor.

**Explanation**

The correct answer is A. The presence of a residual mass (either stable disease or partial response) does not have negative prognostic impact for patients with group III rhabdomyosarcoma. For the patient in the question, therapy should continue, and local therapy should be introduced. The distinction between residual tumor cells and maturing rhabdomyoblasts can be challenging on biopsy. There are also no data on which to base a treatment decision given the biopsy results at this point in treatment.

16. A 16-year-old girl is referred to you with an osteoblastic osteosarcoma in the humerus. When taking a history, you learn that she was treated for vaginal rhabdomyosarcoma when she was 2 years old. Which genetic mutation best explains this cancer pattern?

A. Germline LOH at 11p15.5

B. Germline Rb mutation

C. Germline RECQL4 mutation

D. Germline PAX3 mutation

E. Germline p53 mutation

**Explanation**

The correct answer is E. Osteosarcoma and rhabdomyosarcoma are associated with germline p53 mutations as part of the Li-Fraumeni familial cancer syndrome. Germline LOH at 11p15.5 (option A) is associated with Beckwith-Wiedemann syndrome and a predisposition to rhabdomyosarcoma but not osteosarcoma. Germline Rb mutation (option B) is associated with retinoblastoma and secondary sarcomas, which are predominantly osteosarcomas. Germline RECQL4 mutations (option C) are associated with a predisposition to osteosarcoma but not rhabdomyosarcoma. PAX3 mutations (option D) are associated with Waardenburg syndrome and not specifically with cancer.

17. You are caring for a new patient with a large localized Ewing sarcoma of the soft tissues of the arm. The surgeon believes that the tumor can be resected without amputation but asks whether you can give some chemotherapy to shrink the tumor before surgery.

Which of the following would you tell the surgeon?

A. If the tumor can be resected without amputation, then the best time to do the resection is before any chemotherapy in order to improve the prognosis.

B. You agree with waiting to do the resection until week 12 of therapy and will begin chemotherapy; you recognize that radiotherapy will not be necessary if the tumor is completely resected at week 12 of therapy.

C. You agree with waiting to do the resection until week 12 of therapy and will begin chemotherapy; you recognize that radiotherapy will be necessary even if the tumor is completely resected at week 12 of therapy.

D. If the tumor can be resected without amputation, then the best time to do the resection is before any chemotherapy; you recognize that this is the only way to avoid radiotherapy.

**Explanation**

The correct answer is B. Local control of Ewing sarcoma is generally done after chemotherapy has started. Radiotherapy is not necessary if a complete resection is done after the initiation of chemotherapy. This contrasts with rhabdomyosarcoma therapy, where radiotherapy is recommended for most patients after delayed primary resection.

18. A surgeon refers a patient to you with osteosarcoma of the distal femur. He has already completed what appears to be an appropriate and uncomplicated limb-sparing surgical resection. You complete a staging evaluation that shows no evidence for metastases. The patient’s family has learned that most patients receive some chemotherapy before surgery, and they wonder whether their child should have received chemotherapy before surgery. You indicate that the surgeon should have referred the patient to you before surgery.

In addition, which of the following should you also discuss with this patient’s family?

A. You will treat the patient with high-dose methotrexate, doxorubicin, and cisplatin (MAP) chemotherapy, and the outcome will not be adversely affected by the early surgery.

B. The patient’s prognosis is now definitely worse because you will not be able to optimize the chemotherapy regimen based on the response to chemotherapy.

C. You could have administered preoperative chemotherapy, which would have changed the surgical approach dramatically.

D. You will now have to treat the patient with an intensified chemotherapy regimen that was designed for patients with unresectable, metastatic osteosarcoma.

E. You will treat the patient with MAP chemotherapy and optimize local control by using radiotherapy so that the outcome should not be affected.

**Explanation**

The correct answer is A. This question addresses the role of neoadjuvant chemotherapy. Although neoadjuvant therapy has several theoretical advantages, the effect on outcome is less clear. In this case, the prognostic value of histologic response has been lost; however, it has not been shown that modifying chemotherapy can improve outcome for unfavorable responders (less than 90% necrosis) or that regimens containing additional agents (eg, ifosfamide and etoposide) provide an advantage. Because a limb-sparing surgical resection was accomplished in this case without complication, it is unlikely that the surgical approach or result would have changed with neoadjuvant therapy. There is not a role for radiotherapy in such cases.

19. A 10-year-old presents with a localized Ewing sarcoma of the ilium. Which of the following best describes prognostic features for this patient?

1. Pelvic primary site is the single most unfavorable prognostic feature for Ewing sarcoma.
2. Prognosis for this patient depends primarily on whether surgery or radiotherapy is used as local therapy.

C. Prognosis for this patient has improved with the addition of ifosfamide and etoposide to vincristine, doxorubicin, and cyclophosphamide.

D. This patient’s age is a more important negative prognostic factor than the primary site.

**Explanation**

The best answer is C. The most important unfavorable prognostic feature is the presence of metastases. The pelvis is an unfavorable primary site, and older age (older than 18 years) is also unfavorable. In clinical trials, the patients who have benefited the most from the addition of ifosfamide and etoposide are patients with localized tumors in unfavorable primary sites.

*This question is classified as domain 9, subdomain B2, universal task 2.*

20. You are seeing a 16-year-old with a newly diagnosed grade 3 epithelioid sarcoma of the right forearm. After the biopsy, you obtain an MRI of the forearm that shows the mass to be more than 5 cm in size. Staging evaluations ideally include which of the following?

A. Chest CT scan

B. Chest CT scan, bone marrow aspirate/biopsy

C. Chest CT scan, MRI of the regional lymph node bed

D. Chest CT scan, abdominal CT scan

**Explanation**

The best answer is C. Epithelioid sarcoma has a higher rate of nodal involvement than other nonrhabdomyosarcoma soft tissue sarcomas, and evaluation of nodes is recommended for this disease. If there is nodal enlargement on MRI, then biopsy is recommended. Staging for nonrhabdomyosarcoma soft tissue sarcomas also includes a chest CT scan. Bone marrow involvement is rare, and therefore bone marrow aspirate/biopsy are not part of the standard workup.

21. You are treating a patient with localized osteosarcoma of the distal femur with methotrexate, doxorubicin, and cisplatin (MAP) chemotherapy. At week 10 of treatment the patient undergoes complete resection of the tumor. Pathology demonstrates 40% necrosis.

Which of the following is the most appropriate further therapy?

A. Ifosfamide and etoposide (IE)

B. MAP + ifosfamide and etoposide (MAPIE)

C. Gemcitabine docetaxel

D. MAP

E. Sorafenib

**Explanation**

The best answer is D. Percentage necrosis at the time of resection of osteosarcoma has prognostic value, with less than 90% necrosis considered unfavorable. However, a large randomized trial did not show benefit of intensifying MAP therapy with IE (MAPIE). In fact, patients treated with MAPIE had more toxicity, including some evidence of more secondary malignancies. Although all regimens listed here have activity in osteosarcoma, there is no evidence that switching from MAP to any of them after resection benefits the patient. The failure-free survival for patients with poor necrosis treated with MAP is approximately 50%. It is generally recommended to continue therapy with MAP.

22. You are discussing prognosis with the mother of a patient with stage 3, group III rhabdomyosarcoma. Which of the following is the most unfavorable primary site?

A. Extremity

B. Prostate

C. Infratemporal fossa

D. Neck

E. Biliary tree

**Explanation**

The correct answer is A. The biliary tree and neck are favorable primary sites. The extremity, prostate, and infratemporal fossa are unfavorable primary sites. The least favorable of these sites is consistently the extremity.

23. A 12-year-old patient has been referred to you after complete resection with clean margins of a high-grade malignant peripheral nerve sheath tumor of the shoulder region. The tumor measured approximately 4 cm in greatest dimension. A CT scan of the chest and a PET scan were within normal limits. The patient does not have evidence of neurofibromatosis type 1 (NF1).

Which of the following treatment approaches would you recommend?

A. Chemotherapy with doxorubicin and ifosfamide

B. Radiotherapy

C. Chemotherapy with doxorubicin and ifosfamide plus radiotherapy

D. Observation

**Explanation**

The best answer is D. Optimal therapy for nonrhabdomyosarcoma soft tissue sarcomas remains controversial. The benefit of chemotherapy has been difficult to show. Important prognostic factors include size (5 cm or less or greater than 5 cm), grade, and resectability (group). Generally, patients with small tumors (5 cm or less) that are completely resected are observed without further therapy. Radiotherapy is used in the setting of either microscopic or gross residual disease. Chemotherapy, usually with doxorubicin and ifosfamide, is given to patients with large (greater than 5 cm), high-grade, unresectable tumors of some histologic subtypes. Malignant peripheral nerve sheath tumor is not considered very chemotherapy sensitive. NF1 does not generally change the management.

24. You are completing the initial staging workup for a 9-year-old boy with a paratesticular rhabdomyosarcoma. The primary tumor was completely resected at an outside institution by an appropriate surgery. No other imaging studies had been done before the surgery. You now obtain a CT scan that shows enlarged ipsilateral retroperitoneal nodes that, according to the radiologist, obviously are involved with tumor. No metastatic disease was detected on bone scan, bone marrow, or chest CT.

What is the stage and group of this patient if you initiate chemotherapy at this point?

A. Stage 1, group I

B. Stage 1, group II

C. Stage 1, group III

D. Stage 3, group II

E. Stage 4, group IV

**Explanation**

The correct answer is C. Retroperitoneal nodes up to the level of the common iliacs are regional nodes for a paratesticular primary and may be involved for a significant percentage of patients. Involvement of regional nodes is local/regional disease and does not make the patient stage 4, group IV. The paratesticular site is a favorable primary site, and the stage is therefore 1 (not 3, which includes patients with tumors arising in unfavorable primary sites who have regional lymph nodes involved). Because there are grossly enlarged nodes that have not been resected, the correct group is III. The group assignment is II only if all grossly enlarged nodes have been resected.

25. You are seeing a 5-year-old child who presented with nasal congestion. A CT scan shows a 7-cm tumor centered in the parapharyngeal region. A surgeon has already obtained a biopsy that shows alveolar rhabdomyosarcoma.

What are the most appropriate evaluations to determine the extent of the tumor?

A. MRI of the neck, chest CT, bone scan, and bone marrow aspirate/biopsy

B. MRI of the head and neck, chest CT, bone marrow aspirate/biopsy, and CSF cytology

C. MRI of the head and neck, chest CT, bone scan, and bone marrow aspirate/biopsy

D. MRI of the head and neck, chest CT, bone scan, bone marrow aspirate/biopsy, and CSF cytology

E. MRI of the neck, chest CT, bone scan, bone marrow aspirate/biopsy, and CSF cytology

**Explanation**

The best answer is D. Parapharyngeal rhabdomyosarcoma is classified as parameningeal. Alveolar histology is considered unfavorable. Appropriate staging evaluations for parameningeal alveolar rhabdomyosarcoma include an MRI of the primary site, MRI of the head, chest CT, bone scan, bilateral bone marrow aspirates/biopsies, and CSF cytology. All parameningeal tumors need CSF cytology. The role of PET scan continues to be investigated, and PET scans could replace bone scans for this patient.

26. A surgeon refers a patient to you with a 12-cm pelvic mass after doing a biopsy that shows high-grade undifferentiated sarcoma. The surgeon does not think that the tumor can be resected without considerable functional deficit. You discuss further therapeutic options with the surgeon and a radiation oncologist.

Which of the following treatment approaches do you recommend?

A. Upfront chemotherapy followed by resection or radiotherapy, followed by further chemotherapy

B. Upfront resection in order to avoid radiotherapy, followed by chemotherapy

C. Resection alone

D. Radiotherapy alone

**Explanation**

Answer A is the best answer. This is an unresectable high-grade nonrhabdomyosarcoma. There is evidence that undifferentiated sarcomas are chemotherapy sensitive. The approach that is usually taken with a large (more than 5 cm), high-grade, unresectable (group III) chemotherapy-sensitive nonrhabdomyosarcoma soft tissue sarcoma is chemotherapy (doxorubicin and ifosfamide) followed by radiotherapy or resection (if possible), followed by more chemotherapy. Answer B is an approach taken for rhabdomyosarcoma only if the tumor can be resected without significant functional or cosmetic deficits. Answer C is an approach often used for small (5 cm or less) high grade nonrhabdomyosarcoma soft tissue sarcomas generally if there is not significant functional or cosmetic impairment. Answer D is an approach that is sometimes used for small (5 cm or less) grossly resected (margins positive) nonrhabdomyosarcoma soft tissue sarcomas.

27. A 2-year-old girl is receiving chemotherapy with vincristine, dactinomycin, and cyclophosphamide (VAC) for a stage 3, group III rhabdomyosarcoma of the bladder. After her second course of chemotherapy she is admitted to the hospital with right upper quadrant pain, jaundice, abdominal distension, and weight gain.

Which of the following is the most appropriate next step in the evaluation and treatment of this patient?

A. Echocardiogram

B. Nutrition consult

C. Doppler study of the liver

D. Serum hepatitis screen

E. Urinalysis

**Explanation**

The best answer is C. Sinusoidal obstruction syndrome (or veno-occlusive disease or hepatopathy) is a complication of therapy with dactinomycin and cyclophosphamide. Some rhabdomyosarcoma protocols have rates of sinusoidal obstruction syndrome of 4% to 5%. In addition to elevated bilirubin, weight gain, ascites, hepatomegaly, or right upper quadrant pain, sinusoidal obstruction syndrome may show reversal of portal venous flow on Doppler study of the liver.

28. Biopsy of a bone tumor reveals small round blue cells. Immunostains show that the tumor is CD99 positive. RT-PCR did not identify the t(11;22)(q24;q12). The pathologist asks you about the clinical and radiographic features of the case. You state that the patient is an 11-year-old Caucasian girl and that the tumor arises in the diaphysis of the femur and shows an onionskin pattern on imaging.

You and the pathologist decide to do which of the following?

A. Initiate treatment for small round cell osteosarcoma.

B. Repeat the biopsy.

C. Do FISH using FLI1 break-apart probes.

D. Do RT-PCR for the t(1;13)(p36;q14).

E. Do FISH using EWSR break-apart probes.

**Explanation**

The best answer is E. This question addresses the fact that several translocations have been associated with Ewing sarcoma and that different molecular assays are available to detect translocations (RT-PCR and FISH assays). RT-PCR tests for a specific translocation, whereas FISH break-apart testing will demonstrate that a region is involved in a translocation without specifically identifying the partner. Of the choices given, the best next step is to confirm the diagnosis by FISH testing, which could identify any of the translocations involving EWSR. Although more rare, translocation partners for EWSR could include other ETS family members, such as ERG, FEV, ETV1, or E1AF. EWSR is by far the most common partner that has been described for FLI1 in Ewing family tumors. The common element of the different translocations is EWSR and not FLI1, making FLI1 break-apart probes less useful. Tumor osteoid must be present for a diagnosis of small round cell osteosarcoma. The t(1;13)(p36;14) is found in some alveolar rhabdomyosarcomas.