Chapter 36
Bone Sarcomas

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Abstract Bone sarcomas are primary malignant tumors of osteoid producing cells adjacent to growth plates, which arise more frequently in long bones (Clark J, Rocques PJ, Crew AJ et al: Nat Genet 7:502–508, 1994). Unlike soft tissue sarcomas, which have a wide variety of histological subtypes, bone sarcomas have only three distinct categories: chondrosarcoma, Ewing's sarcoma and osteosarcoma. Bone sarcomas are more common in children and young adults, with some exceptions in later years. The management of bone sarcomas varies considerably, according to histology, degree and stage (Devita H: Rosemberg's cancer: principles & practice of oncology. In: VT DV Jr, Lawewnce TS, Rosemberg SA (eds) Chapter 121 with 404 contributing authors, 10th edn. LWW, New York, 2014).

Keywords Bone sarcoma · Chemotherapy · Radiotherapy

36.1 Introduction

Bone sarcomas are primary malignant tumors of osteoid producing cells adjacent to growth plates, which arise more frequently in long bones [1]. Unlike soft tissue sarcomas, which have a wide variety of histological subtypes, bone sarcomas have

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only three distinct categories: chondrosarcoma, Ewing's sarcoma and osteosarcoma. Bone sarcomas are more common in children and young adults, with some exceptions in later years. The management of bone sarcomas varies considerably, according to histology, degree and stage [2].

36.2 Incidence and Etiology

Bone sarcomas are rare tumors which incidence is <1 per 100.000 people living in the United States each year [3]. The specific incidence of chondrosarcoma is not well established, as low grade lesions are relatively common and there are no accurate records. About high-grade osteosarcoma and Ewing's sarcoma, the incidence is about one per million [2].

The etiology of bone sarcomas is not known [4]. Some conditions increase the risk of developing osteosarcoma, such as the TP53 gene mutation in Li-Fraumeni syndrome [5] and the RB1 gene mutation in patients with retinoblastoma [6].

Environmental factors are also related to the genesis of osteosarcomas, such as ionizing radiation wich is responsible for approximately 3% of cases of bone sarcomas. In addition, treatment with alkylating agents is also known to increase the risk of osteosarcoma [4].

Some benign bone conditions predispose to the development of bone sarcoma, such as Paget's disease of bone [7], fibrous dysplasia, McCune-Albright syndrome and Mazabraud's syndrome [8]. Other benign tumors that can be pre-malignant include giant cell tumor, osteoblastoma and synovial chondromatosis [9]. Even nononcological conditions such as chronic osteomyelitis and bone infarcts may progress to sarcomas [10].

36.3 Clinical Presentation

Patients typically present localized pain, some times that can last several months in duration. Other systemic symptoms, such fever, weight loss and malaise are usually not present. On physical examination, a soft tissues mass may be observed, which is often large and tender palpation. Osteosarcomas have a predilection for the metaphyseal region of the long bones. The most common sites of involvement are: distal femur, proximal tibia, proximal humerus, mid and proximal femur and other bones [11].

Laboratory evaluation is usually normal, except for elevations in alkaline phosphatase, lactate dehydrogenase, and erythrocyte sedimentation rate [12].

Between 10% and 20% of patients present macrometastatic disease at diagnosis. Distant metastases most commonly involve the lungs, but can also involve bone [13].

36.4 Diagnosis and Staging

The evaluation for diagnosis and staging should include an imaging examination of the bone involved. Magnetic resonance imaging (MRI) is preferred in most cases, since it has better definition of soft tissues, particularly neurovascular bundle, joint and marrow involvement [14].

Computer tomography (CT) scans are best suited to assess the presence of metastatic disease to the lung, however, they may underestimate the extent of lung involvement [15]. A PET or PET/CT quantifies the metabolic activity at the primary site and helps to exclude ocult metástases. Its utility in the management of patients with osteosarcoma is well established and should be considered to be a standard of care [16].

Supreme caution must be taken regarding the way the biopsy is performed. Percutaneous fine needle or core procedures, especially when guided by imaging, such as ultrasonography, CT or MRI, can be successful in establishing a diagnosis. This method has the advantage maximizing sampling throughout the mass and minimizing contamination. The material obtained should be sufficient to perform all histological, immunohistochemical, cytometric and cytogenetic studies, allowing an accurate diagnosis, therefore, incisional biopsies are often performed, especially in pediatric cases. Excisional biopsy (resection) can be considered for smaller lesions that can be completely excised with negative margins and without functional impairment [17].

Staging should be performed according to the TNM (tumor, nodule, metastasis) guidelines with the principles established by the American Joint Committee on Cancer [18] (Table 36.1).

36.5 Treatment

36.5.1 Chondrosarcoma

Chondrosarcoma is a malignancy of the matrix producing cartilage with diverse morphological characteristics. Chondrosarcoma occurs most frequently between 40 and 70 years of age. When low grade (about 90% of chondrosarcomas), chondrosarcoma rarely metastasize, but can progress to high-grade, which has a higher metastatizing potential [19].

The surgical treatment offers the only chance of cure for all degrees and subtypes of localized chondrosarcoma. The type of surgery varies according to the histological grade, location and size of the tumor. For tumors with high or intermediate grades, local block excision is the treatment of choice [20]. Low-grade tumors can be treated with less extensive surgeries, intend to minimize the functional disability of these patients [21].

Table 36.1 Bone sarcomas TNM staging AJCC UICC 2017

Primary tumor (T)	
Appendicular skeleton, trunk, skull, and facial bones	
T category	T criteria
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor ≤8 cm in greatest dimension
T2	Tumor >8 cm in greatest dimension
T3	Discontinuous tumors in the primary bone site
Spine	
T category	T criteria
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor confined to one vertebral segment or two adjacent vertebral segments
T2	Tumor confined to three adjacent vertebral segments
T3	Tumor confined to four or more adjacent vertebral segments, or any nonadjacent vertebral segments
T4	Extension into the spinal canal or great vessels
T4a	Extension into the spinal canal
T4b	Evidence of gross vascular invasion or tumor thrombus in the great vessels
Pelvis	
T category	T criteria
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor confined to one pelvic segment with no extraosseous extension
T1a	Tumor ≤8 cm in greatest dimension
T1b	Tumor >8 cm in greatest dimension
T2	Tumor confined to one pelvic segment with extraosseous extension or two segments without extraosseous extension
T2a	Tumor ≤8 cm in greatest dimension
T2b	Tumor >8 cm in greatest dimension
T3	Tumor spanning two pelvic segments with extraosseous extension
T3a	Tumor ≤8 cm in greatest dimension
T3b	Tumor >8 cm in greatest dimension
T4	Tumor spanning three pelvic segments or crossing the sacroiliac joint
T4a	Tumor involves sacroiliac joint and extends medial to the sacral neuroforamen
T4b	Tumor encasement of external iliac vessels or presence of gross tumor thrombus in major pelvic vessels
Regional lymph nodes (N)	
N category	N criteria
NX	Regional lymph nodes cannot be assessed.
N0	No regional lymph node metastasis
N1	Regional lymph node metastasis
Distant metastasis (M)	

(continued)

Table 36.1 (continued)

M category	M criteria			
M0	No distant metastasis			
M1	Distant metastasis			
M1a	Lung			
M1b	Bone or other distant sites			
Histologic grade (G)				
G	G definition			
GX	Grade cannot be assessed			
G1	Well differentiated, low grade			
G2	Moderately differentiated, high grade			
G3	Poorly differentiated, high grade			
Prognostic stage groups				
T	N	M	G	Stage group
T1	N0	M0	G1 or GX	IA
T2	N0	M0	G1 or GX	IB
T3	N0	M0	G1 or GX	IB
T1	N0	M0	G2 or G3	IIA
T2	N0	M0	G2 or G3	IIB
T3	N0	M0	G2 or G3	III
Any T	N0	M1a	Any G	IVA
Any T	N1	Any M	Any G	IVB
Any T	Any N	M1b	Any G	IVB

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As the cytotoxicity of radiotherapy is dependent on cell division and most chondrosarcomas have slow growth, these tumors are considered relatively, but not absolutely, radioresistant. Radiotherapy can be beneficial after an incomplete resection of a high-grade chondrosarcoma and in the palliative context, such as in situations where resection is not feasible or would cause an unacceptable morbidity [22].

Chondrosarcomas are considered chemoresistant tumors, and this characteristic can also be attributed to factors such as slow growth, drug resistance genes expression, difficulty of drugs acessing the tumor, because of large amount of extracellular matrix and poor vascularization and high activity of anti-apoptotic and pro-survival pathways [23, 24].

Although most patients with recurrent or metastatic chondrosarcoma do not respond to chemotherapies used for advanced sarcoma, there are isolated cases of successful treatment with ifosfamide alone, doxorubicin-based chemotherapy or single agent methotrexate. The highest benefit being observed in mesenchymal and dedifferentiated chondrosarcoma [25–27].

36.5.2 Ewing's Sarcoma

Ewing's sarcoma (ES) is a small, blue, round-cell tumor, periodic acid-Schiff positive, and CD99 positive. All ESs are high grade tumors. Molecular biology studies have shown that almost all of these tumors share a common rearrangement of genes involving the EWS gene on chromosome 22, and in most cases it is a recurrent chromosomal translocation, t(11;22)(q24;q12) [28].

ES is the third most common bone cancer. The incidence is higher in the second decade of life and young adults. The most common tumor sites correspond to the lower extremities (45%) followed by pelvic bones (20–25%) [29].

Despite the fact that fewer than 25% of patients have evident metastases at the time of diagnosis, ES is a systemic disease. Before routine chemotherapy use, almost all early diagnosed ES patients developed distant metastatic disease and eventually died. Chemotherapy can successfully eradicate occult metastases, and current treatment plans include chemotherapy, usually given before and after local treatment [30].

Current standard chemotherapy includes Vincristine, Doxorubicin and Cyclophosphamide (VDC) in alternating cycles with Ifosfamide and Etoposide (IE). Doxorubicin is replaced by Dactinomycin when it reaches the cumulative dose of 375 mg/m^2. Cycles are repeated every 2 weeks, and are supported with granulocyte colony stimulating factor (300mcg/day) to facilitate recovery of the bone marrow. Four to six cycles of chemotherapy are given prior to local therapy and, after local treatment, additional cycles of the same treatment are given postoperatively for a total of 14–17 cycles [31].

The local treatment can be surgery, radiation or both. The choice depends on the patient's characteristics, potential damage and benefit (compensation between the functional outcome and the risk of a secondary radiation-induced malignancy) and patient's preference. There are no randomized trials comparing RT and surgery for local control, however, some retrospective series and a systematic review suggest superior local control with surgery [32].

Patients with metastatic disease at diagnosis often respond to the same type of systemic chemotherapy that is used for localized disease, but they present a significantly worse outcome than those with localized disease. The metastases site is an important variable, with better prognosis for patients with isolated lung and pleural metastases [33]. Unlike the experience for patients with localized disease, adding IE to VDC does not improve outcomes of patients with Ewing's Sarcoma of bone with metástases at diagnosis [34].

Patients with recurrent ES had few treatment options. These patients are candidates for clinical trials of new agents, and may be treated with some salvage chemotherapy regimens with activity documented in this setting. Many patients are treated with the same combination chemotherapy regimen used as part of initial therapy [35]. Other data suggest that a higher dose of ifosfamide may be active in patients with recurrent ES who were treated with lower doses of ifosfamide as part of the initial therapy [36]. Other combinations of active agents are Gemcitabine and Docetaxel [37], Topotecan and Cyclophosphamide [38] and Irinotecan and Temozolomide [39].

36.5.3 Osteosarcoma

Osteosarcomas are primary malignant tumors of the bone, characterized by the production of osteoid or immature bone by malignant cells [40]. Although rare, osteosarcoma is the most common primary neoplasm of bone in children and adolescents and the fifth most common malignant disease among adolescents and young adults [41]. In adults older than 65 years, osteosarcoma develops as a secondary malignancy related to Paget's disease [4]. In general, osteosarcoma is classified into three histological subtypes: intramedullary, surface and extraeskelectal [42].

Although osteosarcomas produce a favorable response to chemotherapy, surgery is essential when a curative treatment is intent [43]. The specific surgical procedure is dictated by the location and extent of the primary tumor [44].

The survival of patients with osteosarcomas has improved dramatically in the last 40 years, and this is due to the use of effective chemotherapy. Prior to the routine use of systemic therapy for conventional osteosarcoma, 80–90% of the patients developed metastases despite local tumor control and died of their disease. It was surmised that at diagnosis most patients already present with micrometastases, which can be successfully eradicated if chemotherapy was administered at a time when the disease burden is low [45]. Chemotherapy plays small role in the management of patients with low grade osteosarcoma or surface [2].

The right time for administration of chemotherapy (pre or postoperative) has not been defined, as there is no difference in survival between the two forms. Neoadjuvant chemotherapy is particularly preferred when a limb sparing procedure is intent [46].

There is no a global consensus about a standard chemotherapy regimen for osteosarcoma. Most of the current regimens use Doxorubicin and Cisplatin with or without high-dose Methotrexate (HDMTX) [47]. The combination of Doxorubicin and Cisplatin is most often offered for older patients [48]. However, the tolerability of high doses of Cisplatin and the role of HDMTX remain unanswered questions. A methotrexate-containing regimen is a reasonable standard of care in this population, if patients can tolerate it. Options include a five-week cycle of cisplatin (100 mg/m^2 day 1) and doxorubicin (25 mg/m^2 days 1–3), followed by two weekly doses of HDMTX (6–12 g/m^2 with leucovorin rescue), with 3 cycles administered preoperatively and three postoperatively [47].

Osteosarcoma is considered relatively resistant to radiation therapy. Primary radiation therapy is often inadequate to achieve local control. Whenever possible, surgery is preferred for local control. For patients with tumors in challenging axial sites (skull, spine, sacral base), radiotherapy may be a local control option when surgery is not performed [49].

The prognosis of patients presenting with metastatic disease is poor, contrasting with patients with localized disease [50]. The localization of metastases has prognostic importance, with better results for patients with lung-only metastases [47], and the ability to control all sites of macroscopic disease is essential for successful treatment [51].

There is no single standard approach for the management of patients with metastatic osteosarcoma at diagnosis. The most active drugs are the same used in the metastatic disease setting, however, with low response rates and survival [51].

For patients with resectable metastases at presentation, neoadjuvant chemotherapy is recommended, followed by resection of the primary tumor. Chemotherapy and metastasectomy are included as options for the management of metastatic disease [52].

About 30% of patients with localized disease and 80% of patients with metastatic disease will fail. Some factors may be considered as having a better prognosis, such the presence of single metastases, relapse time and the possibility of complete resection of the metastases [53]. Patients who are not candidates for surgical resection of metastases should be considered for palliative treatment with radiotherapy or chemotherapy [54]. In this setting, combinations of ifosfamide (3 g/m^2/day) and etoposide (75 mg/m^2/day) for 4 days are more active than other agents alone [55]. Cyclophosphamide plus etoposide or gemcitabine plus docetaxel are other options available [56, 57].

Questions

1. **These conditions increase the risk of developing bone sarcomas, except:**

   (a) Paget's disease of bone
   (b) Previous fractures (Answer)
   (c) Fibrous dysplasia
   (d) McCune-Albright syndrome

Comment: Some benign conditions increase the risk of developing bone sarcomas, such as Paget's disease of bone, fibrous dysplasia, McCune-Albright syndrome and Mazabraud's syndrome. Even nononcological conditions such as chronic osteomyelitis and bone infarcts may progress to sarcomas. The only factor that is not related to the increase the risk of developing of bone sarcomas is the existence of a previous fracture.

2. **Among the environmental factors following, it's related to the increased risk of developing osteosarcoma:**

   (a) Ionizing radiation (Answer)
   (b) Smoking
   (c) Alcoholism
   (d) Obesity

Comment: Environmental factors are also known as involved in the genesis of osteosarcomas, such as ionizing radiation, responsible for approximately 3% of cases of bone sarcomas. There are no sufficient data to relate the others factors to the development of osteosarcomas.

3. **Among the laboratory tests below, all may be altered in patients with osteosarcoma, except:**

   (a) Lactate dehydrogenase
   (b) Alkaline phosphatase

(c) Calcium (Answer)
(d) Erythrocyte sedimentation rate

Comment: In patients with bone sarcomas, laboratory abnormalities are not very frequent except for elevations in alkaline phosphatase, lactate dehydrogenase, and erythrocyte sedimentation rate.

4. **About chondrosarcomas, mark the true alternative:**

(a) They are more frequent tumors in children
(b) The most are high grade tumors
(c) They are tumors that never metastasize
(d) They are not responsive to chemotherapy (Answer)

Comment: Chondrosarcoma occurs most frequently between 40 and 70 years of age. About 90% of chondrosarcomas are low grade tumors and they rarely metastasize. Chondrosarcomas are considered chemoresistant tumors, and this characteristic can be attributed to factors such as slow growth, drug resistance genes expression, difficulty of drugs acessing the tumor.

5. **Radiotherapy may be useful in the management of chondrosarcomas in all of the following alternatives, except:**

(a) After a complete resection, in the adjuvante context (Answer)
(b) After an incomplete resection of a high-grade chondrosarcoma
(c) When the resection is not feasible
(d) When the resection would cause an unacceptable morbidity

Comment: Radiotherapy can be beneficial after an incomplete resection of a high-grade chondrosarcoma and in the palliative context, such as in situations where resection is not feasible or would cause an unacceptable morbidity. There is no benefit for treatment with radiotherapy after a complete resection.

6. **Chondrosarcomas are considered chemoresistant tumors. Chose the alternative that not explain this characteristic:**

(a) Drug resistance genes expression.
(b) Slow growth
(c) Tumor heterogeneity (Answer)
(d) Difficulty of drugs acessing the tumor

Comment: Chondrosarcomas are considered chemoresistant tumors, and this characteristic can be attributed to factors such as slow growth, drug resistance genes expression, difficulty of drugs acessing the tumor because of large amount of extracellular matrix and poor vascularization and high activity of anti-apoptotic and pro-survival pathways.

7. **About Ewing's sarcoma, choose the right alternative:**

(a) They are high grade tumors (Answer)
(b) They share a common rearrangement of genes involving the EWS gene on chromosome 19

(c) They are the most common bone cancer
(d) They are more common in elderly people

Comment: All Ewing's Sarcomas are high grade tumors. Molecular biology studies have shown that almost all of these tumors share a common rearrangement of genes involving the EWS gene on chromosome 22, and in most cases it is a recurrent chromosomal translocation, t [11, 22](q24;q12). Ewing's Sarcoma is the third most common bone cancer and the incidence is higher in the second decade? of life and young adults.

8. **About the use of chemotherapy in treatment of Ewing's sarcomas:**

(a) Routine use of chemotherapy did not alter the prognosis of the disease
(b) Because it is a high-grade tumor, has a good response to chemotherapy (Answer)
(c) Chemotherapy is always used in the adjuvant setting
(d) The use of multidrug therapy does not increase the benefit compared to monotherapy

Comment: Before routine chemotherapy use, almost all patients early diagnosed Ewing's Sarcomas developed distant metastatic disease and eventually died, because this is considered a sistemic disease. Chemotherapy can successfully eradicate occult metastases, and current treatment plans include chemotherapy, usually given before and after local treatment, and the standard treatment includes the use of multiple drugs, incluiding Vincristine, Doxorubicin and Cyclophosphamide (VDC) in alternating cycles with Ifosfamide and Etoposide (IE).

9. **Indicate the most appropriate treatment for a patient diagnosed with Ewing sarcoma of the scapula, without evidence of metastatic disease:**

(a) Surgery
(b) Surgery followed by radioterapy
(c) Preoperative chemotherapy (with vincristine, doxorubicin and cyclophosphamide alternating with ifosfamide and etoposide), followed by surgery and adjuvant chemotherapy (Answer)
(d) Preoperative chemotherapy (with vincristine, doxorubicin and cyclophosphamide), followed by surgery and adjuvant chemotherapy.

Comment: Current standard treatment includes Vincristine, Doxorubicin and Cyclophosphamide in alternating cycles with Ifosfamide and Etoposide. Cycles are repeated every 2 weeks for 4–6 cycles before the local therapy and, after local treatment, additional cycles of the same treatment are given postoperatively for a total of 14–17 cycles. The local treatment can be surgery, radiation or both. There are no randomized trials comparing RT and surgery for local control, however, some retrospective series and a systematic review suggest superior local control with surgery.

10. **About osteosarcomas, choose de right alternative:**

    (a) Osteosarcomas are more common in elderly
    (b) In elderly, osteosarcoma can be related to Paget's disease (Answer)
    (c) Osteosarcoma is the third most frequent bone neoplasm
    (d) Osteosarcomas are always low grade tumors

Comment: Osteosarcoma is the most common primary neoplasm of bone in children and adolescents and the fifth most common malignant disease among adolescents and young adults. Otesosarcomas can be low-grade tumors, with better prognosis, or high-grade tumors, with poor prognosis. When osteossarcoma affects the elderly, it can be related to Paget's disease.

11. **About the role of chemotherapy in the treatment of osteosarcoma, choose the correct alternative:**

    (a) The use of chemotherapy does not significantly alter the evolution of patients with osteosarcoma
    (b) Chemotherapy reduces the chance of local recurrence of osteosarcomas
    (c) Routine use of chemotherapy dramatically reduced relapses at a distance (Answer)
    (d) Chemotherapy has an important role in the treatment of low grade osteosarcomas

Comment: The survival of patients with osteosarcomas has improved dramatically in the last 40 years, and this is due to the use of effective chemotherapy, because chemotherapy reduces de risk of distant recurrence. Chemotherapy plays small role in the management of patients with low grade osteosarcoma or surface.

12. **Consider a 28-year-old patient with high-grade osteosarcoma in the left tibia with no evidence of distant metastases. Choose the best treatment strategy for this patient:**

    (a) Surgery
    (b) Radiochemotherapy
    (c) Surgery followed by adjuvant chemotherapy with Cisplatin and Doxorubicin
    (d) Neoadjuvant and adjuvant chemotherapy with Cisplatin, Doxorubicin and high doses of Methotrexate (Answer)

Comment: The right time for administration of chemotherapy (pre or postoperative) has not been defined, as there is no difference in survival between the two forms. Neoadjuvant chemotherapy is particularly preferred when a limb sparing procedure is intente. There is no a global consensus about a standard chemotherapy regimen for osteosarcoma, most of the current regimens use Doxorubicin and Cisplatin with or without high-dose Methotrexate.

13. **About radiotherapy in treatment of osteosarcoma, check the right alternative:**

    (a) Radiotherapy is indicated for adjuvant treatment

(b) Osteosarcomas are considered relatively radioresistant
(c) It can be indicated for local control in tumors which surgery is contraindicated (Answer)
(d) Radioterapy is an option to surgery for local control

Comment: Osteosarcoma is considered relatively resistant to radiation therapy. Primary radiation therapy is often inadequate to achieve local control. Whenever possible, surgery is preferred for local control. For patients with tumors in challenging axial sites (skull, spine, sacral base), radiotherapy may be a local control option when surgery is not performed.

14. **All of the following are considered to be the best prognostic features in metastatic osteosarcoma, except:**

(a) Early relapse (Answer)
(b) Single metastase
(c) Pulmonary metastases only
(d) Possibility of complete resection of metástases

Comment: Are considered as having a better prognosis the presence of single metastases, relapse time and the possibility of complete resection of the metastases. Early relapse is an indicator of poor prognosis.

15. **What is the best treatment strategy for a 19-year-old patient with osteosarcoma of umero with 2 lung resectable lung metástases?**

(a) Chemotherapy only
(b) Neoadjuvant chemotherapy, followed by surgery and adjuvant chemotherapy (Answer)
(c) Surgery followed by adjuvant chemotherapy
(d) Surgery only

Comment: For patients with resectable metastases at presentation, neoadjuvant chemotherapy is recommended, followed by resection of the primary tumor and adjuvant chemotherapy.

Related Clinical Case

A 34-year-old male patient in investigation for backache, associated with anemia and left thigh mass for about 6 months and weight loss of 9 kg in this period, presents with medullary compression syndrome, with paraparesis and urinary retention. MRI of the spine was performed, showing marginal bone irregularity L5 – S1 and protrusion with dural sac compression, hypersignal in L3 – L4, L4 – L5, L5 – S1. Patient was hospitalized and submitted to surgical procedure for decompression of the spinal cord with thoracic spine arthrodesis. In the occasion, a biopsy of the bone lesion was performed. The anatomopathological examination revealed small blue and round cell neoplasm and immunohistochemistry showed positivity for Vimentina and CD 99, compatible with Ewing's Sarcoma. MRI of left thigh showed heterogeneous expansive formation in the proximal and middle diaphyseal region of the left femur, with irregular thickening and permeation pattern

of the cortical bone, presenting a massive soft tissue component involving the part of the musculature of the posterior and medial compartments, and mainly anterior, infiltrating the medial, lateral and intermediate vastus muscles, measuring 19 × 12 × 9 cm (L × AP × LL), establishing close contact with medial bulging of the femoral neurovascular bundle. Other nodular lesions with similar characteristics are observed in the right pubis, posterior region of the left femoral head, and the largest in the minor trochanter measuring 4.5 × 3.3 × 2.3 cm, which within the clinical context may represent secondary involvement. Prominent lymph nodes with globular morphology in the left inguinal chain, measuring up to 1.6 cm. Diffuse edema alteration with edema pattern of the adductor regions and thigh compartments, especially of the extensor musculature, associated to diffuse edema with thickening of the fibroadipous septa of the subcutaneous tissue predominating on the lateral and posterior side of the thigh (Fig. 36.1).

Bone scintigraphy showed hyperconcentration of the radiopharmac in the projection of the cranial calotte (Bone parietal E), thoracic spine (T9, 10 and 12) and heterogeneous distribution of the radiopharmac in the projection of the proximal 2/3 of the left femur. Chest, abdomen and pelvis tomography showed secondary osseous lesions in T5, T10 and T12 and left iliac bone. There was no visceral lesions.

After bone marrow decompression, the patient maintained an important low back pain, paraparesis of the lower limbs and urinary and fecal incontinence.

It was decided to start systemic treatment with chemotherapy with the VDC scheme (Cyclophosphamide 1200 mg/m^2 + Doxorubicin 75 mg/m^2 + Vincristine 2 mg with cycles every 21 days). After the first cycle, patient had improvement of the pain. After the second cycle had improvement of urinary and fecal incontinence. New staging after C3 showed reduction of the mass in the left thigh, now with 15 × 10 × 7 cm. The patient received local control with radiotherapy of the primary and metastatic disease at week 9. The systemic treatment was maintained, and the patient presented important clinical improvement, with recovery of the muscular strength in the gradual and progressive lower limbs. After a cumulative dose of 375 mg/m^2 doxorubicin was replaced by dactinomycin. After administration of C8

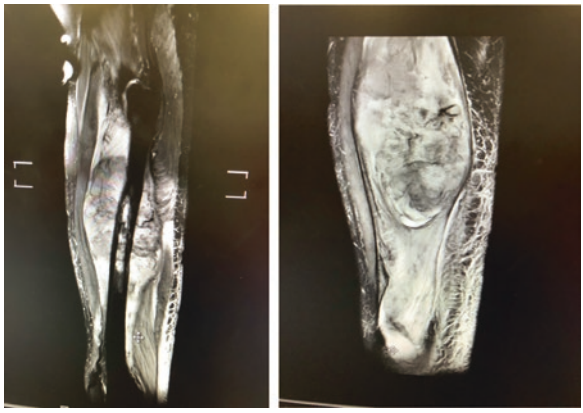

Fig. 36.1 Imaging assessment

the patient was staged, maintaining the response in the left thigh mass (now with 9 × 8 × 5 cm). The treatment was maintained for 17 cycles. After that, with physiotherapeutic treatment, patient completely recovered the muscle strength in the lower limbs and had improve of the fecal and urinary incontinence, in addition to improving pain and recovering functionality.

After 12 months of follow-up, the patient maintains stable disease, with no evidence of visceral disease and with controlled osseous lesions.

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