Osteosarcoma of the Sacrum

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16.1 Introduction

Osteosarcoma and Ewing's sarcoma are the most common primary malignant bone tumors in childhood and adolescence, most occurring during the first two decades [1, 2]. Osteosarcoma rarely involves the spine (1–3% of all osteosarcomas), and the sacrum is one of the most common spinal locations [2–9]. Osteosarcoma is the third most frequent primary malignant tumor of the sacrum after chordoma and Ewing's sarcoma. Secondary osteosarcoma may occur in patients that received pelvic radiation treatment or as sarcomatous degeneration in patients with polyostotic Paget's disease [10–15].

There have been several articles on the treatment of patients with osteosarcoma of the spine [4–7, 16–32]; however, those publications included case reports or selected patients from small series, making the optimal evidence-based therapeutic approach very difficult. Wuisman et al. [23] reported a case of sacral osteosarcoma and performed a review of all reported cases since 1984–2001: they were able to find only 11 patients [7, 18, 25–32]. In the last 15 years, still some data appear in the literature, indicating that the combination of chemotherapy with adequate surgical procedures (hemi/total sacrectomies) may increase survival in this poor prognostic tumor site [4, 20–22, 24].

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16.2 Epidemiology, Presentation, and Diagnosis

Patients with primary spinal osteosarcoma are older than those with osteosarcoma of the extremity (mean age of about 38 years old) [5, 6, 8, 33]. Exposure to radiation is a proven exogenous risk factor for secondary osteosarcoma of the bone. Incidence of sarcomas postirradiation therapy comprises about 0.1% of all cancer cases, and the sarcomas usually appear 10–20 years posttreatment (thus radiation-induced sarcoma is typical of adult age) [10–15]. It has been demonstrated that osteosarcoma could be related to pelvic radiation therapy [10, 13–14].

As well as for other sacral tumors, early diagnosis is difficult and pain and swelling are the most frequent symptoms of sacral osteosarcoma. Neurological symptoms are associated with large tumors. A detailed history with a complete physical exam should be performed prior to any evaluation. Ozaki et al. reported in 2002 their experience in 15 osteosarcomas of the sacrum and 7 of the mobile spine [4]: the duration of symptoms between onset and diagnosis ranged from 2 to 18 months, and the most common was represented by pain (almost all) followed by neurological disorder (half of the cases). The median tumor size in sacral tumors was 8.0 cm. Other reports were results in terms of diagnostic delay and tumor size [8, 34]. The laboratory findings may show an increase in alkaline phosphatase (AP) and lactic dehydrogenase in the serum (about 30% of cases) [35–38]. In some cases mild anemia and high erythrocyte sedimentation rate may also be present at diagnosis [35, 36].

16.3 Imaging

Most spinal osteosarcomas are pathologically osteoblastic, resulting in typical mineralized lesions on radiographs and CT, even if rarely osteolytic lesions also occurred [4, 29, 37, 39]. Computed tomography (CT), magnetic resonance imaging (MRI), angiography, and dynamic bone scintigraphy are used to evaluate the extension of tumors and the involvement of surrounding structures such as vessels, nerves, and soft tissues [40, 41]. CT of the lung is part of the basal staging. MRI is also useful in the assessment of patients with intraosseous tumor spread, particularly in the sacrum or sacroiliac joint, or in the identification of neural compression [8].

Nuclear medicine imaging techniques (bone scans and PET/CT) are being used increasingly to aid in the initial staging/metastatic evaluation and response to therapy. Isotope scans with technetium [41] or thallium [42] are a standard part of the staging because they show the intense hotspot of the tumor and are very sensitive in detecting any skip or distant bony metastases [43]. 18-Fluorodeoxy-glucose positron emission tomography (18FDG-PET) combined with a whole-body CT is being increasingly used in staging and also in treatment monitoring [44–46]. On 18FDG-PET/CT, there is increased uptake within the tumor, which decreases following effective neoadjuvant therapy [44–46]. Whole-body MRI and PET/CT are currently being evaluated for the detection of metastatic disease [47].

Biopsy is a key diagnostic method for sacral osteosarcomas and should be carefully planned according to the definitive surgery, in order to avoid improper

treatments or negative effects on survival [48–50]. Conventional high-grade osteosarcoma is the most frequent variant at histopathologic evaluation. Multicentric osteosarcoma is a rare type of the disease characterized by a synchronous or metachronous appearance of multiple skeletal lesions. Some cases with sacral involvement have been reported [51, 52] with extremely poor prognosis. On the other hand, low-grade osteosarcoma of the sacrum (well-differentiated intraosseous osteosarcoma) has been described in only one report in literature [53].

16.4 Treatment

In recent years, multidisciplinary approach and aggressive adjuvant/neoadjuvant chemotherapy have increased the oncologic outcome of patients with osteosarcoma [5, 6, 35, 37, 54–60], even if spinal involvement has been linked with a very poor prognostic outlook with median survival times of only 10–23 months. Much like with Ewing's sarcoma, a combination of chemotherapy with surgery (when possible) is also the standard therapy in tumors involving the axial skeleton. Some authors suggested that patients with osteosarcoma of the spine should be treated with a combination of chemotherapy and at least marginal surgery [4]. Postoperative radiotherapy can also be applied in the treatment program and may be of benefit in selected patients.

16.4.1 Chemotherapy

Currently, chemotherapy is undoubtedly the method that is likely to cure the greatest proportion of patients with osteosarcoma. However the association with surgery is essential for the local control and the management program of all patients. In fact, in the presence of effective chemotherapy, osteosarcoma is rarely cured without surgical resection [5, 17, 61]. Doxorubicin, cisplatin, high-dose methotrexate, ifosfamide, and etoposide have antitumor activity in osteosarcoma and are frequently used with different protocols as the basis of treatment [54, 57–59, 62]. The selection of postoperative adjuvant chemotherapy based on the degree of the tumor necrosis induced by preoperative therapy improves the patient survival rate [59, 62]. New drugs such as bisphosphonates, interferon, interleukin, and monoclonal antibodies have been trialed in preclinical and clinical studies, showing encouraging results [59]. Specific aspects on protocol of treatment are analyzed in the dedicated chapter.

16.4.2 Sacrectomy

Recent progression of surgical techniques may enable total sacrectomy to improve the survival of patients [63–68]. Patients whose tumors can be completely resected with adequate margins should be approached with curative intent. Simon et al. [29] reported a patient disease-free almost 5 years after surgical excision alone. However,

the surgical intervention is quite challenging given the magnitude of treatment, the significant compromise of neurological status, and the high risk of complications [69–72]. To date, the question whether this type of surgery is really beneficial to the affected patients is still debated. Ozaki et al. [4] show that complete tumor resection may improve their prognosis. In the author's experience, most patients have unresectable or partially resectable tumors, or metastases at presentation, and thus are not good candidates for a surgical treatment (or adequate margins cannot be achieved). Obviously sacral resection in low-grade tumors should be considered the mainstay of treatment and has been successfully reported [53].

There is no absolute contraindication for surgical resection because the decision is dictated by local practice and the surgical expertise of the tumor center. Relative contraindications for resection are large extraosseous extension, major neurovascular involvement, high mortality/morbidity risk with extensive surgery, and unavailability of experienced multidisciplinary team.

16.5 Radiation Therapy

In general, radiotherapy has a limited role in the management of osteosarcoma because of the relative radioresistance and the need for a large dose of radiation to achieve clinical response, but there are anatomical locations in which the possibility of complete surgical resection is unfeasible [73–75]. However, the effect of chemotherapy alone is usually temporary, and there is a need of intensive treatment for local control. In these cases, radiation therapy may be an option to try to extend the progression-free interval. Another possible scenario is the use of adjunctive irradiation in patients who underwent intralesional or inadequate surgery, in which the overall survival was better compared with patients that not received further local treatments [4, 6].

Radiotherapy may provide significant palliation in patients with unresectable sacral osteosarcomas (or patients that refused surgery), even if some cases successfully treated with combination of chemotherapy and radiation have been reported in literature [6, 59, 76, 77].

Considering that high-dose conventional radiation cannot usually be given in the sacrum and new radiation therapy techniques (e.g., proton beam and heavy ion carbon therapy) are available, the role of radiation therapy in osteosarcoma may need to be reinvestigated with modern techniques that may extend indications [78]. Targeted internal radiotherapy with Sm-153-EDTMP could be an additional treatment option for some patients with inoperable tumors [79, 80].

16.6 Oncologic Outcome

Although multimodal treatment, osteosarcoma of the sacrum has a significantly worse outcome than it affects other sites [5, 6, 35, 58, 59]. In the recent ESMO guidelines, primary metastases, axial or proximal extremity tumor site, large

tumor size, elevated serum AP or LDH, and older age are considered adverse prognostic or predictive factors [58].

The median survival for patients with osteosarcoma of the spine has been reported in the range of 6–10 months [5–7, 16]. Shives et al. [6] reported that only 7 of 26 patients treated for their spinal osteosarcomas up to 1980 survived for 1 year. In a large retrospective series of spinal osteosarcomas (15 with tumors of the sacrum and 7 with tumors at other sites), 86% of the patients survived 1 year, but only 3 were alive at 6 years of follow-up [4]. Li et al. [20] reported a series including two cases of osteosarcoma of the sacrum treated with hemisacrectomy and adjuvant chemotherapy: one was alive with disease with local recurrence after resection with marginal margins at 49 months of follow-up, whereas the other was alive with no evidence of disease at 24 months (wide margin). Guo et al. [21] reported a series on en bloc sacrectomies including two patients affected by osteosarcoma: one was alive with disease with local recurrence at 11 months of follow-up and the other alive with no evidence of disease at 20 months. Arkader et al. [22] reported two cases of sacral osteosarcoma in pediatric age, disease-free at 8 years of follow-up after sacrectomy and chemotherapy. Sundaresan et al. [7] suggested that the combination of surgery, chemotherapy, and radiation may increase survival, showing three patients who survived longer than 36 months without evidence of disease.

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References

1. Longhi A, Errani C, De Paolis M, Mercuri M, Bacci G. Primary bone osteosarcoma in the pediatric age: state of the art. Cancer Treat Rev. 2006;32:423–36.
2. Unni KK. Dahlin's bone tumors general aspects and data on 11,087 cases. 5th ed. Philadelphia: Lippincott-Raven; 1996.
3. Weinstein JN, McLain RF. Primary tumors of the spine. Spine. 1987;12:843–51.
4. Ozaki T, Flege S, Liljenqvist U, Hillmann A, Delling G, Salzer-Kuntschik M, Jürgens H, Kotz R, Winkelmann W, Bielack SS. Osteosarcoma of the spine: experience of the Cooperative Osteosarcoma Study Group. Cancer. 2002;94(4):1069–77.
5. Barwick KW, Huvos AG, Smith J. Primary osteogenic sarcoma of the vertebral column: a clinicopathologic correlation of ten patients. Cancer. 1980;46:595–604.
6. Shives TC, Dahlin DC, Sim FH, Pritchard DJ, Earle JD. Osteosarcoma of the spine. J Bone Joint Surg Am. 1986;68:660–8.
7. Sundaresan N, Rosen G, Huvos AG, Krol G. Combined treatment of osteosarcoma of the spine. Neurosurgery. 1988;23:714–9.
8. Green R, Saifuddin A, Cannon S. Pictorial review: imaging of primary osteosarcoma of the spine. Clin Radiol. 1996;51:325–9.
9. Kurugoglu S, Adaletli I, Mihmanli I, Kanberoglu K. Lumbosacral osseous tumors in children. Eur J Radiol. 2008;65(2):257–69.
10. Weatherby RP, Dahlin DC, Ivins JC. Postradiation sarcoma of bone: review of 78 Mayo Clinic cases. Mayo Clin Proc. 1981;56(5):294–306.
11. Iyer R, Jhingran A. Radiation injury: imaging findings in the chest, abdomen and pelvis after therapeutic radiation. Cancer Imaging. 2006;6:S131–9.

12. Longhi A, Barbieri E, FAbbri N. Radiation-induced osteosarcoma arising 20 years after the treatment of Ewing's sarcoma. Tumorigenesis. 2003;89:569–72.
13. Kwon JW, Huh SJ, Yoon YC, et al. Pelvic bone complications after radiation therapy of uterine cervical cancer: evaluation with MRI. AJR Am J Roentgenol. 2008;191(4):987–94.
14. Noh JM, Huh SJ. Two cases of post-radiation osteosarcoma of the sacrum after pelvic irradiation for uterine cervical cancer. Eur J Gynaecol Oncol. 2007;28(6):497–500.
15. Torreggiani WC, Al-Ismail K, Munk PL, Lee MJ. Musculoskeletal case 18. Radiation-induced osteosarcoma of the sacrum. Can J Surg. 2001;44(5):334–5; 346.
16. Mnaymneh W, Brown M, Tejada F, Morrison G. Primary osteogenic sarcoma of the second cervical vertebra. Case report. J Bone Joint Surg Am. 1979;61:460–2.
17. Ogihara Y, Sekiguchi K, Tsuruta T. Osteogenic sarcoma of the fourth thoracic vertebra. Long-term survival by chemotherapy only. Cancer. 1984;53:2615–8.
18. Spiegel DA, Richardson WJ, Scully SP, Harrelson JM. Long- term survival following total sacrectomy with reconstruction for the treatment of primary osteosarcoma of the sacrum. A case report. J Bone Joint Surg Am. 1999;81:848–55.
19. Kawahara N, Tomita K, Fujita T, Maruo S, Otsuka S, Kinoshita G. Osteosarcoma of the thoracolumbar spine: total en bloc spondylectomy. A case report. J Bone Joint Surg Am. 1997;79:453–8.
20. Li D, Guo W, Tang X, Yang R, Tang S, Qu H, Yang Y, Sun X, Du Z. Preservation of the contralateral sacral nerves during hemisacrectomy for sacral malignancies. Eur Spine J. 2014;23(9):1933–9.
21. Guo W, Tang X, Zang J, Ji T. One-stage total en bloc sacrectomy: a novel technique and report of 9 cases. Spine. 2013;38(10):E626–31.
22. Arkader A, Yang CH, Tolo VT. High long-term local control with sacrectomy for primary high-grade bone sarcoma in children. Clin Orthop Relat Res. 2012;470(5):1491–7.
23. Wuisman P, Lieshout O, van Dijk M, van Diest P. Reconstruction after total en bloc sacrectomy for osteosarcoma using a custom-made prosthesis: a technical note. Spine. 2001;26(4):431–9.
24. Zileli M, Hoscoskun C, Brastianos P, Sabah D. Surgical treatment of primary sacral tumors: complications associated with sacrectomy. Neurosurg Focus. 2003;15:E9.
25. Huth JF, Dawson EG, Eilber FR. Abdominosacral resection for malignant tumors of the sacrum. Am J Surg. 1984;148:157–61.
26. Kawai A, Huvos AG, Meyers PA, et al. Osteosarcoma of the pelvis. Clin Orthop. 1998;348:196–207.
27. Krajbich JI, Gillespie R. Complete en bloc resection of the sacrum for osteogenic sarcoma. In: Brown KLB, editor. Complications of limb salvage. Montreal: ISOLS; 1991. p. 395–6.
28. Ritschl P, Missaghi SM, Wurnig C, et al. Operative procedures in tumors of the sacrum: results of 26 cases. Chir Organi Mov. 1990;75(Suppl):111–3.
29. Simon RG, Irwin RB. An unusual presentation of telangiectatic osteosarcoma. Am J Orthop. 1996;25:375–9.
30. Simpson AHRW, Porter A, Davis A, et al. Cephalad sacral resection with a combined extended ilioinguinal and posterior approach. J Bone Joint Surg Am. 1995;77:405–11.
31. Stener B, Guntherberg B. High amputation of the sacrum for extirpation of tumors. Spine. 1978;3:351–66.
32. Tolo VT, Atkinson JB, Sato JK. Resection of sacral Ewing's sarcoma and osteosarcoma in children. In: Brown KLB, editor. Complications of limb salvage. Montreal: ISOLS; 1991. p. 365–70.
33. Murphey MD, Andrews CL, Flemming DJ, Temple HT, Smith WS, Smirniotopoulos JG. From the archives of the AFIP. Primary tumors of the spine: radiologic pathologic correlation. Radiographics. 1996;16:1131–58.
34. Pollock BH, Krischer JP, Vietti TJ. Interval between symptom onset and diagnosis of pediatric solid tumors. J Pediatr. 1991;119:725–32.
35. Link MP, Goorin AM, Horowitz M, et al. Adjuvant chemotherapy of high- grade osteosarcoma of the extremity: updated results of the Multi-Institutional Osteosarcoma Study. Clin Orthop Relat Res. 1991;270:8–14.

36. Hannisdal E, Solheim OP, Theodorsen L, Host H. Alterations of blood analyses at relapse of osteosarcoma and Ewing's sarcoma. Acta Oncol. 1990;29:585–7.
37. Ferrari S, Bacci G, Picci P, et al. Long-term follow-up and post relapse survival in patients with non-metastatic osteosarcoma of the extremity treated with neoadjuvant chemotherapy. Ann Oncol. 1997;8:765.
38. Thorpe WP, Reilly JJ, Rosenborg SA. Prognostic significance of alkaline phosphatase measurements in patients with osteogenic sarcoma receiving chemotherapy. Cancer. 1979;43:2178–81.
39. deSantos LA, Edeiken B. Purely lytic osteosarcoma. Skeletal Radiol. 1982;9:1–7.
40. Thornton E, Krajewski KM, O'Regan KN, Giardino AA, Jagannathan JP, Ramaiya N. Imaging features of primary and secondary malignant tumours of the sacrum. Br J Radiol. 2012;85(1011):279–86.
41. Aisen AM, Martel W, Braunstein EM, McMillin KI, Phillips WA, Kling TF. MRI and CT evaluation of primary bone and soft-tissue tumors. AJR Am J Roentgenol. 1986;146:749–56.
42. Wittig JC, Bickels J, Priebat D, Jelinek J, Kellar-Graney K, Shmookler B, et al. Osteosarcoma: a multidisciplinary approach to diagnosis and treatment. Am Fam Physician. 2002;65:1123–32.
43. McKillop JH, Etcubanas E, Goris ML. The indications for and limitations of bone scintigraphy in osteogenic sarcoma: a review of 55 patients. Cancer. 1981;46:2603–6.
44. McCarville MB, Christie R, Daw NC, Spunt SL, Kaste SC. PET/CT in the evaluation of childhood sarcomas. AJR Am J Roentgenol. 2005;184:1293–304.
45. Volker T, Denecke T, Steffen I, Misch D, Schonberger S, et al. Positron emission tomography for staging of pediatric sarcoma patients: results of a prospective multicenter trial. J Clin Oncol. 2007;25:5435–41.
46. Schulte M, Brecht-Krauss D, Werner M, Hartwig E, Sarkar MR, Keppler P, et al. Evaluation of neoadjuvant therapy response of osteogenic sarcoma using FDG PET. J Nucl Med. 1999;40:1637–43.
47. Hogendoorn PC, Athanasou N, Bielack S, De Alava E, Dei Tos AP, Ferrari S, et al. Bone sarcomas: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2010;21(Suppl. 5):v204–13.
48. Mankin HJ, Mankin CJ, Simon MA. The hazards of the biopsy, revisited: members of the Musculoskeletal Tumor Society. J Bone Joint Surg. 1996;78:656–63.
49. Mavrogenis AF, Angelini A, Vottis C, Palmerini E, Rimondi E, Rossi G, Papagelopoulos PJ, Ruggieri P. State-of-the-art approach for bone sarcomas. Eur J Orthop Surg Traumatol. 2015;25(1):5–15.
50. Mavrogenis AF, Angelini A, Errani C, Rimondi E. How should musculoskeletal biopsies be performed? Orthopedics. 2014;37(9):585–8.
51. Mahoney JP, Spanier SS, Morris JL. Multifocal osteosarcoma: a case report with review of the literature. Cancer. 1979;44:1897–907.
52. Yamamoto T, Fujita I, Kurosaka M, Mizuno K. Sacral radiculopathy secondary to multicentric osteosarcoma. Spine. 2001;26(15):1729–32.
53. Liuhong W, Minming Z. Well-differentiated intraosseous osteosarcoma in the sacrum: a case report. Iran J Radiol. 2013;10(3):175–8.
54. Ferrari S, Smeland S, Mercuri M, et al. Neoadjuvant chemotherapy with high-dose Ifosfamide, high-dose methotrexate, cisplatin, and doxorubicin for patients with localized osteosarcoma of the extremity: a joint study by the Italian and Scandinavian Sarcoma Groups. J Clin Oncol. 2005;23:8845–52.
55. Winkler K, Beron G, Delling G, Heise U, Kabisch H, Purfurst C, et al. Neoadjuvant chemotherapy of osteosarcoma: results of a randomized cooperative trial (COSS-82) with salvage chemotherapy based on histological tumor response. J Clin Oncol. 1988;6:329–37.
56. Winkler K, Bielack S, Delling G, Saltzer-Kuntschik M, Kotz R, Greenshaw C, et al. Effect of intraarterial versus intravenous cisplatin in addition to systemic doxorubicin, high-dose methotrexate, and ifosfamide on histologic tumor response in osteosarcoma (study COSS-86). Cancer. 1990;66:1703–10.

57. Bacci G, Mercuri M, Briccoli A, Ferrari S, Bertoni F, Donati D, et al. Osteogenic sarcoma of the extremity with detectable lung metastases at presentation. Results of treatment of 23 patients with chemotherapy followed by simultaneous resection of primary and metastatic lesions. Cancer. 1997;79:245–54.
58. ESMO/European Sarcoma Network Working Group. Bone sarcomas: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2014;25(Suppl 3):iii113–23.
59. Ta HT, Dass CR, Choong PF, Dunstan DE. Osteosarcoma treatment: state of the art. Cancer Metastasis Rev. 2009;28(1–2):247–63.
60. Gherlinzoni F, Picci P, Bacci G, et al. Limb sparing versus amputation in osteosarcoma. Correlation between local control, surgical margins and tumor necrosis: Istituto Rizzoli experience. Ann Oncol. 1992;3(Suppl 2):S23–7.
61. Jaff N, Carrasco H, Raymond K, Ayala A, Eftekhari F. Cancure in patients with osteosarcoma be achieved exclusively with chemotherapy and abrogation of surgery. Cancer. 2003;95:2202–10.
62. Carrle D, Bielack SS. Current strategies of chemotherapy in osteosarcoma. Int Orthop. 2006;30:445–51.
63. Angelini A, Ruggieri P. A new surgical technique (modified Osaka technique) of sacral resection by posterior-only approach: description and preliminary results. Spine. 2013;38(3):E185–92.
64. Ruggieri P, Angelini A, Ussia G, Montalti M, Mercuri M. Surgical margins and local control in resection of sacral chordomas. Clin Orthop Relat Res. 2010;468(11):2939–47.
65. Tomita K, Kawahara N, Hata M, Mizuno K. Indication and operative method of sacral amputation. In: Kaneda K, editor. Orthopaedic surgery now, no. 22. Surgical techniques for disorders of the thoracolumbar, lumbar and lumbosacral spine. Tokyo: Medical View, Inc.; 1996. p. 188–97.
66. Wuisman P, Lieshout O, Sugihara S, van Dijk M. Total sacrectomy and reconstruction: oncologic and functional outcome. Clin Orthop Relat Res. 2000;381:192–203.
67. Tomita K, Tsuchiya H. Total sacrectomy and reconstruction for huge sacral tumors. Spine. 1990;15:1223–7.
68. Shikata J, Yamamuro T, Kotoura Y, Mikawa Y, Iida H, Maetani S. Total sacrectomy and reconstruction for primary tumors. Report of two cases. J Bone Joint Surg Am. 1988;70:122–5.
69. Ruggieri P, Angelini A, Pala E, Mercuri M. Infections in surgery of primary tumors of the sacrum. Spine. 2012;37(5):420–8.
70. Capanna R, Briccoli A, Casadei R, et al. Sacral resections: experiences of the I.O.R. bone tumor center. Chirurgia Delgi Organi di Movimento. 1990;75(Suppl):114–6.
71. Samson IR, Springfield DS, Suit HD, et al. Operative treatment of sacrococcygeal chordoma: a review of twenty-one cases. J Bone Joint Surg Am. 1993;75:1476–84.
72. Sung HW, Shu WP, Wang HM, et al. Surgical treatment of primary tumors of the sacrum. Clin Orthop. 1987;215:91–8.
73. Delaney TF, Park L, Goldberg SI, et al. Radiotherapy for local control of osteosarcoma. Int J Radiat Oncol Biol Phys. 2005;61:492–8.
74. Mialou V, Philip T, Kalifa C, et al. Metastatic osteosarcoma at diagnosis: prognostic factors and long-term outcome—the French pediatric experience. Cancer. 2005;104(5):1100–9.
75. Loeb DM, Garrett-Mayer E, Hobbs RF, et al. Dose finding study of 153Sm-EDTMP in patients with poor-prognosis osteosarcoma. Cancer. 2009;115(11):2514–22.
76. Aledavood SA, Amirabadi A, Memar B. Non surgical treatment of sacral osteosarcoma. Iran J Cancer Prev. 2012;5(1):46–9.
77. Mahajan A, Woo SY, Kornguth DG, et al. Multimodality treatment of osteosarcoma: radiation in a high-risk cohort. Pediatr Blood Cancer. 2008;50(5):976–82.
78. Blattmann C, Oertel S, Schulz-Ertner D, et al. Non-randomized therapy trial to determine the safety and efficacy of heavy ion radiotherapy in patients with non-resectable osteosarcoma. BMC Cancer. 2010;10:96.
79. Franzius C, Bielack S, Sciuk J, Vollet B, Jurgens H, Schober O. High-activity samarium-153-EDTMP therapy in unresectable osteosarcoma. Nuklearmedizin. 1999;38:337–40.
80. Bruland OS, Skretting A, Solheim OP, Aas M. Targeted radiotherapy of osteosarcoma using 153 Sm-EDTMP. A new promising approach. Acta Oncol. 1996;35:381–4.