PRIMARY EWING’S SARCOMA OF THE SPINE

Case report

Leandro I. Dini1, Rodrigo Mendonça2, Pasquale Gallo3

ABSTRACT - Primary malignant sarcomas of the spine are extremely rare. Because of biological heterogeneity, these tumors have variable sensitivity to radiation and chemotherapy. Adequate local control through complete tumor removal is an important therapeutic goal. However, aggressive resection of tumors in the spinal column must be coupled with restoration of spinal column stability and minimization of neural deficits. The balance of these factors makes treatment of primary sarcomas of the spine challenging, and dictates an individual approach to treatment. We report on a 18 years old man with primary Ewing’s sarcoma of the nonsacral spine. The clinical picture and imaging characteristics were analyzed as well as the management modalities and outcome.

KEY WORDS: Ewing’s sarcoma, primary spine tumor, spine stabilization.

Sarcoma de Ewing primário da coluna vertebral: relato de caso

RESUMO - Sarcomas malignos primários da coluna são extremamente raros. Devido sua heterogeneidade biológica, estes tumores apresentam sensibilidade variada à radioterapia e à quimioterapia. O controle local adequado através da ressecção tumoral completa é um objetivo terapêutico importante. Contudo, a ressecção completa dos tumores da coluna vertebral deve ser realizada com a restauração da estabilidade espinhal e minimização do déficit neurológico. O equilíbrio entre estes fatores torna o tratamento dos sarcomas da coluna desafiador, exigindo-se uma abordagem individualizada para o tratamento de cada paciente. Relatamos um caso de sarcoma de Ewing da coluna não-sacral em um homem de 18 anos. O quadro clínico e características de imagem foram analisados, bem como as modalidades de manejo e o prognóstico.

PALAVRAS-CHAVE: sarcoma de Ewing, tumor espinhal, estabilização espinhal.

Primary malignant sarcomas of the spine are extremely rare. It has been estimated that they account for only 3.5% to 14.9% of all primary bone sarcomas1-5. In the study of primary vertebral Ewing’s sarcoma (ES), the division of the spine into nonsacral and sacral is important and is dictated by the different behavior of ES in these two regions in terms of response therapy and survival rates4. Most studies on ES involving the mobile spine are limited to case reports. A few larger series evaluated patients with primary ES affecting the mobile and nonmobile spine1,6-9. Microscopic examination demonstrates small, round blue cells with a uniform appearance. Electron microscopy, immunohistochemistry, and cytogenetic studies help differentiate ES from other small, round blue cell tumors. The translocation t(11;22)(q24;q12) is identified in most cases of ES10. Adequate treatment of primary malignant spine tumors is aimed at cure rather than palliation whenever possible. The definitive management of Ewing’s sarcoma of the spine, as in other locations, could include three main modalities: surgery, radiotherapy, and combination chemotherapy1.

The purpose of the current study is to report the diagnosis and the treatment of primary sarcomas of the mobile spine.

CASE

A 18-year-old man presented with a 4-month history of progressively worsening back pain, and lower extremity weakness. No constitutional symptoms were present. Bladder dysfunction was presented at admission. Results of a physical examination disclosed bilateral paraspinal ten-
derness with lower extremity paraparesis (Frankel B). Sensibility was decreased below the level L1. The results of laboratory studies, including erythrocyte sedimentation rate were within normal limits. Plain radiographs of the thoracolumbar spine revealed sclerotic L1 vertebra. Computed tomographic (CT) and magnetic resonance imaging (MRI) evaluation of the patient showed a soft tissue mass invading the epidural space (Fig 1). The patient was without evidence of metastatic disease at presentation as determined by staging chest radiographs, chest computed tomography scans and bone scans.

The patient underwent surgery as the first line of management. Subtotal vertebrectomy and decompression was obtained with a combined anterior and posterior approach (Fig 2 and 3). Anterior reconstruction was carried out using a titanium mesh cage filled with autologous bone graft from resected rib (Fig 3C). The patient had histologic confirmation of ES. Small, round blue cells with round to oval nuclei, uniformly packed into broad nests were identified (Fig 3D). Periodic acid-Schiff staining was performed to confirm the presence of intracytoplasmic glycogen. The patient was administered chemotherapy (vincristine, actinomycin D, cyclophosphamide, methotrexate) and additional radiotherapy to T12-L2 (total dose, 40 Gy).
The neurological outcome of surgery was judged good with mild residual deficits. Strength and sensibility in the lower extremities gradually increased, and within 3 months after the surgery, the patient was ambulatory.

The case report was done with the agreement of both the patient and the Ethical Committee of Hospital Centenário.

DISCUSSION

Primary sarcomas of the spinal column are difficult to classify as a clinical entity. The complex neuromusculoskeletal development of the spine may account for a spectrum of malignant tumors with distinct biological behaviors. The differential diagnosis of a small round-cell bone tumor includes, in addition to others, neuroblastoma, primitive neuroectodermal tumor of bone (PNET), malignant lymphoma, and rhabdomyosarcoma. The differentiation between these tumors on basis of light histological data alone may not always be accurate. Current standards dictate that patients with a small round-cell bone tumor be evaluated, in addition to light microscopy and electron microscopy, by immunohistochemical and occasionnaly cytogenetic analysis. Chromosomal data from ES reveals a remarkably consistent chromosomal anomaly, the reciprocal translocation t(11;22)(q24;q12)10,13. Other numerical and/or structural changes have also been reported14,15. Although the differentiation between other tumors based on histologic data alone may not always be accurate, the patient in this report satisfied the histologic criteria required to the diagnosis of ES.

The age at presentation ranged from 12 to 24 years (median, 21 yr)1. Ewing's sarcoma of the spine is a rare condition that appears with a clinical triad of local pain, neurological deficit, and palpable mass. Local back pain usually is the first symptom to occur. Even when initial plain film studies reveal no abnormality, the physician should be alert to the possibility of spinal malignancy, especially when the patient is in the first two decades of life and symptoms, including severe local pain, are not relieved by bed rest, and overlying point tenderness is present.

Plain radiographic signs of ES are late to appear, usually after the neurological signs have become obvious. The most common finding was lytic bone destruction involving the vertebra1. The lytic changes
varied from focal lytic lesion, which is more common, to complete flattening of the vertebral body (vertebra plana)\(^{16}\). Sclerotic changes are also rarely observed. CT is of great value in determining the extent of involvement of both the vertebral bodies and the posterior elements as well as in outlining the soft tissue component. CT-guided needle biopsy of vertebral or paravertebral lesions can be accomplished with accuracy and relative ease. MRI is very sensitive in the early detection of ES in the spine\(^{17,18}\). MRI is superior for visualizing epidural compression and tumor spread to the bone marrow or extension into adjacent soft tissues. The relationship of tumor to adjacent vasculature can also be determined. MRI may be of value in monitoring the effect of chemotherapy on bone sarcomas. MRI, enhanced with gadolinium diethylene-triamine-pentaacetic acid, showed the highest accuracy in determining the response to preoperative chemotherapy\(^{19}\). MRI may be of value in preoperative planning for a reliable definition of the surgical margins of the tumor, which can permit safer and more complete resection.

ES is frequently multifocal. Skeletal scintigraphy before staging is an important step to rule out other foci and also it has been used in the follow-up treatment of primary ES\(^{20}\).

In the Intergroup Ewing’s Sarcoma Study (IESS) experience, lesions of nonsacral spine had a 100% local control rate and an 86% long-term survival rate. Sacrococcygeal primary tumors responded more poorly (they usually are diagnosed at a more advanced stage and are more difficult to supply adequate irradiation to or to achieve total surgical excision of the sacral tumor\(^{21}\)). It is noteworthy that the good outcome reported by the IESS for ES of the nonsacral spine has not been duplicated in many cases reports\(^{1,22,24}\). The definitive treatment of ES should have two goals: local treatment of the primary tumor; maintenance combination chemotherapy to eradicate systemic micrometastasis.

Because of biological heterogeneity, these tumors have variable sensitivity to radiation and chemotherapy\(^{25}\). The classical chemotherapy regimen in ES consists of either VAC-A, that consisted of four agents: vincristine sulfate, dactinomycin, cyclophosphamide and doxorubicin hydrochloride. Treatment consisted of four agents, VAC-A, administered once very 2 weeks for 18 months, or three agents, VAC, administered for 24 months. Other protocols have been used\(^{26-30}\).

It has been suggested that in a neurologically stable patient, initial chemotherapy after biopsy should be administered to shrink the primary tumor before definitive local treatment, be it surgery or radiotherapy, is instituted\(^{23,31,32}\). Preoperative chemotherapy offers three main advantages: bulky or unresectable tumors can be reduced in size and made respectable; early systemic chemotherapy can help eradicate circulating tumor cells and micro metastasis; and the information of the sensitivity of the tumor to the chemotherapy. The histological determinant of prognosis in ES is the histological grade of regression after combination chemotherapy\(^{33-36}\).

Initial chemotherapy has also been tried for acute relief of epidural compression\(^{31}\). Further clinical as well as experimental data are available in support of chemotherapy as the primary modality for epidural decompression in highly chemosensitive tumors\(^{37,38}\); however, the response of ES to initial chemotherapy is not universal (61 to 67%)\(^{21}\). The use of multiantiag chemotheraphy combined with surgery and/or radiation for definitive local control increased disease-free survival rates to 50 to 80%\(^{39-41}\).

Current spinal resection and reconstruction techniques may lead to improved oncologic and clinical outcomes. If the patient is neurologically stable and a tissue diagnosis is required then a large-bore-bone needle biopsy should be considered. Once the diagnosis of ES is confirmed, then chemotherapy can be administered. The soft tissue mass and spinal cord compression usually rapidly diminish. Tumor restaging studies are then performed. If there is no evidence of metastases, then an en bloc spondylectomy should be considered because the risk of local recurrence is lower and long-term survival may be improved compared with an intrasional excision or radiation therapy alone.

When there is epidural compression secondary to ES with rapidly progressing neurological symptoms or impending paralysis, prompt surgical intervention is the only primary alternative if irreversible deficit is to be prevented\(^1\). For tumors involving the anterior vertebral body, an anterior approach is the preferred route to prevent neurological damage and future spinal instability. ES tends to invade the spinal canal from the paravertebral soft tissue component through the intervertebral foramen, compressing the cord circumferentially. This makes laminectomy an effective approach for decompression. So, if the patient is not neurologically stable, then radical anterior decompression with reconstruction and stabilization and/or decompressive laminectomy with stabilization should be considered. Chemotherapy can then
be administered, and definitive local control with radiation therapy should be considered.\textsuperscript{42}

Marco et al.\textsuperscript{42} evaluated the oncological outcome of patients with nonmetastatic Ewing's sarcoma of the mobile spine treated with systemic chemotherapy and radiation therapy for definitive local control. Ten of the thirteen studied patients had a decompressive laminectomy, but none of them had intraslesional excision or bloc spondilectomy. The disease-free survival rate was 49\% and 36\% at 5 and 10 years. Four of the 10 patients (40\%) that had a laminectomy (without spinal instrumentation) developed sinteromatic progressive kyphosis. Decompressive laminectomy alone removes the posterior tension band, which can render the spinal column more unstable. The patient is thus at risk for anterior column collapse, and subsequent development of kyphosis and neurological demise. Spinal stabilization probably decreases the risk of kyphosis and should be considered. The combination of improved resection, stabilization, and fusion techniques allows for more aggressive removal of malignant spinal tumors with acceptable mortality and morbidity. There is a relationship between local control and overall survival. Most of deaths in the current series were attributable to complications from local recurrences.\textsuperscript{43} Residual tumor at the margin, and resection in a piecemeal fashion result in higher recurrence rates that were associated with early mortality.\textsuperscript{43} Therefore, the surgeon should attempt complete en bloc tumor resection whenever possible. Talac et al.\textsuperscript{43} analyzed the relationship between surgical margins and local recurrence in sarcomas of the spine in thirty patients. They concluded that en bloc resection with tumor-free margins provides substantial improvement in overall survival. The local recurrence rate for patients with a negative margin was 16.7\%. The method of tumor removal may have an important effect on local recurrence: an bloc resection with tumor-free margins provides substantial improvement in overall survival. The local recurrence rate for patients with positive margins was 55.6\%.

The risk of local recurrence is probably lower for patients treated with an en bloc surgical excision with adequate margins.\textsuperscript{44-46} Minimizing the risk of local recurrence is especially important around the spinal column because local recurrence can lead to neurological demise. The risk of local recurrence is probably higher with an intraslesional excision compared with en bloc spondilectomy.\textsuperscript{47} However, the advantage of this approach is that many spinal surgeons are familiar with the technique of intraslesional excision, the spinal column remains more stable, and the procedure is less demanding than en bloc spondilec- tomy techniques.

We can summarize the indications for surgery in ES of the spine as follows: epidural decompression in patients with neurological decompression; stabilization for primary instability or for cases with extensive bony involvement by tumor where instability is likely to occur after tumor resection; poor response to initial treatment with chemotherapy or radiotherapy; residual disease.

The role of an intraslesional excision combined with radiation therapy for patients with ES of spine is unclear. The lower survival rates reported with radiation therapy compared with surgery for local control may be related to residual nests of viable tumor within the radiated site. These residual nests of tumor are potential sources of local recurrence or distant relapse.\textsuperscript{48} However, radiation therapy is generally more effective against microscopic disease that macroscopic tumor.\textsuperscript{49,51}

Radiation doses for spinal tumors should not exceed the limit of cord tolerance (45 Gy) to avoid the risk of radiation-induced myelopathy and secondary sarcomas.\textsuperscript{1} The initial use of radiotherapy in patients with epidural compression and severe neurological symptoms will be complicated by edema, which could increase cord compression.\textsuperscript{1} Larges doses of steroids could result in improvement in the neurological deficit. Furthermore, lower doses of radiation are commonly used to treat patients with microscopic residual tumors after an intraslesional excision. A lower dose of radiation probably decreases the risk of developing a radiation-associated sarcoma or myelopathy. Radiosurgery may be a valuable option for recurrent spinal tumors.\textsuperscript{52}

Adequate surgical treatment of primary malignant spine tumors involves wide or radical resection in combination with neoadjuvant chemotherapy and, if responsive, radiotherapy. The aim of preoperative chemotherapy is to reduce the viable tumor mass and to prevent further dissemination. The combination of systemic and surgical treatment offers the patient a good chance of survival with a satisfactory quality of life.

REFERENCES


