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Case Report

Ewing Sarcoma of Tibia in Geriatric patient-Excellent Disease Control without Systemic Therapy

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Abstract

Ewing Sarcoma of long bones is a rare entity in elderly patients. The prognosis and appropriate treatment in this subgroup of patients is not clearly defined. We report a case of 78 years old male treated with surgery followed by adjuvant radiation and had excellent disease control without systemic therapy.

Keywords: Adjuvant radiation, ewing sarcoma, surgery

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Ewing Sarcoma Family of tumors ranks as second commonest primary bone tumor. The highest incidence is seen in adolescence with majority of cases occurring between 10-15 years of age. The current standard of care for treatment of patients with nonmetastatic disease is combination of systemic therapy utilizing multiagent chemotherapeutic drugs and local therapy using Surgery/Radiation. [1] The prognosis and optimal treatment in patients older than 40 years are not clearly defined. Moreover, presence of comorbidities in this subgroup of patients poses massive clinical challenge as many of them are not suitable for intensive chemotherapy regimen.[2] We report a case of 78 years old male diagnosed as Ewing Sarcoma of left Tibia.

Case Report

A 78-year-old male, known diabetic and hypertensive, presented in our clinic with chief complaint of pain left knee for 6 months. Pain was intermittent, relieved with rest and aggravated by walking and bending. There was no history of any trauma. Considering patient's history X Ray (Fig. 1) followed by MRI left knee was ordered which revealed a large expansile lesion in proximal tibial metaphyseal region having narrow sharp zone of transition. The lesion measured 4.8x8.2x6.5 cm showing hypointense signal on T1 and mixed signal on T2 weighted images. There was no associated cortical break, periosteal reaction or fracture. Differential diagnosis included benign giant cell tumor or less likely possibility of metastasis. Biopsy was taken and histopathology turned out to be Small Round Blue Cell Tumor favoring Ewing Sarcoma (Fig. 2). Immunohistochemistry validated strong membranous positivity of CD 99 (Fig. 3), patchy positivity of CK Cam5.2 and S100 and focal positivity of EMA and TLE-1. Metastatic workup was carried out which failed to exhibit any distant spread of tumor. The case was discussed in Multidisciplinary tumor board and in view of his age and comorbidities, he was planned for proximal tibial replacement. However, postsurgery histopathology bared tumor involving proximal bony resection margin and lateral and medial soft tissue margin. Postoperative MRI was advised which demonstrated mild marrow edema

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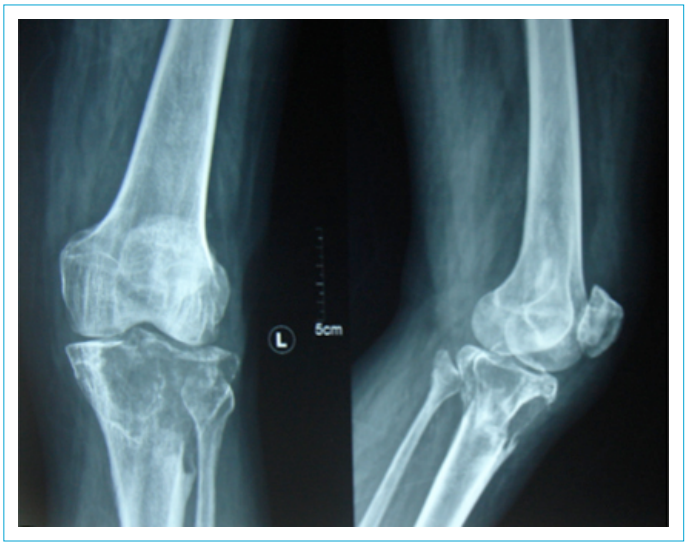

Figure 1. X Ray Left knee showing lytic lesion in proximal tibial metaphseal region.

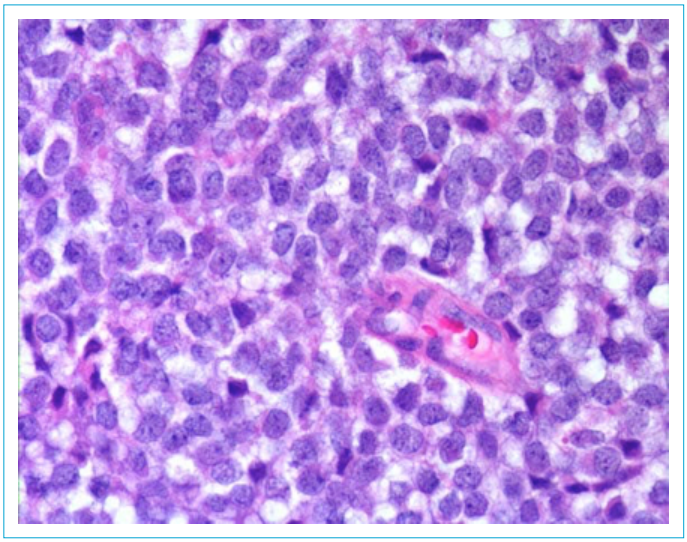

Figure 2. Small Round Blue Cells on H and E Stain.

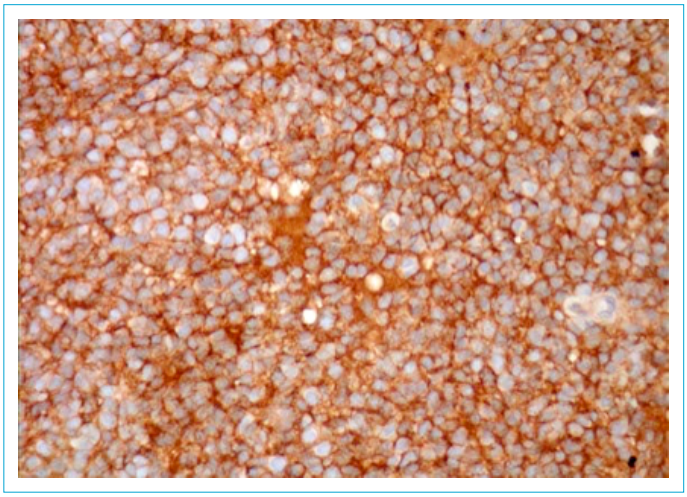

Figure 3. CD 99 positivity.

associated with total left knee replacement. Edema was also noted in deep and subcutaneous soft tissues of distal thigh and proximal visualized leg. Findings more likely favored post-surgical changes. After discussing details of all pros and cons of chemotherapy with patient and his relatives it was finally decided to proceed with radiation alone. He was planned for 1.8 GY/fraction to total dose of 55.8 GY with AP and PA fields in two phases on Linear Accelerator using 6 MV photons. The treatment volume for phase 1 i.e. till 45 GY included presurgical GTV + prosthesis + 1.5 cm margin for CTV 1 and 1 cm margin for PTV 1. The volume was coned down after 45 GY to presurgical GTV + 1.5 cm margin for CTV 2 and 1 cm margin for PTV 2 to complete total dose of radiation to 55.8 GY. The patient tolerated radiation well with no major acute and late side effects of radiation. Though, post radiation he developed mild lymphedema of lower limb which improved with conservative management. He is now on regular 3 monthly follow up for last 24 months with no evidence of local or distant recurrence.

Discussion

Ewing Sarcoma is an aggressive sarcoma seen primarily in children and young adults and accounts for 34% of all primary bone tumors.[3] The standard management scheme for this type of bone sarcoma includes intensive induction chemotherapy using 4-5 drug regimen followed by local therapy with surgery and/or radiation followed by adjuvant chemotherapy.[4] Age, tumor size, tumor site, metastasis at presentation, surgery, and chemotherapy are all well-established prognostic factors. Ewing sarcoma in patients older than 40 years is extremely rare and is associated with worse survival.[5] Due to rarity of disease and lack of randomized clinical trials, the optimal treatment strategy in this subgroup of patients is not clearly defined. The inferior survival seen in geriatric patients is ascribed to usage of less vigorous chemotherapy regimens. Conversely, study conducted by Rochefort et al in patients older than 50 years failed to reveal any overall survival or disease free survival difference between patients receiving aggressive, standard or no chemotherapy.[6] The same held true in our patient. Though, he wasn't offered any chemotherapy because of his comorbidities and personal preference, still he had excellent disease control without systemic chemotherapy. Surgery where possible is the mainstay for local treatment of patients with Ewing Sarcoma. The 5 year Disease free Survival and local control are considerably inferior in patients treated with radiation alone compared to patients treated with surgery only or surgery and radiation combined (48% vs 66%, p=0.002; 80% vs 94% p=0.0001).[7] Adjuvant ra-

diation is suggested in cases of positive margins, poor pathologic response to chemotherapy and intraoperative spillage. The Intergroup Ewing Sarcoma Study (INT-0091) mentions 45 GY dose to presurgery GTV plus 5.4 GY boost to patients with microscopic residual disease and 10.8 GY boost to patients with gross residual disease.[8] As we didn't treat our patient with systemic therapy, therefore, we decided to treat him with slightly higher dose of radiation so as to improve local control and thus survival. Nonetheless, strong evidence for this approach is not existing in literature. Ewing Sarcoma is considered to be radiosensitive tumor, yet survival seen in younger patients is <10% when treated without chemotherapy. The introduction of multidrug chemotherapy had dramatically improved outcome with almost 70% cure rates in patients with localized disease. The evolvement of chemotherapy occurred from single agent Vincristine to VAC (Vincristine, Doxorubicin, Cyclophosphamide) to VAC/IE (Ifosfamide, Etoposide) in cases with nonmetastatic disease.[9] As mentioned earlier patients diagnosed with Ewing Sarcoma who are elderly and more than 40 years of age are usually excluded from large clinical trials. Thus it is not known whether use of single agent or combination chemotherapy provide same survival benefit in this age group of patients as seen in younger population. Consequently, it is the need of hour to design large randomized trials addressing this particular age group so that appropriate treatment guidelines can be defined. Randomization can be done on the basis of risk (High, Intermediate or low risk) or chemotherapy used. Until we have strong evidence based data available, most suitable approach for treatment of elderly patients' especially geriatric patients with Ewing Sarcoma is debatable.

Literature review

A literature review was carried out to see how Ewing Sarcoma is presented in Elderly patients. A survey was done on PubMed database using key words as, "Case report, Elderly, Ewing Sarcoma". Even though we couldn't find a case report similar to one discussed in this report, however, we observed that presentation of Ewing Sarcoma in patients aged more than 60 years is diverse with variable prognosis and different protocols used for treatment. Table 1 summarizes year of publication, site of involvement, treatment and survival of elderly patients with Ewing Sarcoma.

Conclusion

Management of elderly patients with Ewing Sarcoma is not clearly defined. More insight and clinical trials are required in treatment of this rare disease.

Table 1. Summarizing year of publication, site of involvement, treatment and survival of elderly patients with Ewing Sarcoma as stated in case reports

Study Author	Disease Site	Year of Publication	Patient Characteristics	Treatment	Post Treatment Status
Shimosawa et al.[10]	Conus Medullaris	2011	63 years/M	Surgery + Chemotherapy VAC/IE+ RT 14 GY to brain and Spinal Cord 16 GY to local site	Relapsed after 21 months
Wedde et al.[11]	Kidney	2011	73 years/M	Surgery followed by 6 cycles of Chemotherapy VAC/IE	Disease free for 7 months
Shah et al.[12]	Maxillary Sinus	2014	67 years/M	Partial maxillectomy followed by 1 cycle of chemotherapy Cisplatin and Vincristine. Poor tolerability to chemotherapy. Nodal recurrence after 3 months. Salvage Chemotherapy with no response followed by palliative surgery	Died 10 months post 2nd surgery
Mahan et al.[13]	Fifth Metacarpal	2016	Female	Definitive Treatment	Disease free for 22 months
Dutta et al.[14]	Maxillary sinus	2014	67 years/M	Total Maxillectomy followed by adjuvant chemotherapy and radiation Chemotherapy VAC/IE 17 cycles RT Total dose 45 GY	Disease free for 24 months
Toda et al.[15]	Adrenal Gland	2018	74 years/M	Surgery	Died 4 months post surgery
Wygoda et al.[16]	Larynx	2013	68 years/M	Chemotherapy followed by Radiation	Disease free for 30 months
Aydinli et al.[17]	Abdominal wall	2006	65 years/M	Surgery followed by chemotherapy VAC/IE x 6 cycles	Disease free for 12 months
Okada et al.[18]	Urinary bladder	2011	65 years/M	Surgery. Systemic relapse after 8 months. VIDE chemotherapy with no response	Died 22 months post surgery
Monument et al.[19]	10th rib	2015	85 years/F	Radiation alone	Died within 1 year of diagnosis
Mizuguchi et al.[20]	Pulmonary	2016	70 years/M	Chemotherapy	Died 4 months after diagnosis
Shimada et al.[21]	Uterus	2014	63 years/F	Debulking surgery followed by chemotherapy with, Cyclophosphamide Vincristine and Doxorubicin	Disease free for 24 months
Batziou et al.[22]	Small intestine	2006	66 years/M	Excision. Local recurrence after 15 months. Resurgery followed by 4 cycles of Doxorubicin, Cisplatin and Ifosfamide	Disease free for 48 months
Blas et al.[23]	Adrenal Gland	2013	63 years/M	Left adrenalectomy followed by adjuvant chemotherapy VDC/IE	Disease free for 13 months
Soulard et al.[24]	Stomach	2005	66 years/F	Gastrectomy followed by adjuvant chemotherapy	Died 4 months post surgery

Disclosures
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