Original Research Paper

Volume-9 | Issue-2 | February-2019 | PRINT ISSN - 2249-555X

Oncology

CLINICAL PROFILE AND SURVIVAL OUTCOMES OF EWING'S SARCOMA. AN INSTITUTIONAL EXPERIENCE.

Dr D. Bhargavi Assistant professor, Department of Medical Oncology, SVIMS, Tirupati, Chittoor, Andrapradesh. 517507

Dr B. Manilal* Associate professor, Department of Surgical oncology, SVIMS, Tirupati, Chittoor, Andrapradesh. 517507. *Corresponding Author

ABSTRACT

Background: To analyze the disease characteristics and survival outcomes of Ewing's sarcoma family of tumors.
Methods: In this retrospective study, data analysis of Ewing's sarcoma patients between 2013 to 2016 were analyzed. Age, sex, stage, site, skeletal/extra skeletal tissue of origin, and treatment details were recorded. Complications during chemotherapy were recorded. Survival outcomes were analyzed.
Results: Out of the 42 cases, 54.8% were males. The mean age at presentation was 22.7±13.47 years. Majority of patients (66.7%) had limited disease at presentation. Most of the patients (57.1%) had extra skeletal Ewing's sarcoma. VAC/IE and VAC only chemotherapy was given for limited and extensive disease respectively. Only 7 patients received planned cycles of chemotherapy in the limited stage. Symptomatic cardiac failure was observed in 3 patients. Two patients developed deep vein thrombosis of leg during therapy. One patient died due to febrile neutropenia. Two year PFS and OS are 33.3 % and 40% respectively for the whole group.
Conclusion: Extra skeletal involvement comprises a larger number of cases as compared to skeletal Ewing's sarcoma. Survival outcomes are poor owing to poor compliance to the therapy.

KEYWORDS : Ewing's sarcoma, skeletal, extra skeletal, FLI-1

INTRODUCTION:

Ewing sarcoma family of tumors (ESFT) is highly aggressive sarcoma of bone and/or soft tissue. It is the second most common bone tumor in children and adolescents [(1)]. The majority of cases (around 85%) occur in the bones; however about one fourth of cases can occur in the soft tissues as well. The site of disease is the major determinant of the outcome of patients with Ewing's sarcoma, with visceral involvement being an adverse prognostic marker than bone and soft tissue. Involvement of the extremities is reported to have a better prognosis than those located in the axial skeleton in bone and soft tissue Ewing's sarcoma.[(2)] The multimodality treatment strategies have improved the outcomes of localized ESFT [(3,4).] The objective of the study was to assess the clinical profile , and survival outcomes of Ewing's sarcoma patients at our institution.

Materials and Methods:

All the patients with biopsy proven Ewing's sarcoma were analyzed retrospectively from January 2013 to January 2016. This study was done in medical oncology department, Sri Venkateswara institute of medical sciences. Clinical features including age, gender, site, skeletal/extra skeletal tissue origin, stage and treatment details and complications were recorded. Staging evaluation was done with Computed tomography of chest, total body bone scan and bone marrow biopsy. Cardiac evaluation was done prior to chemotherapy. Limited disease is treated with surgery and or radiotherapy and VAC/IE (Vincristine, Adriamycin, Cyclophosphamide/ Ifosphamide, Etoposide) for the duration of one year. VAC (Vincristine, Adriamycin, and Cyclophosphamide) is given in all extensive disease patients. Patients treated with definitive radiotherapy received 54-59.4 Gy. Palliative radiotherapy was given in symptomatic patients. Survival outcomes were analyzed. All the patients were followed till August 2018.

Results:

A total of 42 patients were included for the analysis. Of them, 23 were male and 19 were female. The mean age at presentation was 22.7 ± 13.47 years. Majority of patients (66.7%) were presented at limited stage. Most of the patients (57.1%) had extra skeletal Ewing's sarcoma. Iliac bone was the most common site of involvement in skeletal Ewing's sarcoma (Table 2). Lower extremity was the commonest site of involvement in extra skeletal Ewing's sarcoma (Table 3). Five patients had atypical sites of presentation. The atypical sites being are adrenal gland, Liver, great toe, bladder and nasal cavity. All patients (100%) showed positive staining with FLI-1 on immunohistochemistry and 90% of the patients showed CD99 positivity. Out of 28 patients with limited disease, only 7 patients received planned chemotherapy of 17 cycles. All patients with limited disease and two patients with oligometastatic disease received definitive local therapy. Seven patients received palliative radiotherapy in extensive stage. Symptomatic cardiac failure was observed in 3 patients. Two patients developed deep vein thrombosis of lower limb during therapy. One patient died due to febrile neutropenia. Median follow-up period was 16 months. Two year PFS and OS are 33.3% and 40% respectively. Median survival was not statistically significant between skeletal and extra skeletal Ewing's sarcoma (22months vs 12 months; Log Rank Sig=0.485)

DISCUSSION:

Ewing's sarcoma is an interesting entity that can involve both the skeletal system and the soft tissues of the body. Both the Ewing sarcoma and the peripheral primitive neuroectodermal tumors show the same reciprocal translocation between chromosomes 11 and 22, t (11; 22). In contrary to the current literature data from our institute showed a larger number of extra osseous Ewing's sarcoma (61.9%) as compared to primary bone Ewing's sarcoma [(5).] Reports from previous studies suggest that the Ewing sarcoma and the peripheral primitive neuroectodermal tumors of bone or soft tissue origin are similar and are histogenetically related [(6, 7)]. A study done by Baldini et al reported that Ewing's Sarcoma patients with extra-skeletal primary may be unfavorable predictor for survival, the other adverse predictors being metastasis at diagnosis and older age [(8)]. In the present study we could not find any significant difference in survival between skeletal and extra skeletal Ewing's sarcoma.

Immunohistochemistry studies are important to differentiate Ewing's sarcoma from other small round cell tumors especially lymphoma and Rhabdomyosarcoma. Despite initial promise, CD99 (MIC2) has not proven to be a specific marker. Approximately 90% of ES/PNET have a specific t (11; 22) (q24;q12) that results in fusion of the EWS and FLI-1 genes, and overexpression of FLI-1 protein. Immunohistochemical detection of FLI-1 may be valuable in confirming the diagnosis of ES/PNET in cases in which molecular genetic evaluation is not feasible. FLI-1 protein expression is also helpful in distinguishing ES/PNET from other tumors that may be CD99-positive, such as RMS [(9).] In the present study most of our patients showed positive for CD 99 and FLI-1.

Management of Ewing's sarcoma involves primary induction chemotherapy, followed by local therapy and adjuvant chemotherapy [(10)] . In the present study all limited stage disease patients received 4 cycles of induction chemotherapy followed by local therapy and adjuvant chemotherapy. Patients with extra skeletal disease underwent

upfront surgery followed by chemotherapy. With the current multimodality treatment strategy, overall survival at 5 years typically ranges between 50 and 70% [11]. Most of the mortality is due to metastatic disease, which occurs in approximately 30% of patients [12] .In the present study 2 year overall survival was 40%. Most the patients in the present study could not complete planned cycles of chemotherapy may be the reason for lower survival.

Table 1: Demographic data

Category		Number (N)	Percentage (%)
Age	Range 7-67 years Mean Age at presentation 22.7 ± 13.47 years		
Sex	Male Female	23 19	54.76 45.23
Stage	Limited Extensive	28 14	66.6 33.3
Site	Skeletal Extra skeletal	16 26	38.09 61.9
No. of Patients completed planned cycles of chemotherapy (17 cycles)		9	21.4
No .of patients received definitive local therapy *		30	71.4
IHC	FLI-1 CD 99	42 38	100 90.4

*Two patients in extensive stage received definitive local therapy in view of oligometastatic disease

Table2:- Site of involvement in Skeletal Ewing's sarcoma / PNET (n=18)

Site of involvement	Number of patients
Radius	1
Iliac bone	6
Fibula	1
Great toe	1
Femur	1
Scapula	2
Rib	2
Humerus	1
Spine	2
Spenoid ridge	1

Table3:- Site of involvement in Extra Skeletal Ewing's sarcoma / PNET (n=24)

Site of involvement	Number of patients
Anterior mediastinum	2
Retro peritoneum	3
Pre sacral mass	3
Pre scapular mass	1
Para vertebral mass	1
Lower limb	4
Fore arm	1
Nasal cavity	1
Bladder	1
Adrenal	1
CNS	1
Liver	1
Retro orbital mass	1
Inguinal node	1
Chest wall mass	1
Pelvis	1

REFERENCES:

1. Naomi BJ, Richard BW. Ewing's sarcoma. Lancet Oncol. 2010;11:1 84-92.
2. Obata H, Ueda T, Kawai A, Ishii T, Ozaki T, Abe S, et al. Japanese Musculoskeletal Oncology Group. Clinical outcome of patients with Ewing sarcoma family of tumors of bone in Japan: the Japanese Musculoskeletal Oncology Group cooperative study. Cancer. 2007; 109:767–75.
3. Esiashvili N, Goodman M, Marcus RB., Jr Changes in incidence and survival of Ewing sarcoma patients over the past 3 decades: Surveillance Epidemiology and End Results data. J Pediatr Hematol Oncol. 2008; 30:425–30.
4. Krasin MJ, DavidoffAM, Rodriguez-Galindo C, Billups CA, Fuller CE, Neel MD, et al. Definitive surgery and multiagent systemic therapy for patients with localized Ewing sarcoma family of tumors: Local outcome and prognostic factors. Cancer. 2005; 104:367–73.
5. Xie CF, Liu MZ, Xi M. Extraskeletal Ewing's sarcoma: a report of 18 cases and literature review. Chin J Cancer. 2010; 29:420-44.
6. Applebaum, M. A., Worch, J. , Matthay, K. K., Goldsby, R. , Neuhaus, J. , West, D. C. and DuBois, S. G. (2011), Clinical features and outcomes in patients with extraskeletal ewing sarcoma. Cancer, 117: 3027-3032.
7. Ushigome S, Shimoda T, Nikaido T, Nakamori K, Miyazawa Y, Shishikura A, Takakuwa T, Ubayama Y, Spjut HJ: Primitive neuroectodermal tumors of bone and soft tissue. With reference to histologic differentiation in primary or metastatic foci. Acta Pathol Jpn 1992, 42(7):483-493.
8. Baldini EH, Demetri GD, Fletcher CD, Foran J, Marcus KC, Singer S: Adults with Ewing's sarcoma/primitive neuroectodermal tumor: adverse effect of older age and primary extraosseous disease on outcome. Ann Surg 1999, 230(1):79-86.
9. FolpeAL,HillCE, Parham DM, O'Shea PA, Weiss SW. Immunohistochemical detection of FLI-1 protein expression: a study of 1 32 round cell tumors with emphasis on CD99-positive mimics of Ewing's sarcoma/primitive neuroectodermal tumor. Am J Surg Pathol. 2000; 24:1 657-62.
10. Schuck A, Ahrens S, Paulussen M et al. Local therapy in localized Ewing tumors: results of 1058 patients treated in the CESS 81, CESS 86, and EICESS 92 trials. Int J Radiat Oncol Biol Phys 2003; 55:168–177.
11. P. J. Leavey, L. Mascarenhas, N. Marina et al., "Prognostic factors for patients with Ewing sarcoma (EWS) at first recurrence following multi-modality therapy: a report from the children's oncology group," Pediatric Blood and Cancer, vol. 51, no. 3, pp. 334–338, 2008.
12. H. W. Hense, S. Ahrens, M. Paulussen, M. Lehnert, and H. Jurgens, "Factors associated with tumor volume and primary¨ metastases in Ewing tumors: results from the (EI) CESS studies," Annals of Oncology, vol. 10, no. 9, pp. 1073–1077,1999.