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Original Article

Metastatic Synovial Sarcoma: Experience from a Tertiary Care Center from India

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Abstract

Background: Synovial sarcoma represents 8% of all soft-tissue sarcoma (STS). It is a high-grade STS, and 50% of patients develop metastasis. The most common site of metastasis is the lungs, lymph nodes followed by bones. Ifosfamide-based chemotherapy is associated with improved outcome. In this study, we report our experience of metastatic synovial sarcoma according to primary sites, metastatic pattern, and their outcome. **Materials and Methods:** This was a retrospective observational study carried out at our institute from January 2013 to December 2016. The aim of our study was to evaluate the pattern of metastasis, response to chemotherapy, and survival in patients with metastatic synovial sarcoma. **Results:** Over a period of 4 years, 43 patients with metastatic synovial sarcoma were diagnosed with median age of 30 years. Nearly 70% of patients had lung metastasis, other site of metastasis were lymph node, bone, and liver. Thirty patients received chemotherapy with a combination of ifosfamide and doxorubicin. The overall response rate was 87% with median progression-free survival of 8 months. Patients with lung only metastasis had better survival compared with nonpulmonary metastatic site (18 months vs. 12 months). The median survival was 18 months. **Conclusion:** Metastatic synovial sarcoma is chemoresponsive tumor with lung being the most common metastatic site. Patients with lung only metastasis had a better outcome than nonpulmonary metastasis.

Keywords: *Metastatic synovial sarcoma, sarcoma, synovial sarcoma*

Introduction

Synovial sarcoma represents 8%–10% of all soft-tissue sarcoma (STS). Synovial sarcomas may be diagnosed at any age, but the mostly occurs in young adults, between 15 and 35 years of age, and more commonly in males.[1] Although relatively rare, synovial sarcoma is the third-most common extremity STS. It affects mostly young adults, with a median age of 35 years.[2] Despite its name, synovial sarcoma is a misnomer; it does not originate from synovial tissue. It may sometimes originate near the joint but never within it. Its cellular origin is undefined.[3] Sometimes, it may be encountered in regions without apparent relationship to synovial structures, including the head and neck (<10%), thoracic and abdominal wall (<10%), or intrathoracic sites.[4] Synovial sarcomas are of four subtypes – monophasic fibrous (spindle), monophasic epithelial, biphasic, and poorly differentiated and monophasic subtype being the most common. Biphasic subtype has both, epithelial and spindle cell components.[5] Its unique t(X: 18)(p11.2; q11.2) translocation helps to define the diagnosis and to distinguishes this subtype from other STSs.[6]

Synovial sarcoma is an aggressive STS with a higher propensity for recurrence and metastasis. Overall 50% of patients develop metastatic disease either at initial presentation or later in the disease course. The most common site of metastasis is the lungs (74%–81%), lymph nodes (3%–23%), and bones (10%–20%).[7-9] In this study, we report our experience of metastatic synovial sarcoma according to primary sites, metastatic pattern, and their outcome.

Material and Methods

Study

This was a retrospective descriptive study carried out at Kidwai Cancer Institute, a tertiary care center at Bengaluru, India.

Patient eligibility

Patients of metastatic synovial sarcoma (either at initial presentation or relapsed)

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evaluated at our institute from January 2012 and December 2016 were included in this study. Biopsy from the primary site or accessible metastatic site was performed. The diagnosis was made by histopathological examination and appropriate immunohistochemistry marker such as cytokeratin, epithelial membrane antigen, desmin, vimentin, smooth muscle antigen, and S-100. All patients underwent staging evaluation with computed tomography (CT) scan/magnetic resonance imaging of primary site and CT scan of thorax and abdomen.

Treatment

Patients with the Eastern Cooperative Oncology Group performance status (PS) of 0–2 received chemotherapy. Combination of ifosfamide (1.8 g/m^2 days 1–3) and doxorubicin (75 mg/m^2 day 1) repeated every 21 days was used in all eligible patients. Maximum 6 cycles were planned depending on interim reassessment and tolerability.

Response assessment

Reassessment CT scan was performed at the end of 3 cycles of chemotherapy or on suspected clinical progression. The response evaluation was based on RESIST 1.1 criteria. All patients with stable disease, partial response, or complete response received another 3 cycles of chemotherapy.

Statistical analysis

SPSS software, version 23.0 (SPSS, Chicago, IL, USA) was used for all statistical analysis. The association of different variables was analyzed using the log-rank test. Multivariate analysis was done to test the correlation of different factors with survival. Overall survival analysis was done using the Kaplan–Meier method.

Results

Over a period of 4 years, 43 patients with metastatic synovial sarcoma were diagnosed at our institute.

The median age at diagnosis was 30 years (10–70 years). A female preponderance was seen with a male to female ratio being 1:1.15 [Table 1]. Extremity was the most common site of primary tumor seen in 76% (n = 32) of all patients. Retroperitoneum (7%) and neck (7%) were the next common site of primary tumor [Table 2].

The most common site of metastasis was lung (69.7%) followed by lymph node and bone with the incidence being 18.6% and 11.6%, respectively. Liver metastasis was uncommon and present in only 6.9% of patients.

Thirteen patients did not receive any chemotherapy in view of poor PS. Thirty patients received chemotherapy with a combination of ifosfamide and doxorubicin.

As expected synovial sarcoma being chemoresponsive malignancy overall response rate (ORR) was 87%. One patient showed a complete response to the chemotherapy. The median progression-free survival was 8 months [Table 3]. Second-line chemotherapy on progression was received by only 8 patients. The overall median overall survival was 18 months.

Discussion

Synovial sarcoma occurs most commonly in adolescent and young adults. It occurs most commonly in the soft tissues of the extremities, especially near large joints, but other sites such as head and neck, lung, heart, mediastinum, and abdominal wall sites also have been reported.[10] Patients with synovial sarcoma have relatively high rates of response to chemotherapy. Ifosfamide-based chemotherapy has been associated with improved disease-specific survival

Table 1: Characteristics of metastatic synovial sarcoma patients

Characteristic	*n* (%)
Sex (n=43)	
Male	20 (46.5)
Female	23 (53.5)
Age (years)	
Median age	30
<18	5 (11.7)
18-60	37 (86.0)
>60	1 (2.3)
Histology	
Monophasic	28 (65.2)
Biphasic	13 (30.2)
No data	2 (4.6)
Pattern of metastasis	
Lung	38 (88.9)
Lymph node	3 (6.9)
Bone	2 (4.6)
Liver	2 (4.6)
Chemotherapy	
Received	30 (69.7)
Not received	13 (30.3)

Table 2: Site of primary tumor

Primary tumor	Number of patients (%)
Lower limb	25 (58.1)
Upper limb	8 (18.7)
Trunk	2 (4.6)
Chest wall	2 (4.6)
Retroperitoneum	3 (7.0)
Neck	3 (7.0)

Table 3: Response to chemotherapy

Response	*n* (%)
Complete response	1 (3.3)
Partial response	17 (56.7)
Stable disease	8 (26.7)
Progressive disease	4 (13.3)

with chemotherapy compared with no chemotherapy.[11,12] Ifosfamide appears to be most active agent with ORR of around 30%–55%.[13,14] We found that ORR with ifosfamide and doxorubicin 85% which is higher than as reported by Stefan Sleijfer *et al*.[15] Patients with lung only metastasis had better survival 18 months and 12 months as shown in Figure 1. Similar observation reported by Salah *et al*.[16]

Other newer drugs which showed some efficacy in metastatic synovial sarcoma are pazopanib and sunitinib.[17,18] Pazopanib showed activity in a variety of STS including synovial sarcoma in various phase 2 and phase 3 clinical trials.[19-21] Olaratumab is a recombinant human monoclonal antibody that specifically targets PDGFRα, blocking PDGF-AA, PDGF-BB, and PDGF-CC binding and receptor activation. The result of the phase 1b/2 study, randomizing 133 patients to receive olaratumab plus doxorubicin or doxorubicin alone, showed a median progression-free survival of 6.6 months and 4.1 months. Median survival was 26.5 months and 14.7 months in experimental versus doxorubicin arm.[22]

Immunotherapy has been one of the major breakthroughs in oncology, for both solid and hematological tumors. In the SARC028 phase 2 study, pembrolizumab as a single agent showed activity in unselected STS of all types, with an ORR of 17.5%.[23]

Conclusion

Metastatic synovial sarcoma is a chemoresponsive malignancy with good response to ifosfamide and doxorubicin. Patients with extrapulmonary metastasis have dismal prognosis. There is a need for better novel agents for achieving better treatment outcomes.

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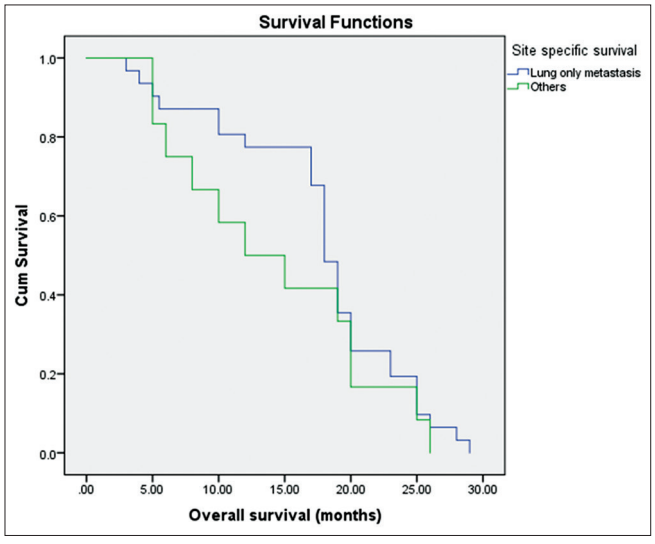

Figure 1: Survival curve comparing lung only metastasis versus other site of metastasis

Conflicts of interest

There are no conflicts of interest.

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