ORIGINAL RESEARCH PAPER

Volume-8 | Issue-2 | February-2019 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

CLINICOPATHOLOGICAL AND IMMUNOPHENOTYPIC STUDY OF SPINDLE CELL SARCOMAS.

Pathology

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ABSTRACT

Malignant mesenchymal tumours are rare. 60 cases of spindle cell sarcoma were recruited during January 2014- May 2015 and differentiated into subtypes based upon histo-pathological features and immuphenotyping. MPNST (Malignant Peripheral Nerve Sheath tumour) was found to be the most common type with lower extremity as the most common site. Grade 3 tumours had higher propensity to metastasize and lung was found to be the most common site of metastasis. This study highlights the importance of histologic grade as the single most important independent prognostic parameter for predicting the tumor behaviour.

KEYWORDS

Introduction

Malignant mesenchymal neoplasms amount to less than 1% of overall human burden of malignant tumors but they are life threatening and may pose a significant diagnostic and therapeutic challenge[1,2].The close interaction between surgical pathologists,surgeons and oncologists has brought about a significant increase in disease free survival for tumours which were considered fatal .Careful physical examination and radiologic evaluation to evaluate the size,depth and location of the mass,along with signs of neuro vascular involvement are essential for designing the best therapeutic approach. Amongst the sarcomas,spindle cell sarcomas comprise almost one third of the total sarcomas.The most common spindle cell sarcomas in the adult population are Malignant peripheral nerve sheath tumor,synovial sarcoma,leiomyosarcoma and fibrosarcoma.

In this study we have analyzed a group of 60 adult patients with spindle cell sarcomas.The main objective was to study the clinico-pathological parameters affecting spindle cell sarcomas.

Methods and materials

The aim of the study was to differentiate the various subtypes of spindle cell sarcoma based upon the histological features and aided with Immunohistochemistry (IHC). This was a prospective study comprising of 60 adult patients of Spindle cell sarcoma, reported by the pathology department of our institute, during January 2014 - May 2015.

Inclusion criteria:

1. Age >14 years
2. Patients with soft tissue sarcoma showing spindle cell morphology on H&E (Haematoxylin and Eosin) stain.

Exclusion Criteria:

1. Benign spindle cell tumour
2. Tumours which mimicked spindle cell tumor
3. Visceral spindle cell tumors (lesions arising from visceral organs)

Patient details:

All clinical information like age, presenting symptoms, clinical stage and residual disease was obtained from the case files. Biopsy was available for all the cases, for examination. Specimens of a few cases were obtained for histo-pathological examination. Special stain like Periodic Acid Schiff's (PAS) stain was used in a few cases to aid the diagnosis. IHC was used in all cases for final diagnosis. A pre-treatment TNM staging (AJCC 7th edition) was done for all patients by doing an MRI/CT scan of the primary tumor site, chest X-ray and a CECT of the thorax. The duration of survival was measured up to the date of death or last date of follow up.

Procedure for histo-pathological evaluation:

Formalin fixed, paraffin embedded and H&E stained biopsy slides were examined. Histological types were diagnosed according to the WHO classification of soft tissue sarcoma. The tumour was graded according to FNCLCC grading system. Histological parameters like mitosis/10HPF (high power field) , necrosis and pleomorphism were noted. Immunohistochemistry (IHC) was done in all the cases.

Treatment modality:

The treatment received by every patient was noted .e.g surgery, radiotherapy, chemotherapy or a combination of any of these modalities. All the patients were followed up in the entire study period. Any incidence of local recurrence or distant metastasis was noted.

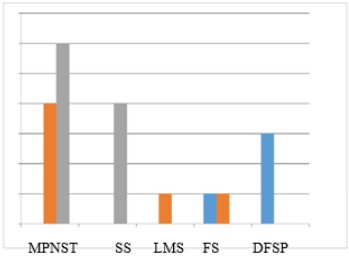
Results

25,345 new cancer cases were registered at our institute between January 2014-May 2015. Out of this, 229 cases were diagnosed as soft tissue sarcoma, accounting to 0.9% of total tumor burden. 60 cases out of this, were diagnosed as adult spindle cell sarcoma, which were included in our study. Table 1and 2 shows the parameters of these patients.

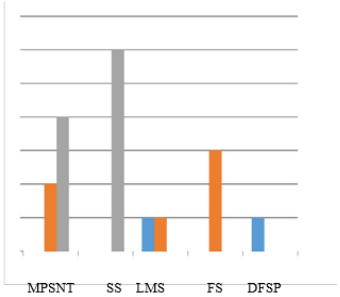
Table 1 showing parameters of the patients

No.	Parameters	% of patients
1	Median age in years(range)	43.8 years(15-85 years)
2	Sex Female Male	 47% 53%
3	Site Lower extremity Upper extremity Retroperitoneum Head and neck Abdomen-pelvis Chest wall	44% 18% 8% 12% 10% 8%
4	Median size in cm	6cm(1.2-12cm)
5	Location Superficial Deep	 15% 85%
6	Histo-pathological diagnosis MPNST SS LMS Fibrosarcoma DFSP others	 35% 28% 18% 12% 5% 2%

7	Histological grade Grade 1 Grade 2 Grade 3	 12% 40% 48%
8	Recurrence	33%



Graph 1 shows the relation between grade and recurrence.



Graph 2 shows the relation between grade and metastasis.

Discussion

In the current study,60 cases of spindle cell sarcomas presenting at GCRI over a duration of January 2014 to May 2015 were studied. Median age of patients for spindle cell sarcomas in our study was 43.8 yrs,which was in accordance with the study by takafumi et al whose median age for soft tissue sarcomas was 44 years. The commonest site for spindle cell sarcomas was the lower extremities(44%) which was in agreement with takafumi et al(46%)stating it to be the commonest site for soft tissue sarcomas as well .Location is an important factor guiding the tumor behaviour as locations like extremities,head and neck are superficial tumors ;as they present at an early stage and are hence associated with a better prognosis.Where as the tumors with deeper locations like retroperitoneum present at a later stage and are hence of higher grades. The 3 major clinicopathological parameters that establish the risk profile for a given patient are tumor size,anatomic depth(relative to the investing fascia or body musculature wall) and histologic grade. Tumor depth is an important independent prognostic factor for predicting survival rates.Deep seated tumors present late and at a higher grade.In our study 85% were deep seated, In our study 62% patients had tumor size more than 5 cms Larger tumor size is associated with a higher local recurrence rate,distant metastasis and aggressive tumor behaviour. Histologic grade is currently the most important prognostic factor for spindle cell sarcomas. grade III tumors had higher recurrence and metastasis,making grade of sarcomas as an important prognostic parameter.

As per the literature,the survival rates for spindle cell sarcomas are substantially higher for grade I tumors and subsequently lower for the higher grades.This fact is supported by our study,in which grade 3 tumors behave aggressively and have shown higher local recurrence and metastasis. This higher rate of recurrence in attributed to the effect of local reseeding by systemically circulating tumor cells that deposit at the primary site after its removal.Local recurrence may also result in case of inadequate treatment ,because the tumor has given rise to satellite tumors (local metastasis)outside the resected margin.In either case,residual tumor cells probably explain the higher recurrence rate in majority of the cases.Increased metastasis and local recurrence reflect combined local and distant aggressiveness of highly malignant tumors.Other reasons to support higher recurrence rates are inadequate surgical excision due to approximation to the vital structures or multicentricity,inadequate or no neoadjuvant chemotherapy or RT or previous surgery at an inexperienced center.

In our study Grade III spindle cell sarcomas show higher propensity to metastatize which is in concordance with the literature[3,4,5,6]. 12/18 cases as per our study have metastatised via the hematogenous route supporting various literatures that these tumors mainly spread via the hematogenous route and the most common site is the lung.Synovial sarcoma followed by MPNST were the most common tumors to metastatize to the ung. As per the literature,[7,8,9,10], sarcomas rarely metastatize to the lymph nodes.The soft tissue sarcomas commonly showing lymphatic spread are synovial sarcoma,MPNST, rhabdomyosarcoma,clear cell sarcoma and epitheloid sarcomas.Our study had synovial sarcoma ,MPNST and DFSP showing lymphatic spread. In our study, only 3 cases of DFSP were obtained. All 3 cases showed CD34 positivity and recurrence.However,the data is too small to comment on.The higher rate of recurrence can be explained by suggesting that a fibrosarcomatous area within DFSP leads to higher recurrence and more aggressive behaviour.To diagnose sarcoma arising in DFSP we have to look for a constellation of features:atleast 5-10% sarcomatous area,fascicular architecture,plump spindle cells of higher nuclear grade,higher mitosis (7-15/hpf)detected by higher MIB1 index and diminished immunoreactivity for CD34. Hence with the help of proper sampling,immunohistochemistry and adequate excision we can avoid higher local recurrence rates.

As per our study,85% of patients underwent surgery along with other adjuvant therapy ,making it the main stay of treatment for spindle cell sarcomas. Novel molecular markers have emerged as a newer promising diagnostic and prognostic modality in some spindle cell sarcomas. In synovial sarcomas,SYT-SSX translocation helps in distinguishing it from other primitive sarcomas and predicts tumor behaviour.

Conclusion

To conclude, the current 60 case study of spindle cell sarcomas,has illustrated the clinicopathological characteristics of spindle cell sarcomas,presenting at our institute.The median age at presentation was 43.8 years.Most common site involved by spindle cell sarcomas was the lower extremities(44%).The most common spindle cell sarcoma histologically was MPNST(35%).Most cases presented as grade III tumors(48%).Grade III tumors had more recurrence and metastasis compared to grade I tumors.This highlights the importance of histologic grade as the single most important independent prognostic parameter for predicting the tumor behaviour.Most common site to metastatize was the lung via the hematogenous route.IHC proved vital in clinching the diagnosis.Surgery is the corner stone for the treatment of all spindle cell sarcomas.neoadjuvant CT and RT help in improving patient survival. A multi disciplinary approach is advisable with the pathologist,radiologist and the oncosurgeons joining hands to achieve better results and improving patient survival in cases of spindle cell sarcomas.

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