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Retroperitoneal Sarcomas – A Pathological Study

Dr.N.V.Vanitha, M.D.(Path.)[1], Dr.K.Deepa, M.D.(Path)[2]
[1](Sr.Asst.Prof., Institute Of Pathology, Madras Medical College, Chennai, India).
[2](Sr.Asst.Prof., Institute Of Pathology, Madras Medical College, Chennai, India).

Abstract: *Retroperitoneal sarcomas comprise heterogeneous groups of neoplasms, generally presenting late in the disease course, associated with poor patient survival and less amenable to complete surgical excision.*
Aim Of The Study*: To analyse the clinicopathological features of different types of retroperitoneal sarcomas and the role of immunohistochemistry in the diagnosis of selected cases.*
Materials and methods*: This is a retrospective study of retroperitoneal sarcomas reported in a tertiary care hospital (Institute of Pathology, Madras Medical College, Chennai) from January 2007 to August 2014. The cases were studied with reference to age, sex, tumor size, histological type and grade. The immunohistochemical evaluation done in selected cases reviewed.*
Results*: Retroperitoneal sarcomas studied showed a male preponderance with majority of cases in the fifth and sixth decades. The tumors are generally large with advanced histological grade. The liposarcomas are the most common tumors. Immunohistochemistry appropriately done with a panel of markers selected based on the clinical picture and histomorphology aid in the diagnosis.*
Conclusion*: Retroperitoneal sarcomas constitute a difficult diagnostic and management problem. With the increasing availability of more sensitive and specific antibodies to identify the different lineages of tumors, immunohistochemistry has acquired a major role in the precise diagnosis of soft tissue sarcomas, hence improving the patient prognosis.*
Keywords: *immunohistochemistry, retroperitoneum, sarcomas, soft tissue tumors.*

I. Introduction

The retroperitoneum is the portion of the lumboiliac region limited anteriorly by the peritoneal covering, posteriorly by the posterior abdominal wall, superiorly by the twelfth rib and vertebra, inferiorly by the base of the sacrum and iliac crest, and laterally by the side borders of the quadratus lumborum muscles. It contains, embedded in a meshwork of loose connective tissue, the adrenal glands, kidneys and ureters, aorta and its branches, inferior vena cava and its tributaries, and numerous lymph nodes.[2]

The neoplasms arising in the kidney, adrenal gland and retroperitoneal lymph nodes are actually the most common primary tumors in retroperitoneum in the adults.[2]The soft tissue tumors are relatively less common in the retroperitoneum. The retroperitoneal sarcomas constitute 15% of all primary sarcomas; retroperitoneum being the second most common site for sarcomas after the deep tissues of lower extremities.[1]

Both primary and metastatic tumors in the retroperitoneum grow silently for a considerable period of time before clinical signs and symptoms appear. This is due to the availability of potential large space with abundant loose connective tissue and relative paucity of vital structures. In general the clinical presentation is vague and related to the compression/invasion of neighbouring structures and obstructive phenomena.[2]

The diagnosis of retroperitoneal soft tissue tumors is generally based on clinical, radiological and histological features. However in certain tumors with overlapping histological features and in high grade sarcomas with poor phenotypic differentiation accurate diagnosis is a challenge, where in, immunohistochemistry for specific antigens or cytogenetic analysis to detect tumor specific genetic alterations contribute to the definitive diagnosis.

II. Aim Of The Study

To analyze different types of retroperitoneal soft tissue sarcomas with reference to clinicopathological features – age, sex, tumor size, histological type and grade.

To evaluate the diagnostic role of immunohistochemistry in appropriate cases, where needed.

III. Materials And Methods

This was a retrospective study including retroperitoneal sarcomas reported over a period of 92 months (from January 2007 to August 2014) in the Institute of Pathology, Madras Medical College, Chennai. The 25 cases retrieved from the medical records include 14 excised specimens and 11 biopsies. The cases are analyzed with reference to clinicopathological parameters of age, sex, tumor size, histological type and grade. Correlation

with clinical and radiological features reviewed. Formalin fixed paraffin embedded tissue sections stained with hematoxylin and eosin were studied and immunohistochemical evaluation done in appropriate cases analyzed.

IV. Results

Out of 25 cases studied, 14 were excised specimens and 11 were biopsies. The age range was from 23 yrs to 68 yrs with a mean age of 48 yrs. The study group included 17 male patients and 8 female patients with male: female ratio of 2:1. The tumor size ranged from 6cm to 40cm; average size of the tumor being 21cm. The distribution of tumors as to the age, sex and tumor size is given in the Table.1 below:

Table-1

Patient characteristics	No. of tumors(percentage)
Age	
21- 40yrs	07(28%)
41- 60yrs	16(64%)
61- 80yrs	02(08%)
Sex	
Male	17(68%)
Female	08(32%)
Tumor size	
≤ 10cm	06(24%)
10 – 20cm	07(28%)
≥ 20cm	12(48%)

Liposarcomas constitute the most common tumors (36%) followed by undifferentiated pleomorphic sarcomas (20%) and leiomyosarcomas (16%). The different tumors encountered and the tumor categorization according to the FNCLCC grading system are given in the Table-2. The predominant tumors were of high grade. Accurate diagnosis was made in 11 cases (44%) based on histological examination with routine H&E stained sections. Immunohistochemical evaluation was required in 14 cases (56%), of which 3 cases could not be analyzed due to inadequate tissue and included in 'others' in the Table-2; one was a case of High grade GIST/Poorly differentiated sarcoma and two cases were spindle cell sarcoma. The tumors were evaluated with a panel of antibodies including positive and negative markers for the suspected correct diagnosis and also markers to rule out the tumors considered in differential diagnosis.

Table-2

Tumor type	No. of tumors (percentage)
Liposarcoma	**09(36%)**
Well differentiated liposarcoma	04
Pleomorphic liposarcoma	02
Myxoidliposarcoma	
Dedifferentiated liposarcoma	01
Undifferentiated pleomorphic sarcoma	**05(20%)**
Leiomyosarcoma	**04(16%)**
Gastrointestinal stromal tumor	**03(12%)**
Malignant peripheral nerve sheath tumor	**01(04%)**
Others	**03(12%)**
GIST–high grade / poorly differentiated sarcoma	01(04%)
Spindle cell sarcoma	02(08%)
Histological grade	
Grade I	05(20%)
Grade II	07(28%)
Grade III	13(52%)

Liposarcomas were diagnosed with histomorphology (Fig.1&2). Leiomyosarcomas showed diffuse positivity for SMA and desmin (Fig.4,5&6). GISTs showed diffuse CD117 positivity (Fig.9&10) and focal SMA positivity in 2 cases. Focal expression of CD68 and absence of CD117, SMA, desmin, S100 was observed in undifferentiated pleomorphic sarcoma. Malignant peripheral nerve sheath tumors showed focal S100 positivity (Fig.7&8).

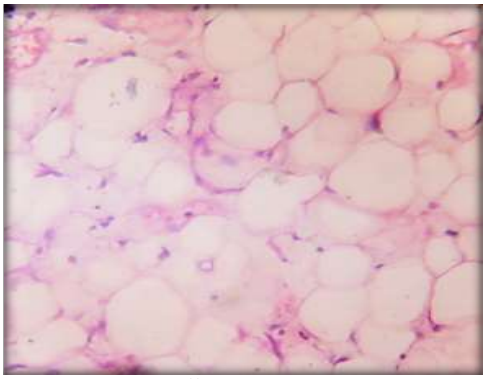

Fig.1 Well differentiated liposarcoma,H&E

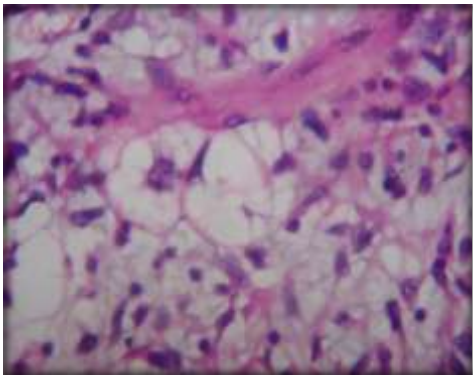

Fig.2 Multivacuolated lipoblasts in pleomorphic liposarcoma, H&E

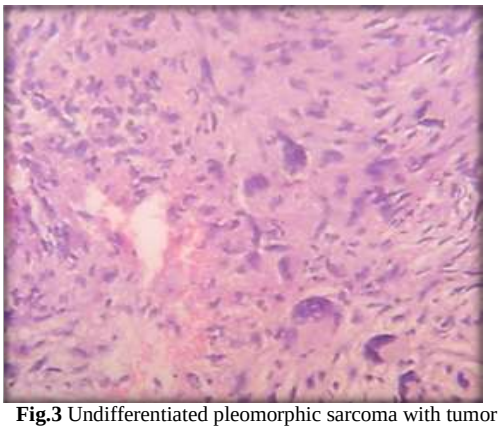

Fig.3 Undifferentiated pleomorphic sarcoma with tumor giant cells, H&E

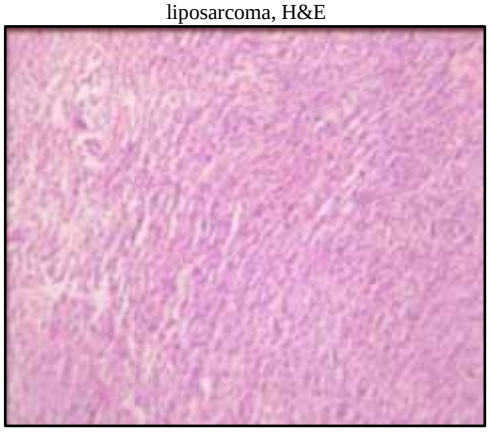

Fig. 4 Leiomyosarcoma, H&E

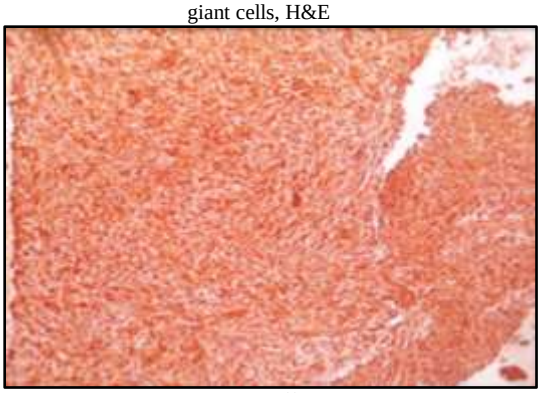

Fig.5 Leiomyosarcoma, diffuse SMA positivity

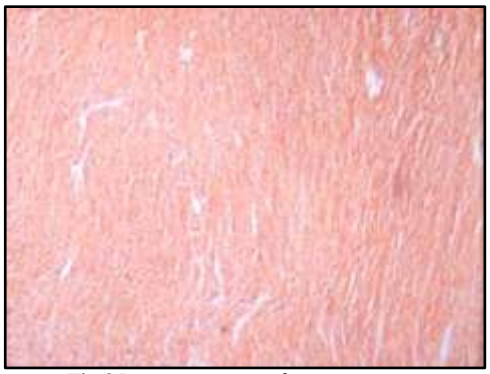

Fig.6 Leiomyosarcoma, desmin positivity

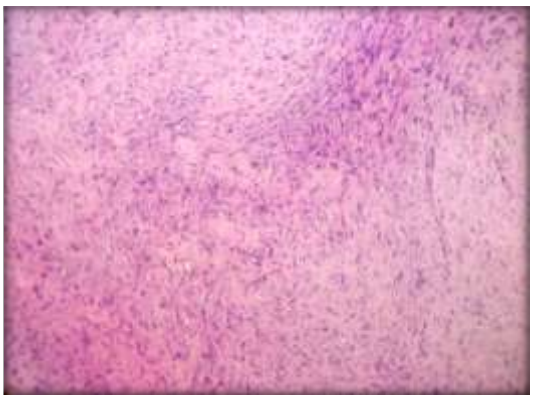

Fig.7 Malignant peripheral nerve sheath tumor,H&E

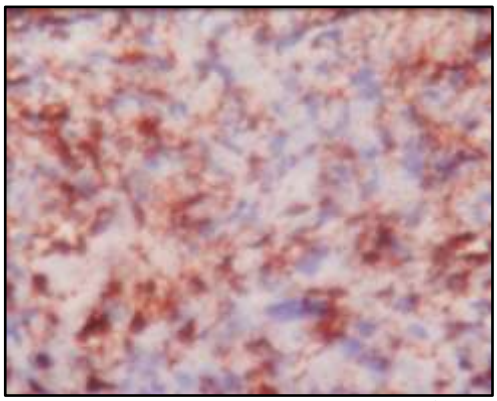

Fig.8 Malignant peripheral nerve sheath tumor, focal S100 positivity

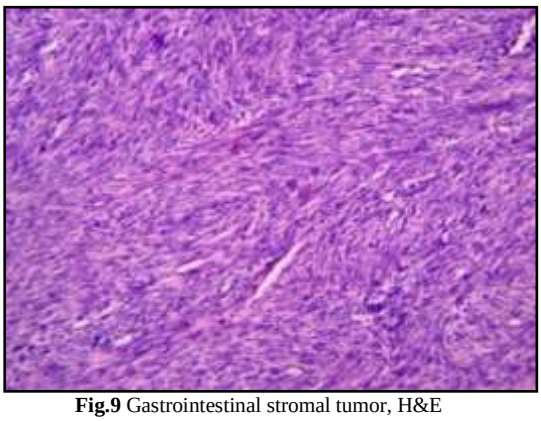

Fig.9 Gastrointestinal stromal tumor, H&E

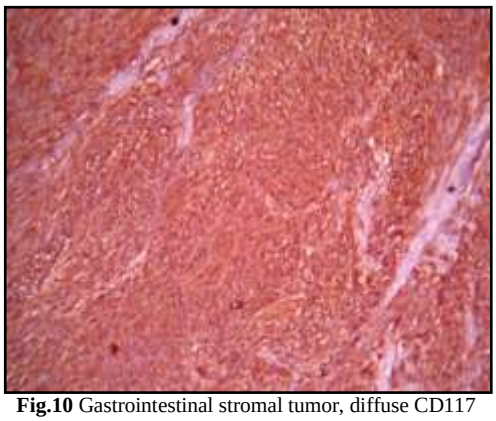

Fig.10 Gastrointestinal stromal tumor, diffuse CD117 positivity.

V. Discussion

Retroperitoneal sarcomas include complex heterogeneous groups of neoplasms, presenting a diagnostic challenge to pathologists in many instances.However, the range of commonly encountered soft tissue neoplasms in the retroperitoneum is more limited; the most common being of lipomatous, smooth muscle or neural differentiation.[1, 2] Malignant tumors are four times more frequent than benign tumors in retroperitoneum. This is in contrast to the occurrence of soft tissue neoplasms elsewhere in the body, where benign tumors predominate.[1] They should be distinguished from the more common retroperitoneal tumors, the lymphoproliferative disorders and parenchymatous epithelial tumors.[2]

The retroperitoneal sarcomas because of late clinical presentation and poor accessible location constitute a difficult management problem. Complete surgical excision is the primary modality of treatment for most primary and recurrent tumors.[3] Current chemotherapy is less effective and radiotherapy is limited by toxicity to adjacent structures.[4,5] The prognosis[6] depends on the tumor size, histological type and grade, surgical margins, clinical stage, DNA ploidy, cell proliferation index and genetic alterations. The primary retroperitoneal liposarcomas carry worse prognosis compared to those that arise in the trunk and extremities.[1] Also the leiomyosarcomas encountered in the retroperitoneum are more aggressive.[1]

In the current study, the predominant tumors (64%) occurred in the fifth and sixth decades with a M:F ratio of 2:1. The tumor size in most cases (48%) was ≥ 20cm with average size of 21cm. The liposarcomas constitute the common histological type followed by undifferentiated pleomorphic sarcoma and leiomyosarcoma which correlated with literature.[1,2] Majority of the tumors were of high grade. Routine histological examination with clinical picture aided the definitive diagnosis in 11 cases; 14 cases required immunohistohemical evaluation with a panel of antibodies for categorization.The results of this study were concordant with various studies conducted in the past and compared with some of the studies here in the Table 3.

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Table-3

Parameters	Stoeckle et al, 2001[7]	Van Dalen et al, 2001[8]	Lewis et al, 1998[3]	Gronchi et al, 2004[9]	Current study
No. of patients	165	142	500	167	25
Male:female ratio	1.0:1.2	1.0:1.22	1.34:1.0	1.2:1.0	2:1
Age(yrs)					
Median	54	60	58	53	50
Range	16-82	18-88	16-88	15-82	23-68
Tumor size (cm)					
Median	15	-	-	-	21
Range	2-70	-	-	-	6-40
Histology (%)					
Liposarcoma	26	38	41	57	36
Leiomyosarcoma	23	29	27	17	16
MFH	17	-	7	8	20
MPNST	8	-	3	8	4
Others	15	33	22	10	12
Grade (%)					
Low	16	45	36	35	20
Intermediate	41	36	-	-	28
High	43	16	64	65	58

Liposarcomas, the most frequent of the retroperitoneal sarcomas are generally diagnosed based on morphology.[10] In well differentiated liposarcomas(WDL) the identification of stromal cells with a requisite degree of atypia is more diagnostic than the identification of lipoblasts.[1]The recurrence rate with retroperitoneal WDL approaches 100% and the risk of dedifferentiation 10–15%.[1] The dedifferentiated liposarcomas occur more commonly in the retroperitoneum than in the soft tissues of extremities(3:1).The pleomorphic liposarcomas are equally distributed between the retroperitoneum and the deep soft tissues of the extremities. The dedifferentiated liposarcomas are composed of areas of WDL juxtaposed to areas of high grade nonlipogenic sarcoma, usually resembling either a fibrosarcoma or MFH. The pleomorphic liposarcomas, generally of two hisological patterns, pleomorphic spindle cell or pleomorphic round cell morphology with bizarre giant cells, have in addition, the characteristic univacuolated or multivacuolated lipoblasts. Both these types require adequate tissue sampling for a definitive diagnosis.[1] Myxoid liposarcomas are less common in the retroperitoneum.[1]

Undifferentiated pleomorphic sarcoma (MFH), the second most common sarcoma of retroperitoneum usually shows pleomorphic spindle cell morphology. It should be distinguished from dedifferentiated liposarcoma, pleomorphic liposarcoma, pleomorphic leiomyosarcoma, pleomorphic rhabdomyosarcoma, anaplastic carcinoma.[1] The diagnosis requires adequate tissue sampling and morphological evaluation; immunohistochemistry when employed includes a panel of antibodies to exclude the tumors considered in differential diagnosis. Undifferentiated pleomorphic sarcomas may show focal expression of intermediate filaments like keratin, desmin and neurofilament protein.[1]

Leiomyosarcomas of the retroperitoneum constitute one-half to three-quarters of the soft tissue leiomyosarcomas; occur more commonly in elderly females.[1] These tumors are generally malignant spindle cell neoplasms with microscopic features of smooth muscle differentiation showing intersecting fascicles of spindle cells with eosinophilic cytoplasm, cigar shaped nuclei and less interstitial collagen; need to be differentiated from fibrosarcoma, undifferentiated pleomorphic sarcoma(malignant fibrous histiocytoma), malignant peripheral nerve sheath tumor, GIST and monophasic synovial sarcoma. Immunohistochemically, they show diffuse positivity for desmin, smooth muscle actin (SMA), muscle specific actin (MSA), h-caldesmon, calponin and smooth muscle myosin (SMM); generally negative for CD34, CD117, and S100.[1]

The malignant peripheral nerve sheath tumors show focal positivity for S100, also expresses CD56/57 and SOX-10, a more specific marker for MPNST than S100.[11] Synovial sarcomas are positive for CD99, EMA, focally positive for CK and minority cases label focally for S100; TLE1 has emerged as a potentially useful marker in synovial sarcoma.[1] GISTs show diffuse cytoplasmic and membranous positivity for CD117.

Immunohistochemistry has a valuable role in the diagnosis of soft tissue tumors. The soft tissue tumors are categorized based on the neoplastic cell differentiation and the mature mesenchymal tissue they resemble. The principal morphological groups seen are spindle cell, epithelioid cell, small round cell and pleomorphic cell tumors, which when required apart from the routine morphological study, need to be evaluated with a panel of immunohistochemical markers or molecular and cytogenetic studies to be further characterized.

The two most prevalent grading systems of soft tissue sarcomas[1] include the FNCLCC grading system developed by the French Federation of Cancer Centers Sarcoma Group and the NCI (National Cancer Institute) grading system, United States. The FNCLCC system is based on three histological parameters including tumor differentiation, mitotic rate and tumor necrosis. The NCI system based on a combination of histologic diagnosis, cellularity, cellular pleomorphism, and mitotic rate as criteria for grading, also included necrosis as an important determinant for predicting recurrence and survival rates. Both the systems have demonstrated prognostic value.[1]

VI. Conclusion

Retroperitoneal sarcomas constitute a difficult diagnostic and management problem. The diverse morphological groups of tumors generally present late in the course of disease with an advanced histological grade. They need to be appropriately diagnosed for a better prognosis and patient survival. Nowadays immunohistochemistry is a main diagnostic tool in the evaluation of soft tissue sarcomas. Based on the clinical presentation and histomorphology, an appropriate panel of antibodies should be employed to arrive at a definite diagnosis. In sarcomas associated with specific translocations, even antibodies to fusion proteins are now available allowing a more precise diagnosis.

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