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Immunohistochemical study for typing of soft tissue neoplasms: Experience at a tertiary care institute

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Abstract

Immunohistochemistry (IHC) plays an important role in soft tissue tumors diagnosis. It is important that immunohistochemical evaluation must be employed with the clinical picture, the morphology and when necessary, other ancillary techniques such as molecular genetics and cytogenetic. The present study was conducted to include the morphological typing of the soft tissue tumors with the help of Immunohistochemistry markers. Immunohistochemistry provides an additional tool by which one can analyse poorly differentiated sarcomas and characterize them. Its specificity, sensitivity, cost effectiveness and applicability to routinely processed material, clearly make it an essential part of diagnostic pathological studies for soft tissue tumors. Also an attempt to categorise the soft tissue neoplasm according to World Health Organization [WHO] 2013 classification.

Keywords: immunohistochemistry, soft tissue neoplasm

Introduction

Over the years, application of immunohistochemistry (IHC) in surgical pathology has increased tremendously. Introduced in the early 1980s, immunohistochemistry is now a standard tool for evaluating the diagnosis and prognosis of tumors [1]. The impact of immunohistochemistry in pathology may be explained by three major advances: the availability of numerous good quality antibodies applicable on routine formalin-fixed tissues; improvements in antigen retrieval techniques and particularly heat-induced epitope retrieval (HIER) which provides consistent and reliable results; and the availability of sensitive detection systems. Immunohistochemistry (IHC) plays an important role in soft tissue tumors diagnosis. The first approach consists in ruling out a non mesenchymal tumor, followed by trying to define mesenchymal cell lineage. This approach, achieved with a panel of commonly used antibodies, helps narrow down the differential to a more manageable level. The present study was conducted to include the morphological typing of the soft tissue tumors with the help of Immunohistochemistry markers and attempts to classify according to WHO 2013 classification [2-5].

Material and Methods

This prospective study was performed over period of three years. During this period total 262 surgical specimens were received from patients clinically diagnosed to have soft tissue tumors for histopathological examination. All the cases of melanoma were excluded. Histopathological diagnosis was achieved using the microscopic examination of slides stained with Haematoxylin and Eosin stains. Formalin fixed paraffin embedded tissues were selected for IHC. 3 μ sections were cut on APES/ poly L-lysine coated slides. The sections were marked with a PAP pen to avoid future running off of the reagents. These slides were then kept for overnight incubation at 37 °C. Following markers were used.

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Histogenesis		Markers
1	Mesenchymal (general)	Vimentin
2	Epithelial	CK, EMA
3	Smooth muscle	Desmin, SMA
4	Skeletal muscle	Desmin, myogenin
5	Fibrohistiocytic	Vimentin, CD ₆₈
6	Melanocytes	HMB45, S-100
7	Neuronal	S-100, NSE
8	Endothelial/vascular	CD ₃₄ , CD ₃₁
9	Neuroendocrine Ewing sarcoma/PNET	NSE, CD99, Chromogranin

Table 1: Categorewise distribution of soft tissue tumor cases

Type	Benign Cases (%)	Malignant Cases (%)	Total Cases (%)
Adipocytic	106 (40.4%)	03 (1.2%)	109 (41.6%)
Fibrous	39 (14.8%)	05 (2.0%)	44 (16.8%)
Fibrohistiocytic	24 (09.1%)	04 (1.6%)	28 (10.7%)
Smooth Muscle	03 (01.1%)	02 (0.8%)	05 (1.9%)
Skeletal Muscle	Nil	06 (2.2%)	06 (2.2%)
Peripheral nerve and nerve sheath tumor	57 (21.8%)	Nil	57 (21.8%)
Tumors of uncertain differentiation	05 (01.9%)	08(03.0%)	13 (4.9%)
Total	234 (89.3%)	28 (10.7%)	262 (100%)

Distribution of histomorphologically diagnosed soft tissue tumor cases submitted for IHC (N=45). Out of 45 cases of soft tissue tumors submitted for IHC, 9 cases of schwannoma followed by 8 cases of spindle cell lesions, 7 cases of round cell lesions, 4 cases of fibrohistiocytic tumor, 3 cases each of rhabdomyosarcoma, pleomorphic sarcoma, hemangiopericytoma and dermatofibrocytic protuberans, 2 cases of liposarcoma and one case each of fibrolipoma, Infantile fibromatosis, cutaneous leiomyoma.

Out of 2 cases of liposarcoma, one case expressed focal reactivity for S100 and in 2nd case S100 was positive while vimentin was positive in both cases of liposarcoma. [Fig No 1]. In myxoid liposarcoma S100 was focally positive and in pleomorphic liposarcoma both S100 and CD₃₄ were positive. [Fig. No.2]

One case was histomorphologically diagnosed as infantile fibromatosis. IHC was applied for one case of infantile fibromatosis.

Panel of antibodies applied – SMA, Desmin, Vimentin and Caldesmon.

IHC study in one case of infantile fibromatosis SMA was positive and Desmin, S-100, CD68, Vimentin and Caldesmon were negative. [Fig. No 4] Three cases were histomorphologically diagnosed as dermatofibrosarcoma protuberans. IHC was applied in all three cases of dermatofibrosarcoma protuberans.

Panel of antibodies applied for dermatofibrosarcoma protuberance – SMA, S-100, CD₃₄, Vimentin and CD₁₁₇.

In 3 cases of dermatofibrosarcoma protuberans CD₃₄ was positive in all cases and SMA, S100, CD₆₈, vimentin and CD₁₁₇ were negative. [Fig. No.6]

Four cases were histomorphologically diagnosed as fibrohistiocytic tumors, out of them, 3 cases were diagnosed as malignant and one case as benign. IHC was applied for one benign and three malignant fibrohistiocytic tumors.

Panel of antibodies: Applied for fibrohistiocytic tumors – CK (Pan), SMA, Desmin, S100, Vimentin and CD68.

In 4

Following overnight incubation standard protocol was followed. Antigen retrieval is done by microwave method. For each antibody, a known positive control was kept to rule out false negative results.

Results and Observations

262 specimens clinically suspected of soft tissue neoplasm and diagnosed as soft tissue neoplasm on his pathological examination.

cases of fibrous histiocytoma, vimentin and CD68 were positive and CK, SMA, Desmin and S100 were negative. [Fig.no.7] One case was histomorphologically diagnosed as cutaneous leiomyoma. IHC was applied.

Panel of antibodies: Applied in one case of cutaneous leiomyoma – CK (Pan), SMA, Desmin and Vimentin. IHC study in one case of cutaneous leiomyoma, SMA and vimentin were positive. CK and Desmin were negative.[Fig. No.8]

IHC was done for histomorphologically diagnosed three cases of rhabdomyosarcoma, which included one case of embryonal rhabdomyosarcoma, composed of numerous rhabdomyoblast with brightly eosinophilic cytoplasm and occasional multinucleated strap cells seen. One case of alveolar rhabdomyosarcoma composed of collagenous fibrovascular septa divide mixture of undifferentiated tumor cells and rhabdomyoblast into discrete nests. Another one case was pleomorphic rhabdomyosarcoma composed of round to spindle cells and polygonal cells with abundant cytoplasm and bizarre nuclei seen.

Panel of antibodies used for rhabdomyosarcoma – CK (Pan), SMA, Desmin, Myogenin, S100 and LCA. In 3 cases of rhabdomyosarcoma, desmin and myogenin were positive and CK, SMA, S-100 and LCA were negative. The findings were similar in all the three cases irrespective of variant (type) of rhabdomyosarcoma. [Fig. No.9 and 10]

IHC was applied for histomorphologically diagnosed nine cases of schwannoma.

Panel of antibodies used – S100 and NSE.

Result of IHC in 9 cases of schwannoma. all positive for S100, Only two positive for NSE IHC study in 9 cases of schwannoma showed S-100 was positive in all 9 cases (100%). NSE was positive only in 2 cases (22.2%) out of 9 cases of schwannoma. [Fig. No.11] IHC was applied for histomorphologically diagnosed four malignant spindle cell lesions and four benign spindle cell lesions.

Panel of antibodies used for 4 malignant and 4 benign spindle cell lesions – SMA, Desmin, S100, CK, CD34, NSE, CD99 and CD117. Out of 4 malignant spindle cell lesions one case was dermatofibrosarcoma protuberans in which CD₃₄ and vimentin were positive and SMA, S100 and CD₁₁₇ were negative. One case was myofibroblastic sarcoma in which SMA, Desmin and Vimentin were positive and S-100 and CD₃₄ were negative. Out of 4 spindle cells lesions in 2 cases CK and CD₉₉ were positive and SMA, Desmin, S-100 and CD₃₄ were negative and diagnosed as synovial sarcoma. In 4 benign spindle cell lesions S100 and NSE were positive and they were diagnosed as schwannoma. With the help of IHC study out of eight spindle cell lesions, four cases were diagnosed as schwannoma, one case was diagnosed as dermatofibrosarcoma protuberans, one case was diagnosed as Myofibroblastic sarcoma and two cases were diagnosed a synovial sarcoma. Seven cases were histomorphologically diagnosed as malignant round cell tumors. IHC was applied in all 7 cases of malignant round cell tumors.

Panel of antibodies used for 7 cases of malignant round cell tumors- CK (Pan), LCA, Desmin, CD99, Myogenin and S100. With the help of IHC study out of 7 malignant Round Cell lesions in one case there was Desmin and myogenin positive and CK, LCA and CD₉₉ were negative that diagnosed as alveolar rhabdomyosarcoma. In 6 cases out of 7 malignant round cell lesions, CK, CD₉₉ and S-100 were positive and LCA, Desmin were negative and these cases were diagnosed as Ewing's sarcoma/PNET. With the help of IHC out of 7 cases of malignant round cell tumors, 1 case was diagnosed as alveolar rhabdomyosarcoma and 6 cases diagnosed as Ewing's sarcoma/ PNET.

Three cases were histomorphologically diagnosed as pleomorphic sarcoma. IHC was applied in all three cases of pleomorphic sarcoma.

Panel of antibodies used for pleomorphic sarcoma – CK (Pan), SMA, Desmin, S-100, Vimentin, CD68 and Myogenin. Out of 3 pleomorphic sarcoma, one case diagnosed as malignant fibrous histiocytoma and other 2 cases were diagnosed as pleomorphic rhabdomyosarcoma. In malignant fibrous histiocytoma vimentin and CD₆₈ were positive and CK, SMA, Desmin and S-100 were negative. In 2 pleomorphic rhabdomyosarcoma cases, Desmin, myogenin and vimentin were positive and CK, SMA and S-100 were negative. Final diagnosis of 3 pleomorphic sarcoma with help of IHC, 1 case was diagnosed as malignant fibrous histiocytoma and 2 cases were diagnosed as pleomorphic rhabdomyosarcoma.

Spindle cell lesion cases: With the help of IHC study out of eight spindle cell lesions, four cases were diagnosed as schwannoma, one case was diagnosed as dermatofibrosarcoma protuberans, one case was diagnosed as Myofibroblastic sarcoma and two cases were diagnosed a synovial sarcoma.

Round cell lesion cases :With the help of IHC out of 7 cases of malignant round cell tumors, one case was diagnosed as alveolar rhabdomyosarcoma and 6 cases diagnosed as Ewing's sarcoma/ PNET[Fig. No.12]. Final diagnosis of 3 pleomorphic sarcoma with help of IHC was

made as one case of malignant fibrous histiocytoma and 2 cases of pleomorphic rhabdomyosarcoma.

All the histomorphologically diagnosed cases of liposarcoma (2 cases), fibrolipoma (one case), hemangiopericytoma (3 cases), infantile fibromatosis (one case), DFSP (3 cases), fibrohistiocytic tumor (4 cases), schwannoma (9 cases), rhabdomyosarcoma (3 cases) and cutaneous leiomyoma (one case) revealed histomorphological features which correlated with IHC findings.

Discussion

Soft tissue tumors are defined as mesenchymal proliferations that occur in soft tissue which is nonepithelial extra skeletal tissue of body exclusive of reticuloendothelial system, glia and supporting tissue of various parenchymal organs. Soft tissue is represented by voluntary muscles, fat and fibrous tissue along with vessels. By convention it also includes peripheral nervous system^[3] This prospective study was performed over period of three years from October 2016 to October 2018. We have compared our results with similar studies in India and abroad^[15], Although clinical information regarding age, site, size of the lesions are critical for the diagnosis of STTs, but histological examination remains the cornerstone for their diagnosis. However, certain complementary methods like EM and immunohistochemical examination (IHC) may be needed to confirm the diagnosis and to establish their classification.⁹ (Bashar AH, 2010.) In this study immunohistochemistry (IHC) was applied for total 45 cases of soft tissue tumors were studied, of which 19 (42.2%) cases were benign and 26 (57.8%) cases were malignant.

Table 2: Comparison of histomorphological types of all soft tissue tumors reported in various studies.

Author (year)	No. of tumors	Benign (%)	Malignant (%)	B:M ratio
Kransdorf <i>et al.</i> (1995) ^[15]	31,047	18,677 (60.2%)	12,370 (39.8%)	1.5:1
Bashar <i>et al.</i> (2010) ^[5]	93	70 (75.2%)	23 (24.8%)	3:1
Beg <i>et al.</i> (2012) ^[26]	126	105 (83.3%)	21 (16.7%)	5:1
Present study	262	234 (89.3%)	28 (10.7%)	8.3:1

In present study the frequency of benign tumors was 89.3% and malignant tumors was 10.7% which was nearer to Beg *et al.* (2012)^[26]. Out of 262 cases, 45 cases (17.17%) were selected for IHC studies in which morphological typing needed IHC confirmation. With the help of IHC study out of eight spindle cell lesions, four cases were diagnosed as schwannoma, one case was diagnosed as dermatofibrosarcoma protuberans, one case was diagnosed as Myofibroblastic sarcoma and two cases were diagnosed a synovial sarcoma. With the help of IHC out of 7 cases of malignant round cell tumors, one case was diagnosed as alveolar rhabdomyosarcoma and 6 cases diagnosed as Ewing's sarcoma/ PNET. Final diagnosis of 3 pleomorphic sarcoma with help of IHC was made as one case of malignant fibrous histiocytoma and 2 cases of pleomorphic rhabdomyosarcoma. All the histomorphologically diagnosed cases of liposarcoma (2 cases), fibrolipoma (one case), hemangiopericytoma (3 cases), infantile fibromatosis (one

case), DFSP (3 cases), fibrohistiocytic tumor (4 cases), schwannoma (9 cases), rhabdomyosarcoma (3 cases) and cutaneous leiomyoma (one case) revealed histomorphological features which correlated with IHC findings.

1. IHC study of adipocytic tumors:

Josefine Haim-Hall *et al.* (2008) stated IHC plays a relatively minor role in diagnosis of adipocytic tumors. In myxoid liposarcoma showed focally CD₃₄ positivity. Cyril Fisher (2011)^[17] showed the distinction between lipoma and atypical lipomatous tumor (ALT)/well differentiated liposarcoma can be difficult which is facilitated by the demonstration of immunohistochemical positivity for products of the murine double minute type 2 (MDM2) and cyclin-dependent kinase 4 (CDK4) genes^[7, 8]. Wael Al-Daraji *et al.* (2009)^[16] showed no specific markers for fatty tumors.. Often fatty tumors such as well-differentiated liposarcoma and spindle cell non-lipogenic components of fatty tumors (including some dedifferentiated liposarcoma) may show CD₃₄. In present study cases of lipoma were diagnosed on histologically and with clinical details hence were not submitted for IHC. However, 2 cases diagnosed histomorphologically as liposarcoma were taken for IHC because one case revealed features like myxoid areas and lipoblast seen. In other case histomorphological reveal pleomorphic sarcoma with lipoblast. The pleomorphic variant revealed diffuse positivity for vimentin, S-100 and CD₃₄. The myxoid variant revealed diffuse positivity for vimentin and CD₃₄ whereas S-100 was focally positive (Fig. No.)

2. IHC study of fibrous and fibrohistiocytic tumors:

IHC was applied for one case of fibrolipoma, one case of infantile fibromatosis, three cases of hemangiopericytoma, three cases of dermatofibrosarcoma protuberans and four cases of fibrohistiocytic tumors which were histomorphologically diagnosed^[6]

i) IHC study for fibrolipoma: Wael Al-Daraji *et al.* (2009)^[16] showed the haemosiderotic fibrolipomatous tumor is histologically characterized by the presence of mature adipose tissue and spindle cell component. The spindle cell component of these lesions is generally positive for CD₃₄ and negative for CD₆₈, S100, SMA and desmin. In present study in one case of fibrolipoma CD₃₄ was positive and SMA, desmin, CD₉₉ were negative.

ii) IHC study of infantile fibromatosis: Josefine Haim-Hall *et al.* (2008) stated fibrous STTs are a heterogeneous group of spindle cell proliferations composed of a mixture of fibrocytes, fibroblasts, and myofibroblasts. In present study on IHC the case of infantile fibromatosis was positive for SMA and was negative for desmin, S100, CD₆₈, vimentin and Caldesmon.

iii) IHC study of hemangiopericytoma: Josefine Haim-Hall *et al.* (2008) showed, originally considered a tumor of pericytic origin, hemangiopericytoma (HPC) of soft tissue is now grouped with solitary fibrous tumor (SFT). Markers frequently expressed include CD₃₄ (positive in 44%-95%) and CD₉₉ (positive in 64%-91%. Smooth muscle actin is only rarely positive (<15%), and desmin is usually negative.

Endothelial markers CD₃₁ is uniformly negative. Wael Al-Daraji *et al.* (2009)^[16] mentioned about solitary fibrous tumor is defined histologically, comprises a group of benign and borderline tumors that present in a wide variety of locations, the most common being retroperitoneum and extremities.

Cyril Fisher (2011)^[17] showed solitary fibrous tumor is diffusely positive for CD₃₄ in 95% of cases, as well as for bcl-2, CD₉₉ and betacatenin. In present study 3 cases were selected for IHC out of them one case showed atypical cells, area of necrosis and mitotic figures hence the case was considered to be malignant. The panel of antibodies applied were SMA, CD₃₄, CD₉₉ and CD₃₁. All these cases were positive for CD₃₄ and CD₉₉ and were negative for SMA and CD₃₁

iv) IHC study of dermatofibrosarcoma protuberans: Coindre J.M. (2003)^[19] described cases of dermatofibrosarcoma protuberans and giant cell fibroblastoma. These two related tumors are consistently positive for CD₃₄. Diagnosis of DFSP is usually made on histological features. CD₃₄ is not specific but does not stain benign fibrous histiocytoma which enters into the differential diagnosis of DFSP, particularly on microbiopsies. Jose fine Haim-Hall *et al.* (2008) stated dermatofibrosarcoma protuberans is generally factor XIIIa negative and CD₃₄ positive, whereas DF shows the opposite staining. In the present study, IHC was applied for 3 cases of dermatofibrosarcoma protuberans CD₃₄ was positive in all the 3 cases and SMA, S100, CD₆₈, vimentin and CD₁₁₇ were negative. Four cases were histomorphologically diagnosed as fibrohistiocytic tumors out of them 3 cases were diagnosed as malignant and one case as benign. Panel of antibodies applied were CK (pan), SMA, desmin, S-100, vimentin and CD₆₈.

Wael Al-Daraji *et al.* (2009)^[16] showed, malignant fibrous histiocytoma (MFH) is a designation used for poorly differentiated sarcomas that do not show any specific differentiation, except perhaps fibroblastic differentiation. In present study, IHC was applied in 4 cases of fibrous histiocytoma showed, vimentin and CD₆₈ were positive and CK, SMA, desmin and S100 were negative.

3. IHC study of smooth muscle tumors: Wael Al-Daraji *et al.* (2009)^[16] showed, leiomyomas are typically positive for muscle actin when evaluated with the monoclonal antibody HHF-35 or with antibodies to alpha-SMA. However, both antibodies also react with myoepithelial cells and the latter also with myofibroblasts, as seen, for example, in the myofibroblast-rich nodular fasciitis. Therefore, strong SMA-reactivity itself is not diagnostic of a smooth muscle cell tumor. Typical leiomyosarcomas generally show prominent actin reactivity similar to that seen in benign leiomyomas, but desmin reactivity is variable and may be absent. Approximately 70% of leiomyosarcomas are desmin positive and the reactivity is often focal. In present study IHC was applied for one case of cutaneous leiomyoma showed SMA and vimentin were positive and CK and desmin were negative. (Fig. No. - Table No).

4. IHC study of skeletal muscle tumors: Coindre J.M. (2003)^[19], in his study showed desmin and myogenin are positive in more than 90% of rhabdomyosarcomas and in

virtually all embryonal and alveolar type. Jha R. (2010)^[18] stated rhabdomyosarcoma group of tumors with skeletal muscle differentiation. These tumors are divided into 3 main biologically distinct categories like embryonal rhabdomyosarcoma (ERMS), alveolar rhabdomyosarcoma (ARMS), and pleomorphic rhabdomyosarcoma (PRMS). In present study, 3 cases were histomorphologically diagnosed as rhabdomyosarcoma which included one case each embryonal, alveolar and pleomorphic variant. All 3 cases of rhabdomyosarcoma, desmin and myogenin were positive and CK, SMA, S-100 and LCA were negative. The findings were similar in all the three cases irrespective of variant (type) of rhabdomyosarcoma.

5. IHC study of peripheral nerve and nerve cell sheath tumors: Wael Al-Daraji *et al.* (2009) showed the neoplastic spindle cell components are almost uniformly S-100 protein positive, whereas CD34 is seen only in the pericapsular area and loose, degenerative areas. Schwannomas commonly express glial fibrillary acidic protein (GFAP) and are sometimes positive for keratins. Granular cell tumor of soft tissues is believed to be a Schwannian derivation. This tumor is consistently S-100 protein positive and also reacts with CD68 (KP1) because of its high content of lysosomes. Roholl *et al.* ((1985), neuron-specific enolase was found for instance in many types of tumors of the central nervous system, ductal carcinomas and fibroadenomas of the breast, schwannomas, rhabdomyosarcomas. In the present study IHC was applied for 9 cases of schwannoma in which S-100 was positive in all cases and NSE was positive in 2 cases.

6. IHC study of spindle cell lesions: According to Cyril Fisher (2011)^[17], the differential diagnosis of the principal benign soft tissue tumors is straightforward when the lineage is obvious. Jha R. (2010)^[18] the list of differential diagnosis for spindle cell malignant is long some being leiomyosarcoma, gastrointestinal stromal tumor (GIST), malignant peripheral nerve sheath tumor (MPNST), monophasic synovial sarcomas, spindle cell melanomas, sarcomatoid carcinomas and so on. Leiomyoma and leiomyosarcomas (LMS) are generally strongly and uniformly positive for smooth muscle actin (SMA) and HHF35. 70-80% of leiomyosarcomas are desmin positive. To define a poorly differentiated spindle cell sarcoma as LMS, at least 2 of 3 muscle markers (using for example SMA/desmin/HHF35 or SMA/desmin/calponin) should be positive. In the present study IHC was applied for histomorphologically diagnosed four malignant spindle cell lesions and four benign spindle cell lesions. Out of 4 malignant spindle cell lesions one case was dermatofibrosarcoma protuberans in which CD34 and

vimentin were positive and SMA, S-100 and CD117 were negative. One case was myofibroblastic sarcoma in which SMA, desmin and vimentin were positive and S100 and CD34 were negative. Out of 4 spindle cell lesions in 2 cases CK and CD99 were positive and SMA, desmin, S-100 and CD34 were negative and diagnosed as synovial sarcoma. In 4 benign spindle cell lesions S-100 and NSE were positive and they were diagnosed as schwannoma.

7. IHC study of malignant round cell tumor: Jha R. (2010) studied morphologic differential diagnosis of malignant small round cell tumors include Ewing's sarcoma/PNET, neuroblastoma, rhabdomyosarcoma, desmoplastic small round cell tumor, lymphoma, leukemia, small cell osteosarcoma, small cell carcinoma (either undifferentiated or neuroendocrine), olfactoryneuroblastoma, cutaneous neuroendocrine carcinoma, (Merkel-cell carcinoma), small cell melanoma and mesenchymal condrosarcoma. Cyril Fisher (2011), showed round cell tumors of soft tissue neoplasms includes Ewing sarcoma/primitive neuroectodermal tumor (ES), desmoplastic small round cell tumor (DSRCT), alveolar rhabdomyosarcoma (ARMS), neuroblastoma (NB) and poorly differentiated synovial sarcoma (PDSS). In the present study, IHC was applied for 7 malignant round cell tumors. With the help of IHC study, out of 7 malignant round cell tumors in one case there was desmin and myogenin positive and CK, LCA, CD99 were negative that diagnosed as alveolar rhabdomyosarcoma. In 6 cases out of 7 malignant round cell lesions, CK, CD99 and S-100 were positive and LCA, Desmin were negative and these cases were diagnosed as Ewing's sarcoma/PNET.

8. IHC study of pleomorphic Sarcoma: Cyril Fisher (2011)^[17] showed pleomorphic sarcomas include liposarcoma (pleomorphic and dedifferentiated). Rhabdomyosarcoma, MPNST, leiomyosarcoma, myofibrosarcoma and undifferentiated pleomorphic sarcoma (also known as pleomorphic malignant fibrous histiocytoma or MFH). Undifferentiated or sarcomatoid carcinoma, melanoma and rarely lymphomas can also have similar microscopic appearances. In the present study, IHC was applied for 3 cases histomorphologically diagnosed as pleomorphic sarcoma. Out of 3 pleomorphic sarcoma in one case vimentin and CD68 were positive and CK, SMA, desmin and S-100 were negative and diagnosed as malignant fibrous histiocytoma. Remaining 2 cases showed desmin, myogenin and vimentin positivity and whereas CK, SMA and S-100 were negative and thus were diagnosed as pleomorphic rhabdomyosarcoma

Pleomorphic liposarcoma

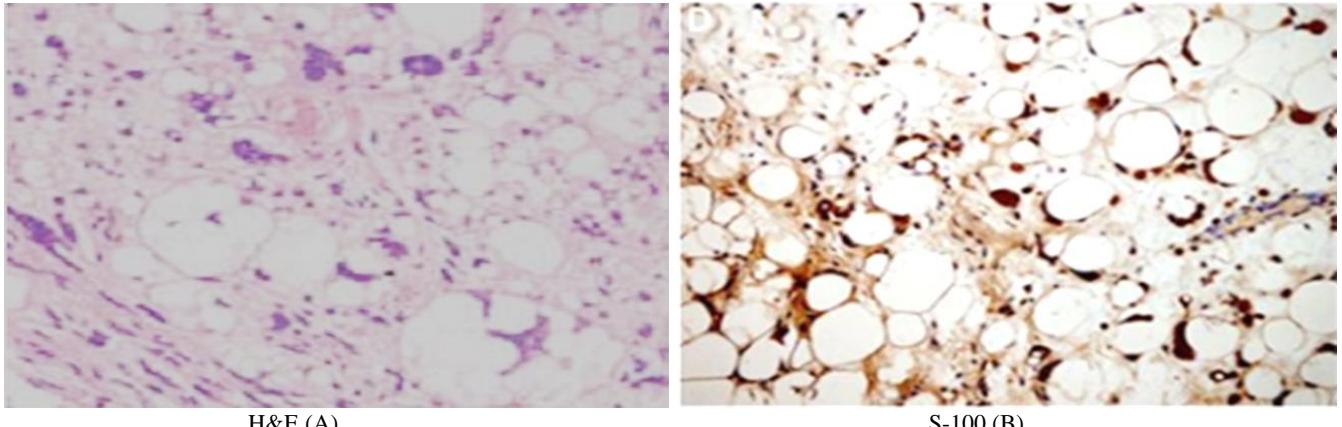


Fig 1: (A) H&E, X400 showing pleomorphic spindle cells with pleomorphic multi vacuolated lipoblast with bizarre hyperchromatic nuclei.
(B) S-100 is positive in tumor cells (X400).

Myxoid liposarcoma

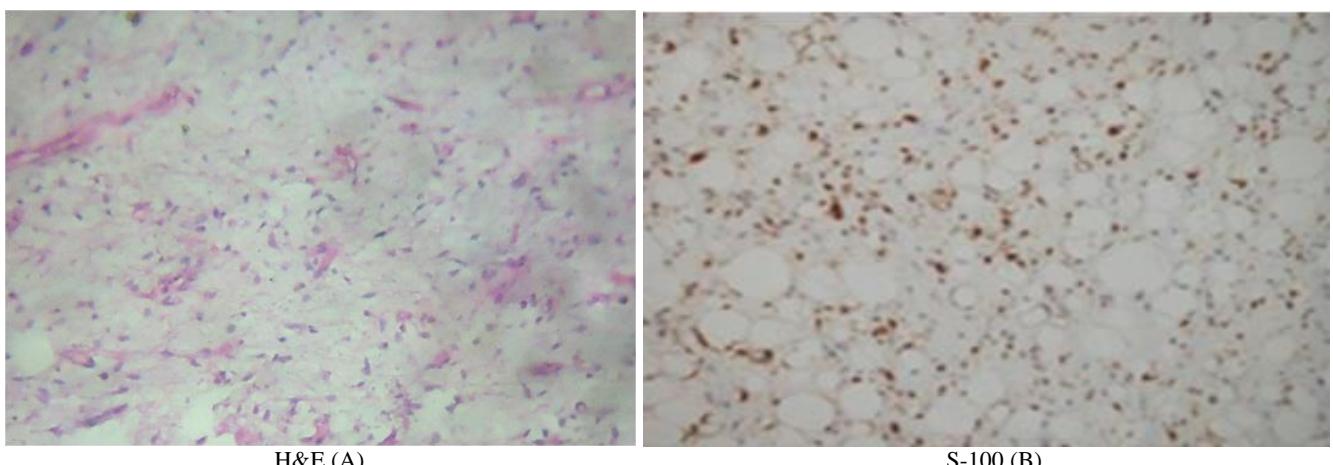


Fig 2: (A) H&E, x20 - showing Tumor tissue arranged in diffuse and small nodules. Tumor tissue comprised of lipoblast with eccentric nucleus and vacuolated cytoplasman and myxoid stroma. (B) Positive Immunohistochemical staining for S-100 (B,IHC X100).

Fibrolipoma

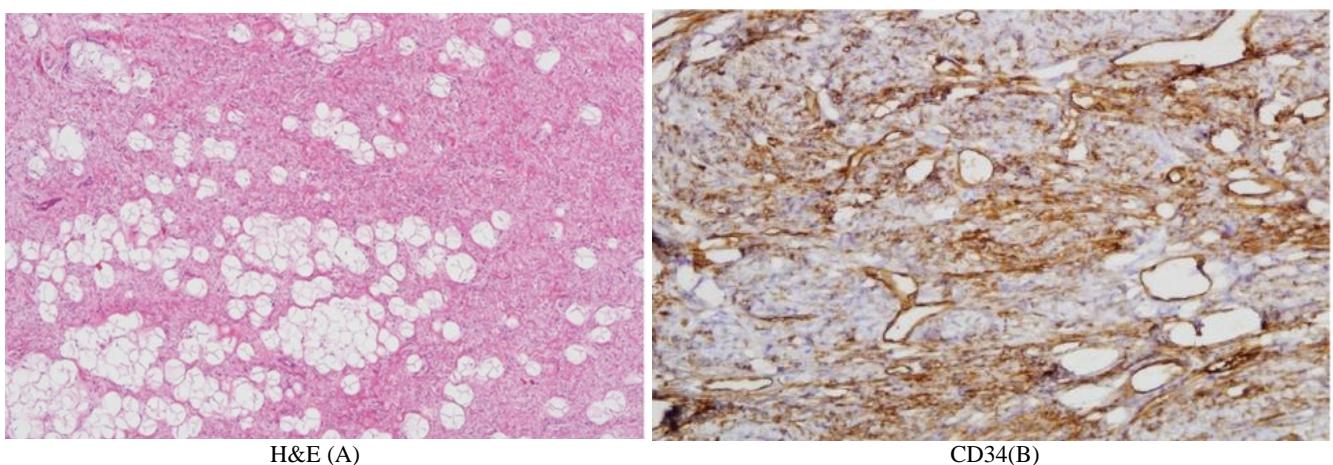


Fig 3: (A) H&E, X100 - The tumor consists of a relative equal mixture of mature fat and spindle cells. (B) The spindle-shaped cells show strong positivity on CD34 immunostaining, IHC, X100).

Infantile fibromatosis

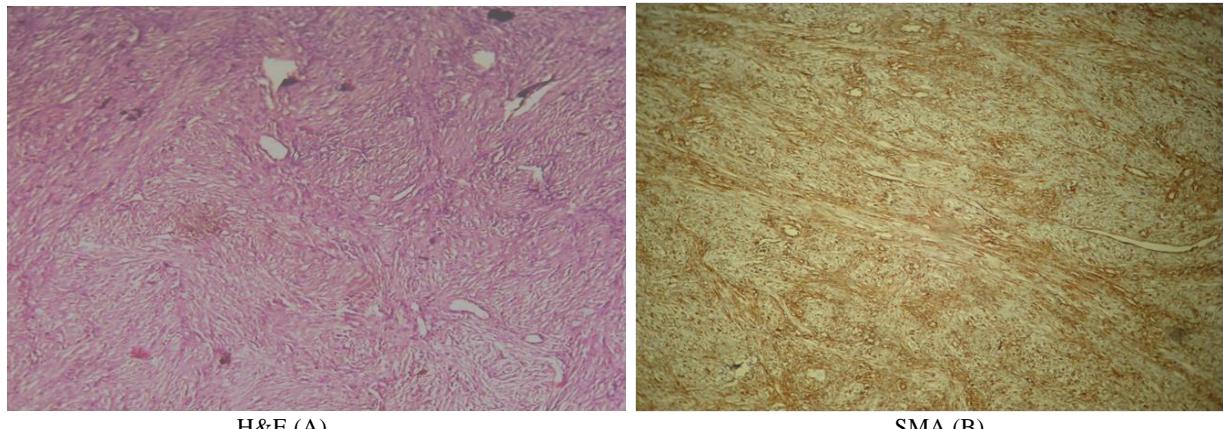


Fig 4: (A) H&E,X20 shows spindle to oval cells with bland nuclei are arranged in fascicles and bundles. (B)SMA is positive in tumor cells (IHC,X20).

Hemangiopericytoma

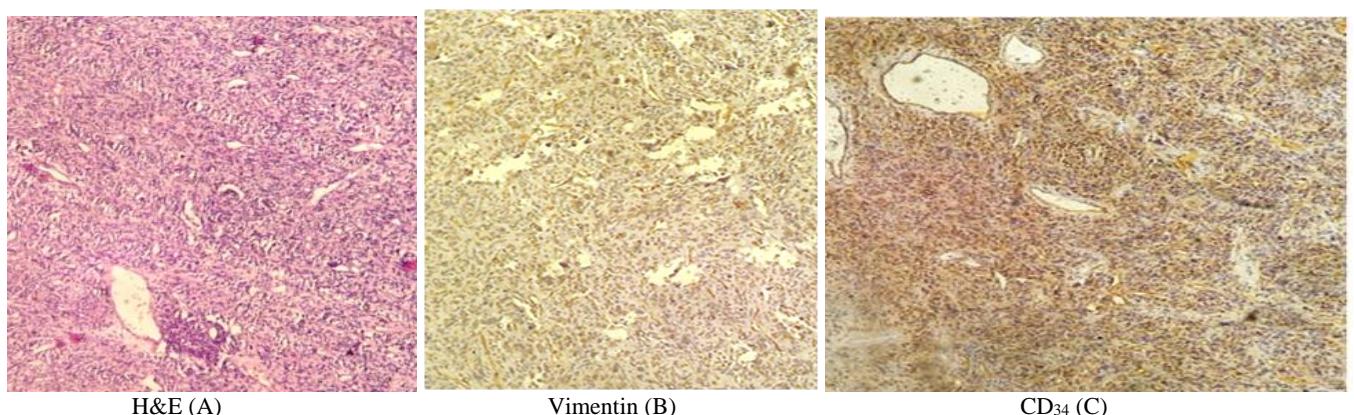


Fig 5: (A) H&E, X20 Slit-like vessels with hemangiopericytomatus pattern, Plump spindle-shaped cells, (B,IHC,X20) vimentin is positivity in tumor cells, CD34 is positive in tumor cells and endothelial lining of blood vessels (C, IHC, X20).

Dermatofibrosarcoma protuberans

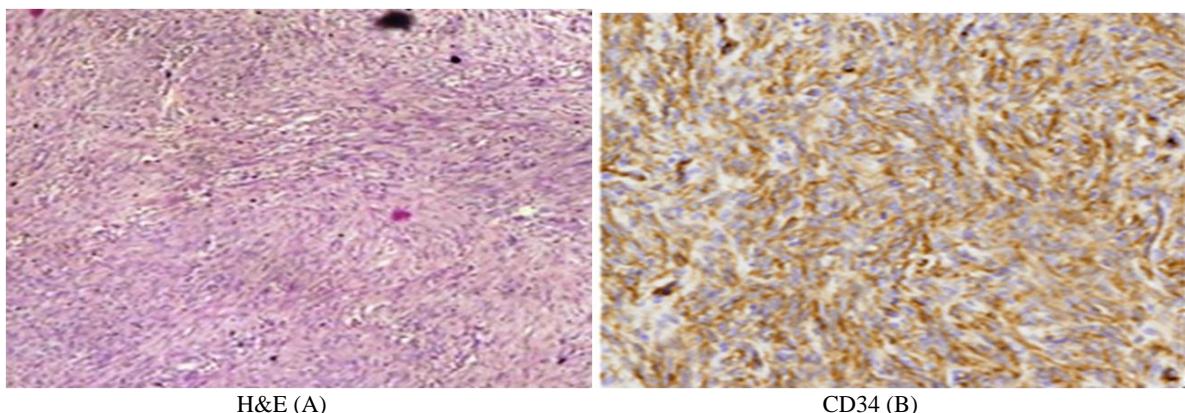


Fig 6: (A) H&E,X20slide shows tumor comprised of storiform tumor cells, highly cellular spindle cells, nuclei are thin.(B) CD34 is positive in tumor cells (IHC,X100).

Malignant fibrous histiocytoma

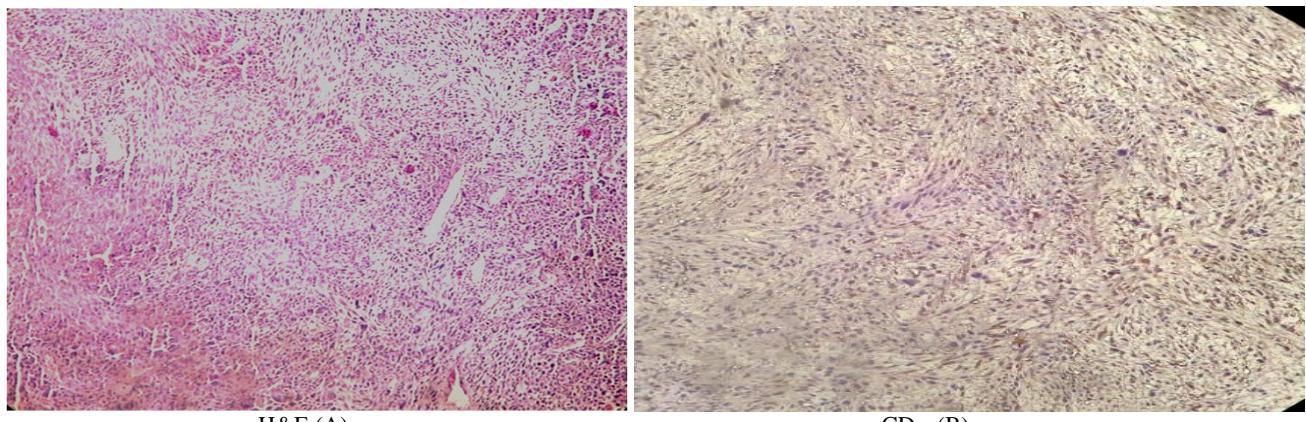


Fig 7: (A) H&E X40 showing spindle cells and histiocytes like cells, inflammatory infiltrates and brisk mitosis. (B) CD68 is positive in tumour cells (H&C, X40).

Cutaneous leiomyoma

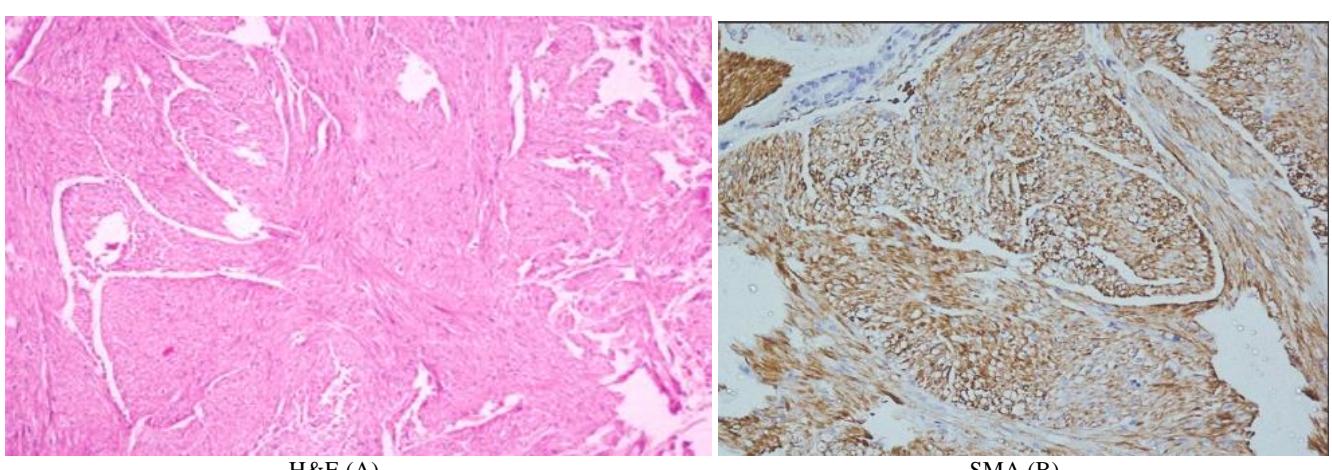


Fig 8: (A) H&E, X40 Interlacing fascicles of bland spindle cells with elongated nuclei. Smooth muscle cells with blunt-shaped nuclei and eosinophilic cytoplasm. (B) Smooth muscle actin stain showing positive staining for smooth muscle fiber (IHC, X100).

Alveolar rhabdomyosarcoma

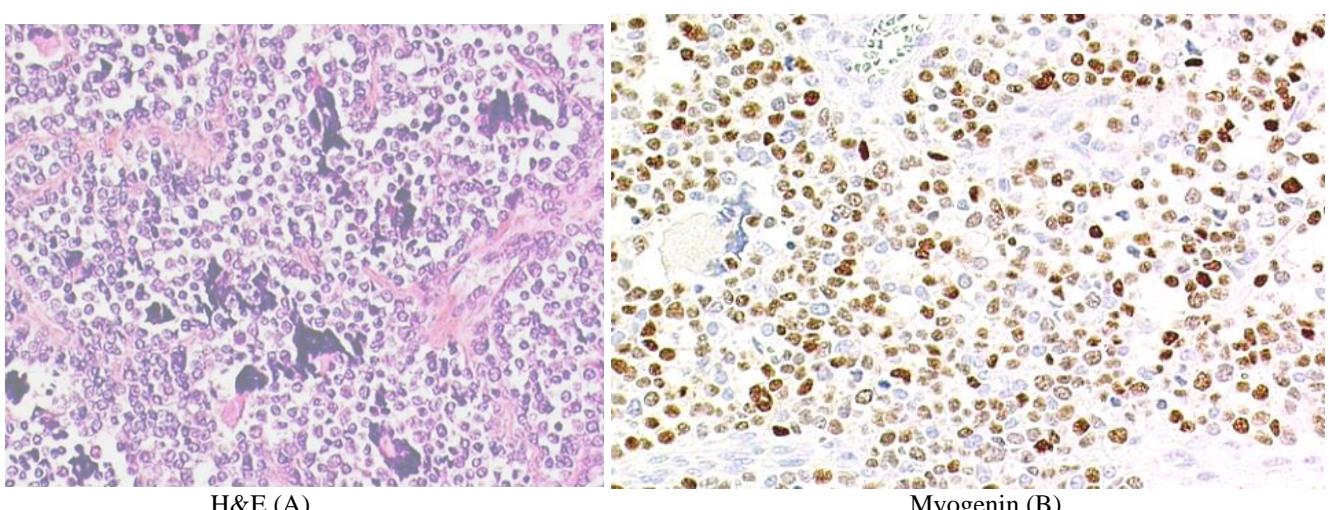


Fig 9: (A) H&E, x400 slide shows fibrovascular septa separate the tumour cells which are round to oval arrangement in alveolar pattern and discrete nests. (B) Alveolar rhabdomyosarcoma myogenin positive (IHC, X400)

Pleomorphic rhabdomyosarcoma

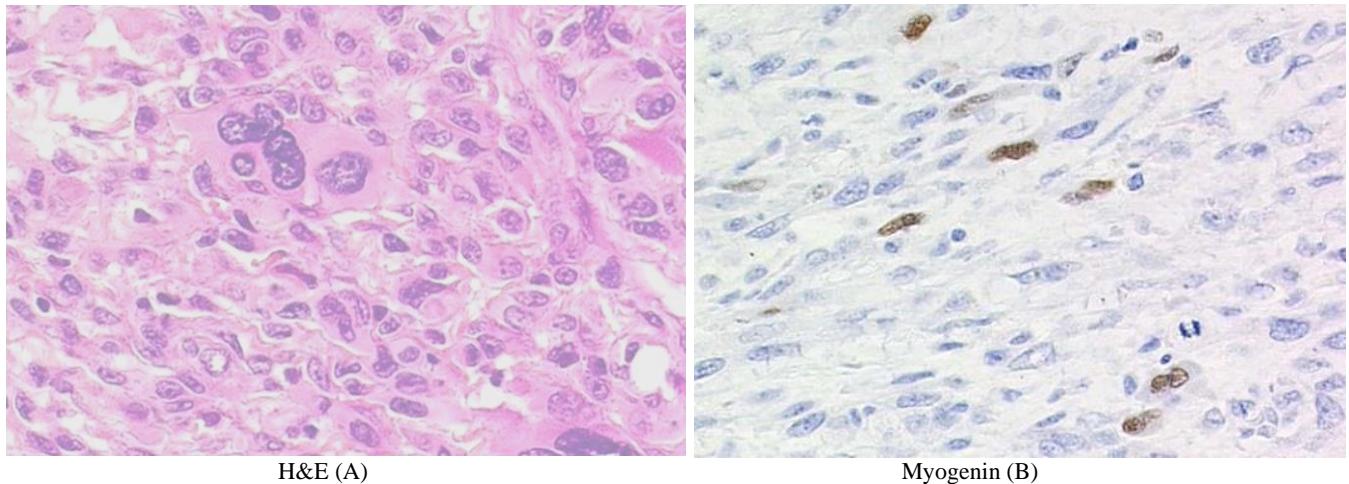


Fig 10: (A) H&E, X400 shows pleomorphic nature of the cells are seen. Large bizarre polygonal an spindle shaped rhabdomyoblast seen. (B) Myogenin staining is positive (IHC,X400).

Schwannoma

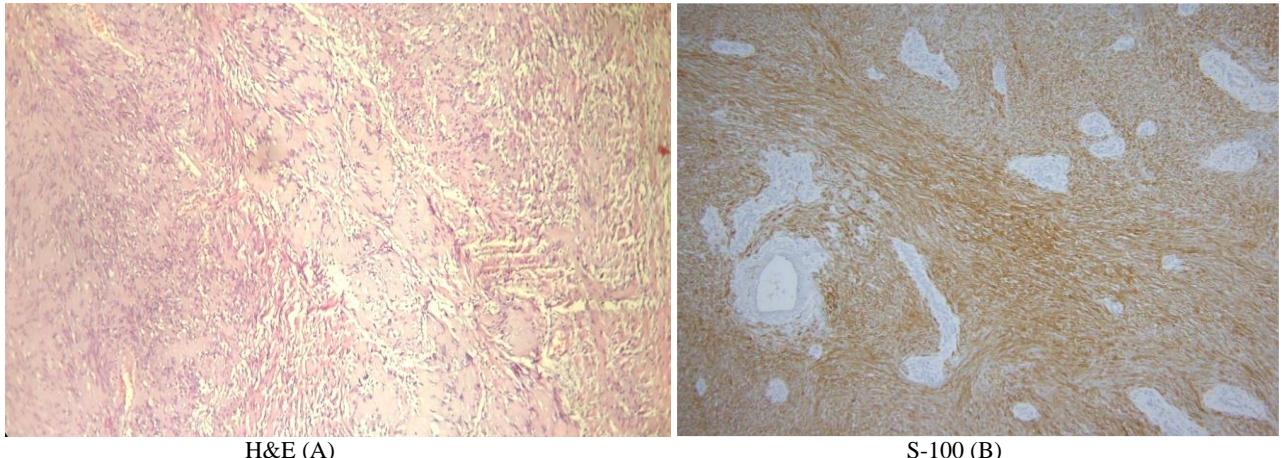


Fig 11: (A) H&E,X40neoplastic cells form short palisades with interposed fibrillary collections of cell processes, designated as verocay bodies. (B) Schwann cells exhibiting intense intranuclear S-100-P positivity. (IHC,X40).

PNET

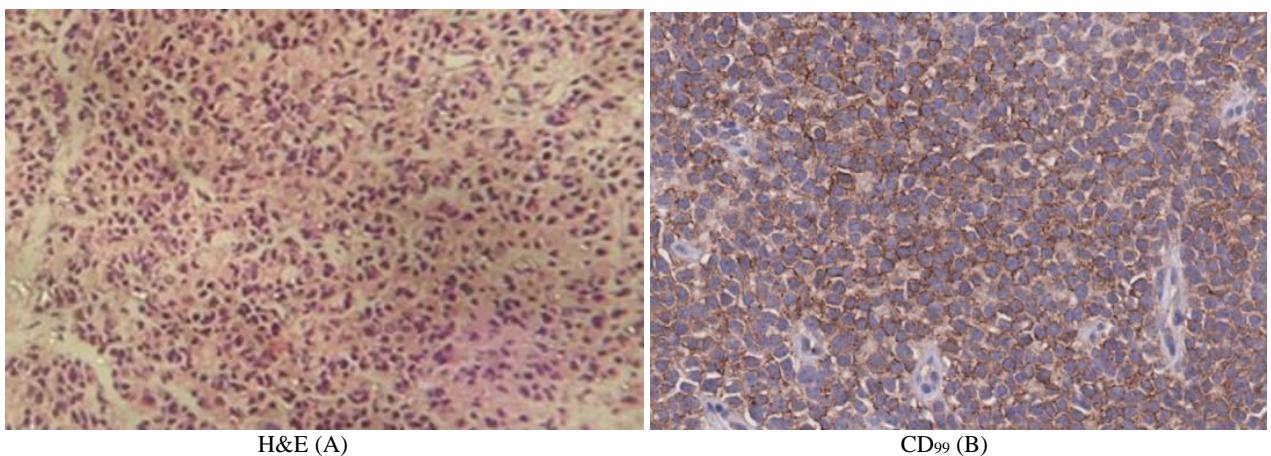


Fig 12: (A) H&E,X20 showing round cell sarcoma where the nuclei are incredibly uniform round to oval. (B)CD99 is positive in tumor cells (IHC, X 100).

Conclusions

Immunohistochemistry plays an important role in the diagnosis of soft tissue tumors. One of its major utilities is to correctly identify a tumor as being of mesenchymal or non mesenchymal origin. Once mesenchymal origin has been established, histologic subtyping according to specific cell lineage may be achieved with the use of lineage-specific markers. The careful histopathological examination and clinical correlation remains the cornerstone of morphologic diagnosis. The immunostaining is usually able to support or rule out one or more of possible differential diagnosis. Immunohistochemistry has made a significant contribution to the diagnosis of soft tissue sarcomas. It provides an additional tool by which one can analyse poorly differentiated sarcomas and characterize them. Its specificity, sensitivity, cost effectiveness and applicability to routinely processed material, clearly make it an essential part of diagnostic pathological studies for soft tissue tumors.

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