# Soft Tissue Sarcomas: A review of 40 cases

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## ABSTRACT:

**BACKGROUND:**

Soft tissue sarcoma (STS) represents a heterogeneous group of rare malignant tumors. Many diagnostic problems and difficulties are often encountered in the differential diagnosis of these tumors. The variety of appearance gives a wide range of tumor types and subtypes with a high discrepancy rate in tumor typing among pathologists.

**METHODS:**

This study was conducted at the Military Medical Academy (EGYPT) during the period from (1989-1990). The study aimed to reexamine a routinely processed H and E stained slides of cases previously diagnosed as STS by a group of pathologist and match the old and new diagnoses, with the application of some special stains; histochemical and immunohistochemical, then evaluate the results. Forty cases previously diagnosed as STS were reexamined and classified according to the criteria of Enzinger and Weiss. A descriptive or morphological classification was also used; as spindle, round, myxoid and pleomorphic STS. The results were compared to, and matched with the previous diagnoses. Histochemical stains used are, Picro Sirius red (PSR), Masson trichrome (MT), and Periodic-acid schiff stain (PAS). Myoglobin was used as immunohistochemical marker for the detection of cross-striated muscle cell differentiation by peroxidase antiperoxidase method (PAP).

**RESULTS:**

Agreement in diagnosis between the previous and the recent diagnosed STS was found to be **47.5%.** For spindle cell malignant tumors the agreement was **58.8%,** while for round cell malignant tumors was **33.3%.** Agreement in diagnosis in mixed malignant soft tissue tumors was **62.5%**. PSR and MT demonstrate the amount and distribution of collagen. MT also demonstrates muscle fibers. Using Myoglobin immunohistochemical marker in the previously diagnosed STS: one out of four cases diagnosed as Rhabdomyosarcomas gave a positive result, while two cases from the unsuspected group gave positive results. In the recently diagnosed tumors: all cases diagnosed as Rhabdomyosarcoma gave positive results, while from the unsuspected group one gave positive result.

**CONCLUSION:**

While the ordinary H and E stain will suffice to permit recognition of many of STS, it will not do so for all. Limitation of diagnosis of these tumors, especially the rare ones, to specialized centers or highly qualified pathologists is recommended. Histochemical stains are supportive rather than exclusive for the diagnosis of STS. Myoglobin immunohistochemical marker could be used to aid in the diagnosis of rhabdomyosarcomas. Definite diagnosis of many STS needs further special stains and/or electron microscopy and other sophisticated procedures.


**KEY WORDS:** Myoglobin, Periodic-Acid Schiff stain, Rhabdomyosarcoma, Soft Tissue Sarcomas.

## INTRODUCTION:

Sarcomas of the soft tissues account for less than 1 percent of all malignant neoplasms but have been the subject of medical attention out of proportion to their frequency. [1] Earlier classifications have been largely descriptive and based more on the cellular configuration than the nature of type or tumor cells. These morphological classifications have the advantage of simplicity; they include round cell, spindle cell, pleomorphic and myxoid. But tumors with similar tissue patterns may have different prognosis. So morphological classifications may be diagnostically convenient but should be discouraged because they are meaningless and convey little information as to the nature and potential behavior of a given tumor. [2]

Traditionally, STS have been classified according to a histogenetic concept (e.g., Fibrosarcoma as a tumor arising from fibroblasts, and so on). Experimental data instead suggest that most if not all sarcomas arise from primitive multipotential mesenchymal cells, which in the course of neoplastic transformation undergo differentiation along one or more lines. [3,4,5] So it has been suggested that the simplest step for diagnosis of STS is to classify them on a simple descriptive basis as spindle cell sarcomas, myxoid sarcomas, pleomorphic sarcomas, and round cell sarcomas. The second step is to range these tumors according to current histogenetic classification. [2,5,6,7, 8] The third step is histopathologic grading, which was found to be useful for determining the prognosis

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particularly of spindle cell sarcomas. [5,8,9] There are special techniques that have been successfully applied to increase diagnostic accuracy of STS; these include conventional special stains, electron microscopy, immunohistochemistry, cytogenetics, and molecular methods. [5,10] Rhabdomyosarcoma is the most common soft-tissue sarcoma in the first two decades of life; however, relatively few cases are seen in any one institution. Hence, in the United States of America a collaborative Intergroup Rhabdomyosarcoma Study Group (IRS) was established to investigate biology and treatment of the tumor. [10,11] . To overcome the diagnostic difficulties in Rhabdomyosarcoma, several immunohistochemical markers have been introduces. Only Myoglobin, skeletal muscle myosin, and skeletal muscle actin have been found to be specific markers in the detection of cross-striated muscle cell differentiation in tumors. [7,12,13,14] .

## MATERIAL AND METHODS:

This study was conducted at the Military Medical Academy. The material was collected from Military Maadie Hospital, Kubry el-Ubba hospital, and Military Central Medical Laboratories after reviewing the records of patients referred to these centers. All the clinical informations in the request forms with gross and histopathological findings in the histopathological reports have been reported. All tissue specimens of the selected cases, have already been fixed in 10% formalin and routinely processed for paraffin embedded-sections. The cases were numbered as case 1,2,3… New sections stained with H and E stain have been reexamined by a group of pathologist to determine the histologic type. The previous diagnoses matched with the new ones. Special histochemical stains including PSR for collagen identification, Masson Trichrome for skeletal or smooth muscle differentiation and PSA for glycogen identification. Myoglobin was used as immunohistochemical marker for the detection of cross-striated muscle cell differentiation by peroxidase antiperoxidase method (PAP). It was supplied by DAKO OAO kit$_{TM.}$ Kit size-system 20.Cod No.K542.

The cases included in the detection of Myoglobin, were these which had more than one differential diagnosis and all the cases diagnosed as rhabdomyosarcomas, the new and previous cases. A rose-red to light brown sensitive staining should be observed in the skeletal muscle fibers (control) and the same stain or slightly less intense in tumor tissue should be detected to interpret positive results. All results were interpreted and summarized in Tables as will be mentioned later in the results.

## RESULTS:

**Table-1** shows the previously diagnosed STS matched with the new diagnoses according to the histogenetic nature of these tumors.

Some cases in the new diagnoses have more than one differential diagnosis, the Ist one was the most agreed on by the group of pathologists.

We used the Ist diagnosis to compare with the previous one. Agreement in diagnosis was **47.5%** (19 out of 40 cases).

**Table1: Previous and new diagnoses of different STS .**

| Case Number | Previous Diagnosis | Recent Diagnosis |
|---|---|---|
| **1** | Fibrosarcoma | Fibrosarcoma |
| **2** | Fibrosarcoma | Malignant Schwannoma |
| **3** | MFH* | Extraabdominal Fibromatosis |
| **4** | Neurofibrosarcoma | DFP** |
| **5** | MFH | MFH (storiform-pleomorphic) |
| **6** | Rhabdomyosarcoma | MFH (myxoid) |
| **7** | Malig. Mesothelioma | Malig. Mesothelioma |
| **8** | Leiomyosarcoma | Leiomyosarcoma |
| **9** | Leiomyosarcoma | Leiomyosarcoma |
| **10** | Wilm's tumor | Neuroblastoma |
| **11** | Liposarcoma | Malignant Mesothelioma |
| **12** | Neurogenic sarcoma | Ewing's Sarcoma<br>Neuroepithelioma |
| **13** | Rhabdomyosarcoma | Alveolar soft part sarcoma<br>Rhabdomyosarcoma (embryonal) |
| **14** | Rhabdomyosarcoma | Rhabdomyosarcoma (alveolar) |
| **15** | Rhabdomyosarcoma | Rhabdomyosarcoma (embryonal) |
| **16** | MFH | Rhabdomyosarcoma (pleomorphic)<br>Liposarcoma (Pleomorphic) |
| **17** | Reticulum cell sarcoma | Angiosarcoma<br>Malignant melanoma |
| **18** | Rhabdomyosarcoma | Rhabdomyosarcoma (alveolar) |

| | | |
|---|---|---|
| **19** | DFP | DFP |
| **20** | Fibrosarcoma | Malignant Schwannoma |
| **21** | Soft tissue sarcoma | Lymphoma |
| **22** | Fibrosarcoma | Synovial sarcoma |
| **23** | Neurofibrosarcoma | Neurofibrosarcoma |
| **24** | Neurogenic sarcoma | Rhabdomyosarcoma (embryonal)<br>Neuroepithelioma |
| **25** | Myxoid liposarcoma | Myxoid liposarcoma |
| **26** | Myxoid liposarcoma | Myxoid liposarcoma |
| **27** | Malig. haemangiopericytoma | Extraskeletal mesenchymal chondrosarcoma |
| **28** | Fibrosarcoma | DFP |
| **29** | Fibrosarcoma | Fibrosarcoma |
| **30** | Leiomyosarcoma | Leiomyosarcoma |
| **31** | Synovial sarcoma | Synovial sarcoma |
| **32** | Malig. Schwannoma | Malig. Schwannoma |
| **33** | Liposarcoma | Liposarcoma |
| **34** | Fibrosarcoma | MFH |
| **35** | Clear cell sarcoma | Clear cell sarcoma |
| **36** | Haemangioendothelioma | Bronchial carcinoid |
| **37** | Alveolar soft part sarcoma | Lymphoma<br>Merkel cell carcinoma |
| **38** | Fibrosarcoma | MFH |
| **39** | Rhabdomyosarcoma | Angiosarcoma<br>Anaplastic carcinoma |
| **40** | Leiomyosarcoma | Leimyosarcoma |

* MFH: Malignant fibrous histeocytoma
** DFP: Dermatofibrosarcoma protuberance

On the bases of cell morphology **(Table-2)**, the soft tissue neoplasms were subdivided into:

1. **Spindle cell malignant neoplasms**. Different histologic types, according to the histogenetic nature, summarized in **Table-3.**
2. **Round cell malignant neoplasms**. Different histologic types, according to the histogenetic nature, summarized in **Table-4.**
3. **Myxoid malignant neoplasms.**
4. **Pleomorphic malignant neoplasms.**

We are left with a group of **mixed malignant soft tissue tumors**.

**Table- 5** summarizes the malignant soft tissue tumors, which have more than one prominent morphological type.

**Table2: General morphological appearance of the malignant soft tissue tumors**

| General morphology | Number | Percentage % |
|---|---|---|
| **Spindle cell tumors** | 17 | 42.5% |
| **Round cell tumors** | 12 | 30.0% |
| **Myxoid tumors** | 2 | 5.0% |
| **Pleomorphic tumors** | 1 | 2.5% |
| **Mixed tumors** | 8 | 20.0% |
| **Total** | 40 | 100% |

**Table3: Spindle cell sarcomas of soft tissue; Histological types**

| Case. no | Previous diagnosis | Recent diagnosis |
|---|---|---|
| **1.** | Fibrosarcoma | Fibrosarcoma |
| **2.** | Fibrosarcoma | Malig. Schwannoma |
| **3.** | MFH | Aggressive Fibromatosis |
| **4.** | Neurosarcoma | DFP |
| **7.** | Malignant Mesothelioma | Malig. Mesothelioma |
| **8.** | Leiomyosarcoma | Leiomyosarcoma |
| **9.** | Leiomyosarcoma | Leiomyosarcoma |
| **19.** | DFP | DFP |
| **20.** | Fibrosarcoma | Malig. Schwannoma |

| | | |
|---|---|---|
| **22.** | Fibrosarcoma | Synovial sarcoma |
| **23.** | Neurofibrosarcoma | Malig. Schwannoma |
| **28.** | Fibrosarcoma | DFP |
| **29.** | Fibrosarcoma | Fibrosarcoma |
| **30.** | Leiomyosarcoma | Leiomyosarcoma |
| **32.** | Malig. Schwannoma | Malig. Schwannoma |
| **38.** | Fibrosarcoma | MFH |
| **40.** | Leiomyosarcoma | Leiomyosarcoma |

**Table4: Round cell malignant tumors of soft tissue; Histological types**

| Case no. | Previous diagnosis | Recent diagnosis |
|---|---|---|
| **10** | Wilm's tumor | Neuroblastoma |
| **12** | Neurogenic sarcoma | Ewing's sarcoma |
| **13** | Rhabdomyosarcoma | Alveolar soft part sarcoma |
| **14** | Rhabdomyosarcoma | Rhabdomyosarcoma |
| **17** | Reticulum cell sarcoma | Angiosarcoma |
| **18** | Rhabdomyosarcoma | Rhabdomyosarcoma |
| **21** | Soft tissue sarcoma | Lymphoma |
| **24** | Neurogenic sarcoma | Rhabdomyosarcoma |
| **35** | Clear cell sarcoma | Clear cell sarcoma |
| **36** | Hemangioendothelioma | Bronchial carcinoid |
| **37** | Alveolar soft part sarcoma | Merkel cell carcinoma |
| **39** | Rhabdomyosarcoma | Angiosarcoma |

**Table5: Mixed malignant soft tissue tumors; Histologic types**

| Case no. | Previous diagnosis | Recent diagnosis | Morphological types |
|---|---|---|---|
| **5** | MFH | MFH | Spindle & pleomorphic |
| **6** | Rhabdomyosarcoma | Myxoid MFH | Spindle & myxoid |
| **11** | Liposarcoma | Malig. Mesothelioma | Round & spindle |
| **15** | Rhabdomyosarcoma | Rhabdomyosarcoma | Round & myxoid |
| **31** | Synovial sarcoma | Synovial sarcoma | Round & spindle |
| **33** | Liposarcoma | Liposarcoma | Round & myxoid |
| **27** | Malignant haemangiopericytoma | Mesenchymal chondrosarcoma | Spindle & myxoid |
| **34** | Soft tissue sarcoma | MFH | Spindle & pleomorphic |

Out of the above listed tables, we can summarize the results in few points:

**1.** In 10 out of 17 cases of spindle cell sarcomas, the new diagnosis agreed with the previous ones, which constitutes about 58.8%. On the other hand, in round cell malignant tumors, the agreement was in only 4 cases out of 12, which constitutes about 33.3%.

**2.** The two myxoid tumors were diagnosed as myxoid liposarcomas without difficulty, **Fig-1, Myxoid liposarcoma (case no.26).**

**3.** Only one case of pleomorphic tumor, which was diagnosed previously as MFH, was recently diagnosed as rhabdomyosarcoma (pleomophic).

**4.** Agreement in diagnosis in mixed malignant tumors was 62.5% (5 cases out of 8), **Fig-2&3, Mesenchymal chondrosarcma (case no.27)**

Regarding the use of histochemical stains, the result of ***PSR*** staining drew attention to the following interesting observations:

**A.** Findings concerned with the amount of collagen produced; as in aggressive Fibromatosis (case. no 3) produce abundant collagen in relation to individual cells in comparison with fibrosarcoma.

**B.** Findings concerned with the distribution of collagen fibers, as in fibrosarcoma the collagen is evenly distributed in contrast to all the other spindle sarcomas where the distribution was heterogeneous. Also in some cases fine collagen separate groups of cells giving an alveolar or pseudo alveolar pattern, **Fig-4, Alveolar rhabdomyosarcoma (case no.18).**

**C.**PSR stain was found to demonstrate the vascular pattern of the tumors. Most of our STS were found to be highly vascular which was more prominent in round cell tumors.

The result of ***Masson trichrome*** stain drew attention to the following interesting observations:

**A.** Results regarding the amount, distribution and pattern of collagen fibers were comparable to that detected in PRS, **Fig-5, Leiomyosarcoma (case no.9).**

**B.** As regarding skeletal muscle cells, only case no. 15 was intensely stained with MT, **Fig-6, Embryobnal rhabdomyosarcoma (case no. 15).**

**C.** Leiomyosarcomas stained typically with MT. The results of ***PAS*** stain, we had +ve staining results in case no. 12,13, and 27. In case no. 22, the secretions in glandular like spaces stained +ve. The result of immunohistochemical stain for ***Myoglobin*** can be summarized, as shown in **Table-6,** as follow:

**A.** It shows positive staining results in 5 cases. Four cases were mainly round cell sarcomas, while the 5th case was pleomorphic sarcoma.

**B.** Strong reactivity was found in well-differentiated myoblasts with abundant cytoplasm and in giant cells (Fig-6).

**Table6: Myoglobin staining results in previously and recently diagnosed cases of rhabdomyosarcomas.**

| Case no. | Previous diagnosis | Recent diagnosis | Myoglobin staining results |
|---|---|---|---|
| **14** | Rhabdomyosarcoma | Rhabdomyosarcoma Rhabdomyosarcoma | +ve |
| **15** | Rhabdomyosarcoma | Rhabdomyosarcoma | +ve |
| **16** | MFH | Rhabdomyosarcoma | +ve |
| **24** | Neurosarcoma | Haemangioendothelioma | +ve |
| **18** | Rhabdomyosarcoma | Myxoid MFH | +ve |
| **6** | Rhabdomyosarcoma | Alveolar soft part sarcoma | -ve |
| **13** | Rhabdomyosarcoma | Angiosarcoma | -ve |
| **39** | Rhabdomyosarcoma | | -ve |

## DISCUSSION:

Agreement in the diagnosis between the previous and the recent STS, based on routinely processed slides, was 47.5%. This proves the diagnostic problems and difficulties, which are often encounter in the diagnosis of STS. This has been manifested by many researchers [2,7] .The crude proportion in agreement observed by Coinder et al. [8] was 61% for the diagnosis of different STS by ordinary stained slides. Some STS as myxoid liposarcoma and mesenchymal chondrosarcma could be diagnosed with ease depending on the characteristic cytoarchitectural features. Some others need other supportive and sophisticated investigations and measures for diagnosis. Agreement in the diagnosis of spindle cell sarcomas in this study was 58.8%. The main disagreement was in fibrosarcoma. Enzinger and Weiss [2&7] summarizes the causes of over diagnosis of fibrosarcoma:

1. The introduction of MFH as a specific lesion
2. The separation of Fibromatosis as a specific entity.
3. The separation of fibrosarcoma from malignant Schwannoma and Synovial sarcoma. Most disagreement in this study was encountered in the diagnosis of round cell sarcomas (or round cell malignant soft tissue tumors). The agreement in diagnosis was only 33.3%. The differential diagnosis of small round blue cell tumors includes rhabdomyosarcoma, neuroblastoma, lymphoma, Ewing sarcoma, and others. [6,14] Problems were encountered in the diagnosis of rhabdomyosarcomas, because many of these tumors presented as primitive round cell tumors without distinct rhabdomyoblastic differentiation. This difficulty in the diagnosis of round cell sarcomas, especially in children, has been asserted by many researches. [2,16,17] Neurogenic sarcoma/ Neuroepitheioma/ peripheral neuroepitheioma/ peripheral neuroblastoma, is a primitive malignant neuroectodermal tumor (PNET) consisting of primitive neuroepithelial cells which are capable of differentiation in neuronal and /or neuroglial directions [15] We observe the use of these terms is variable from one pathologist to others, depending on the experience of the pathologist, the clinical informations as age of the patient and site of the tumor, and the availability of special stains**.** Regarding histochemical stains used in this study, we could consider PSR stain as a supportive staining procedure rather than an exclusive one for the diagnosis of different STS, especially the spindle cell type. MT on the other hand, was found to be helpful in documenting smooth and some skeletal muscle tumors.

The usage of PSA was helpful in confirming or favoring the diagnosis of some STS as in case no.22 (Synovial sarcoma). These satins have been applied to increase diagnostic accuracy. [5] Regarding the use of myoglobin imunoperoxidase marker, we could conclude the following;

1. The 1st two cases (case no.14&15) considered as morphologically classical rhabdomyosarcomas, were documented by +ve myoglobin staining results.

**2.** The remaining cases were morphologically less classical. From the results we can see that some suspected rhabdomyosarcomas from the previous diagnoses have –ve staining results, as case no. (6, 13 & 39). On the other hand unsuspected case in the recent diasgnoses get +ve results (case no. 18). Many points should be considered in evaluating the results of myoglobin immunohistochemical staining results.

**a.** Myoglobin is a protein appears specific for striated muscle differentiation. But unfortunately it is expressed only when the tumor cell has acquired a high degree of differentiation. It is therefore often negative in poorly differentiated tumors. [5,13,18]

**b.** Rhabdomyoblastic differentiation is also a feature of many malignant neoplasms, for example, malignant Schwannoma, malignant ectomesenchymoma, nephroblstoma and others.

**c.** Also residual muscle fibers may give false positive results. [5, 7] So careful examination of the slides must precede the interpretation of this technique.

**d.** Negative staining results of Myoglobin marker, on the other hand, dose not exclude rhabdomyosarcoma. Myosin was found to be more sensitive in the detection of muscle differentiation in rhabdomyosarcoma than Myoglobin. [13,14] .

## CONCLUSION:

The variety of appearances of STS leads to a wide range of possible tumor types and subtypes. This variety gives a high discrepancy rate in tumor typing even among experienced pathologists. Limitation of diagnosis of these tumors, especially the rare ones, to specialized centers or highly qualified pathologists is recommended. The interpretations of special stains, especially the immunohistochemical, need careful and precise study with correlation of results with the H and E sections.

Applications of further special stains, immunohistochemical markers and/or other sophisticated techniques, as electron microscopy, are required for definite diagnosis of STS.

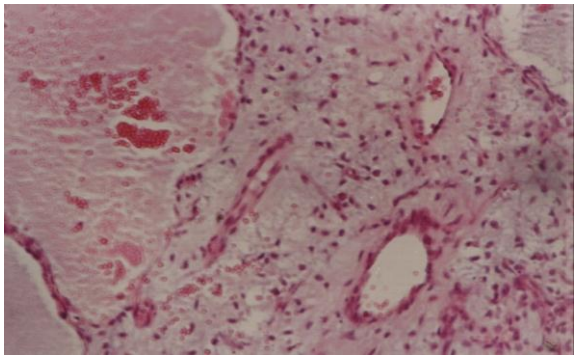

**Fig1: Myxoid sarcoma (Myxoid liposarcoma, case no. 26). Note the prominent plexiform capillary pattern and abundance of myxoid material between vessels and tumor cells with large pools of mucin. (H&E x 100) .**

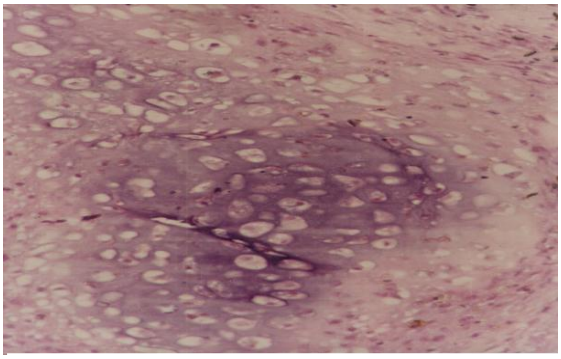

**Fig2: Extraskeletal mesenchymal chondrosarcma (case no. 27), showing well circumscribed islet or nodule of well-differentiated cartilaginous tissue with central calcification surrounded by primitive mesenchymal tissue characteristic of this tumor. (H&E x100) .**

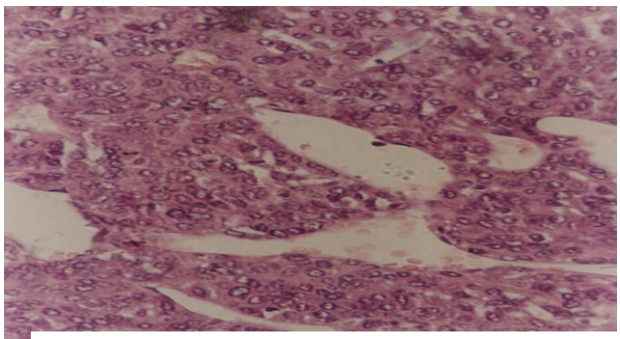

**Fig3: Extraskeletal mesenchymal chondrosarcma (case no. 27). Note the hemangiopericytoma-like arrangement of tumor cells characteristic of this sarcoma. (H&Ex200) .**

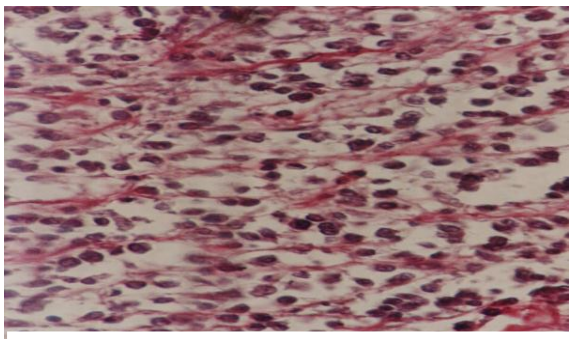

**Fig4: Alveolar rhabdomyosarcoma (case no.18). Poorly differentiating round cells separated by collagen fibers into prominent alveolar pattern. (PSR with haematoxylin counterstain x200) .**

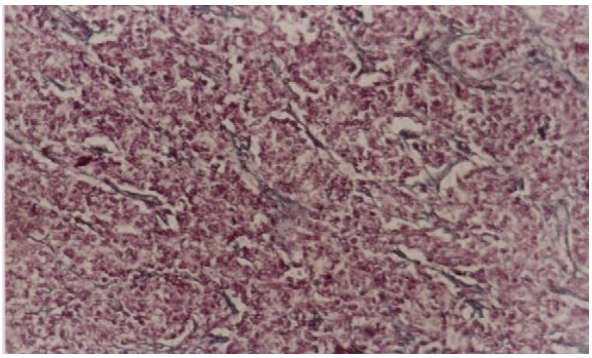

**Fig5: Leiomyosarcoma (case no.9). The greenish collagen fibers are sharply demarcating the reddish violet smooth muscle fascicles (Masson trichrome X 40).**

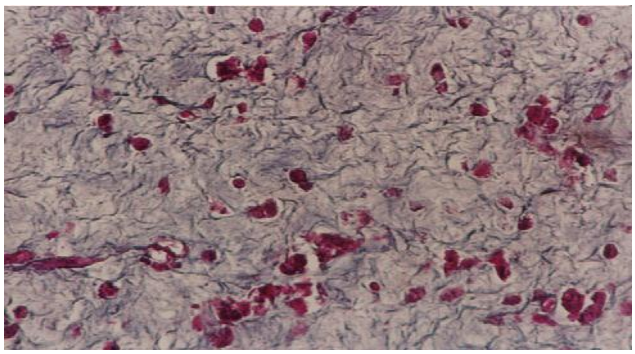

**Fig 6: Embryobnal rhabdomyosarcoma (case no. 15). Note the distinct positive stain in most tumor cells. (Masson trichrome x200)**

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