

Subtyping and Grading of Synovial Sarcomas: A Cyto-Histopathologic Correlation Study

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ABSTRACT

Introduction: Synovial sarcoma is a mesenchymal spindle cell tumor which displays variable epithelial differentiation, including glandular formation and has a specific chromosomal translocation t(X; 18). Fine-needle aspiration cytology (FNAC) is increasingly accepted as a valid screening technique with high sensitivity and specificity in establishing the presence of malignancy and determining the mesenchymal nature of a lesion.

Aims and Objectives: In this present study, cytological features, subtyping and grading were studied retrospectively from the histologically confirmed 14 cases of synovial sarcomas and then subsequently correlated our findings from histology section.

Methods: This is a retrospective study conducted in Central Institute of Orthopedic (CIO) laboratory. A total 14 cases with a diagnosis of synovial sarcomas from CIO laboratory from past 4 years were retrieved and reviewed for cytohistological correlation, subtyping and grading of synovial sarcoma.

Results: Out of total 14 cases of histological proven synovial sarcomas, 12 cases were exactly subtype on cytology. The cytological grading was only similar in 7 of 13 cases that were graded.

Conclusion: FNAC is an important and useful tool in diagnosing and subtyping synovial sarcoma.

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Introduction

Synovial sarcoma (SS) is a mesenchymal spindle cell tumor which displays variable epithelial differentiation, including glandular formation and has a specific chromosomal translocation t(X; 18).[1] The preoperative diagnosis of synovial sarcoma should always be established in a manner that does not compromise the radical surgical treatment. The diagnosis of synovial sarcoma can be obtained in a variety of ways, including fine needle aspiration cytology (FNAC), core biopsy or open biopsy. Each of these diagnostic tools has advantages and disadvantages. FNAC when applied with respect to anatomic compartment boundaries is the least invasive method to obtain diagnostic material. It is an outpatient procedure with almost no complications. It is easy to perform and gives a rapid diagnosis. Also, the risk for sarcoma-cell spread is negligible and multiple aspirations from different parts of large heterogeneous tumors have been found to be more informative than small single biopsy samples.[2,3] The last few years have seen publication of several reviews and editorials on cytodiagnosis of soft tissue tumors indicating that aspiration cytopathology can prove to be an accurate and minimally invasive method for the evaluation of soft tissue tumors, particularly in the backdrop of a multidisciplinary approach (appropriate clinicoradiologic correlation). The present study is aimed at evaluating the success and limitations of FNAC in diagnosing STT with special emphasis on subtyping and grading of SS.

Materials and Methods

This is a retrospective study conducted in Central Institute of Orthopedic (CIO) laboratory Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi. The cytological aspirates of all STTs received in Orthopedic (CIO) Laboratory in the last 10 years (period commencing from 2001 to 2011) were retrieved and reviewed blindly to diagnose and subtype STTs as well as grade STS.

The study material included in all, 14 cases of synovial sarcoma received during the duration of this study. FNAC smears were studied in the backdrop of the available clinicoradiologic details of the patients. In the retrospective cases, the patient details including clinicoradiological data were retrieved from the archives. A definite plan for comparative study between cytology and histopathology of STTs was adopted in taking up each case for the study.

The smears were examined first under low power to assess their cellularity and cellular distribution. They were then studied under high power with respect to cellular size and shape, cohesiveness, nuclear-cytoplasmic ratio, nuclear size and shape, chromatin pattern, presence or absence of nucleoli, mitotic figures and presence of naked nuclei. The

cytological diagnosis was made in each case and compared with histopathological diagnosis to find out the diagnostic accuracy of cytology.

The cytological specimens were assessed for the following:

A. Adequacy: Smears having at least 5 clusters of 10 unobscured cells, each were considered adequate.

B. Background: Presence of necrosis, myxoid, chondroid or osteoid material was noted.

C. Cellular arrangement: Arrangement of cells in a particular pattern, e.g. fascicular, storiform, papillary, alveolar or dispersed was observed.

D. Principal smear pattern: Based on the principal smear pattern, the tumors were classified in the following categories, namely, pleomorphic, spindle, myxoid, small round cell or epithelioid.

The cases were blinded as to patient identification and graded without any knowledge of prior diagnosis or grade originally assigned. Each neoplasm was cytologically graded using the grading system shown in Table 1.[3] After cytological grading the corresponding surgical biopsy/specimen was graded without any knowledge of the cytological grade or histological grade originally assigned. Pitfalls on cytology were evaluated keeping histopathology as gold standard. Cytological and histological diagnoses were made strictly according to the latest WHO classification.[4]

Table 1: Protocol for cytological grading

Features	Point assigned
Cellularity	1 (low), 2 (moderate), 3 (high)
Nuclear atypia	1 (minimal), 2 (moderate), 3 (marked)
No. of mitotic fig./200cells	1 (0–2), 2 (3–5), 3 (>5)
Tumor necrosis	1 = absent, 3 =present
Grade 1 =	4–6
Grade 2 =	7–9
Grade 3 =	10–12

Result

Our series included a total of 14 cases of histologically confirmed SS (9 biphasic, 4 monophasic and 1 poorly differentiated). The age of the affected patients ranged from 10 to 60 years, with the average affected age being 33.5 years. There were 8 males and 6 females. The sites involved were foot, forearm, knee, ankle, elbow and leg. The average maximum dimension of tumor was 6.93 cm with 12 of 14 lesions having a maximum dimension of >5 cm.

Cytologically, the yield was good in all cases. The smear pattern varied from being epithelioid to spindle cell in biphasic tumors (Figure 1), round or spindle cell type in monophasic tumors (Figure 2) and round cell type in the poorly differentiated tumor (Figure 3). The cells were arranged in tissue fragments and as dispersed cells. Epithelial elements were represented by round to ovoid cell with few gland-like formations within otherwise solid tissue fragments. Occasional findings included presence of calcific spherules, squamous differentiation, mast cells, necrosis, prominent nuclear atypia and secretory mucin. No necrosis was appreciated in any case except the one case of poorly differentiated SS. Minimal nuclear pleomorphism, bland nuclei and inconspicuous nucleoli were typical. On review cytology the number of cases showing cytohistological correlation was 12. Two cases were wrongly typed. On comparing with the histology it was noted that epithelial like cells and secretory mucin were restricted to biphasic SS only, whereas, round to poorly differentiated cells and comma like nuclei were essentially seen in monophasic SS. (Table 1)

The study comprised of 14 cases of histologically proven SS. One recurrent lesion was not graded as grading on recurrent and metastatic lesions is not recommended as per existing literature (these neoplasms are known to show a higher grade as compared to the primary lesion). A total of 14 sarcomas were graded on histology and review cytology, and the results were compared. There were zero grade I, seven grade II and six grade III cases on histology. There were two grade I, nine grade II and two grade III cases on cytology.

No agreement of grade I on review cytology and histology was found. Agreement of grade II on review cytology

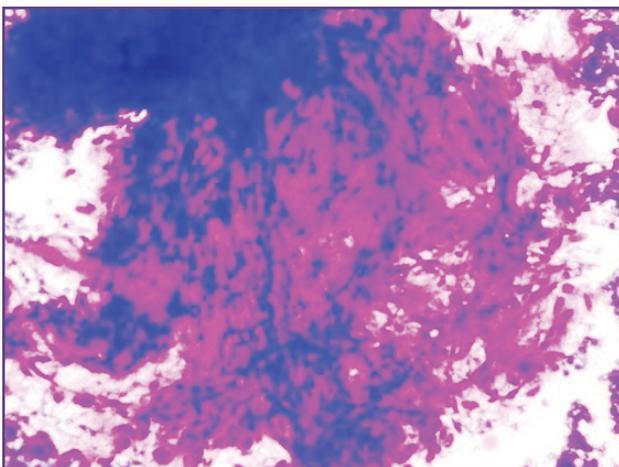


Fig. 1: Photomicrograph showing classic pattern in synovial sarcoma. Branching tumor tissue fragments.

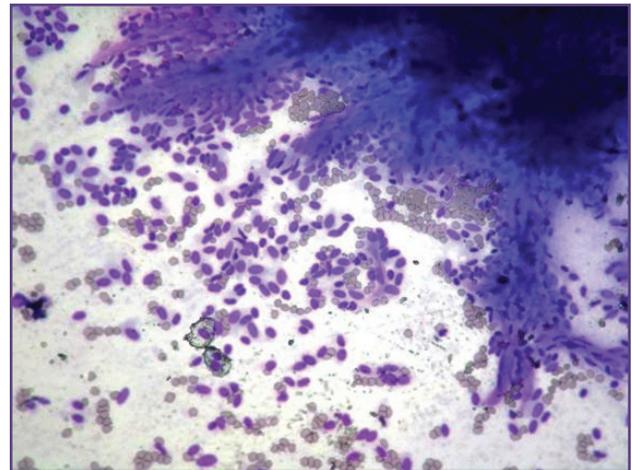


Fig. 2: Photomicrograph showing classical pattern in monophasic synovial sarcoma with three dimensional cell cluster, oval to spindle shape cells with bland chromatin, inconspicuous nucleoli.

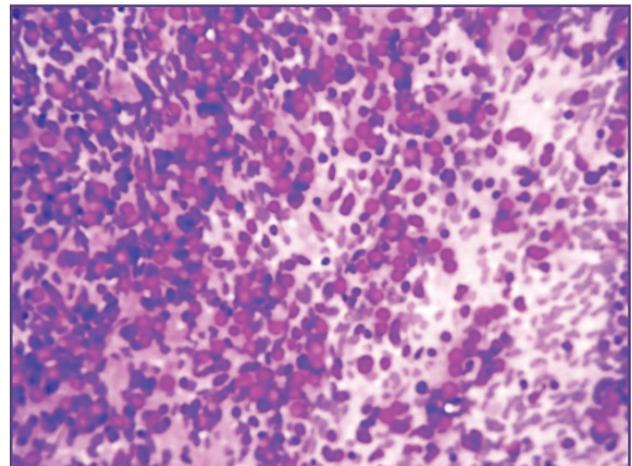


Fig. 3: Photomicrograph showing poorly differentiated synovial cell sarcoma with hyperchromatic, pleomorphic round cells.

and histology was found in a total of 5 cases, 2 biphasic synovial sarcoma, and 3 cases of monophasic synovial sarcoma. Agreement of grade III on review cytology and histology was found in a total of 2 cases of synovial sarcoma including 1 monophasic synovial sarcoma and 1 poorly differentiated synovial sarcoma.

Discussion

The exact type specific diagnosis on review cytology was achieved in 12 of 14 SS, with an accuracy of 85.71%. High accuracy of exact subtyping was achieved because of the fact that evaluation of smears was done taking into account the available clinical and radiological details, and smears were interpreted based on cytological features like background, smear pattern, cell arrangement, cellularity

and nuclear details including presence and absence of nucleoli and other special cytological features associated with various tumors.

There are only a few studies documenting how well FNAC can subtype previously undiagnosed soft tissue sarcoma and the results vary widely, with an average of 50 to 70% success rate.[5,6,7] In a series carried out by Kilpatrick, et al.[5] on 140 patients, to evaluate the role of FNAC in the primary diagnosis of STS, it was found that the accuracy of FNAC for subtyping of STS with the use of ancillary studies was greater for pediatric sarcomas (92%) than for adult sarcomas (52%). The authors further showed that if one is able to subtype or at least, place the sarcoma into the proper cytomorphological group based on smear pattern (pleomorphic, spindle, etc.), then a specific grade was not needed for the initiation of treatment because in most cases, the histological grade is readily apparent.

The exact success rate for subtyping of STS was found to be lower (20%) in the study done by Costa and co-workers.[8] According to Nagira, et al.[9] (specific FNAB diagnoses were correct in 151 of 279 cases, that is, 54%, in combination with clinical and radiologic findings). Kilpatrick, et al.5 also gave similar results for subtyping with a 54% success rate.

We received 14 cases of histologically confirmed SS (9 biphasic, 4 monophasic and 1 poorly differentiated). The age of the affected patients (10 to 60 years, with the average affected age being 33.5 years) was in accordance with the study of Ackerman[10] who stated that SS can occur at any age, but most cases are found between the ages of 10 and 35 years as well as Enzinger[11] who stated that 15 to 40 years is the peak affected age group. A male predominance was noted similar to the observation of Enzinger.[11] The anatomical distribution and average size of the tumor was consistent with that found by Ackerman[12] and Enzinger.[11] An important clue to the diagnosis was the location of the tumor in the region of joints, tendons, and ligamentous structures (especially acral parts). Also synovial sarcomas may seem to be dormant for a long period of time before behaving aggressively, and may have irregular, small flecks of calcification in their substance, which sometimes provides a radiographic clue regarding their diagnosis, as was found in this study.[11]

Comparative studies based on histologic and cytological features to account for morphologic heterogeneity of these tumors are limited to a few series.[10,13] The diagnostic/characteristic cytological features were similar to those described by other authors.[14,15,16] The smears were cell-rich and stroma-poor, the tumor cells showed striking uniformity, lacking nuclear pleomorphism. Branching papillary-like tumor tissue fragments with vessel stalks, acinar-like structures, and comma-like nuclei were also found. Epithelial elements were represented by round to ovoid cell with few gland

like formations within otherwise solid tissue fragments. On cytology only two cases were wrongly typed. It was inferred that ancillary diagnostic methods are necessary in the diagnosis of poorly differentiated SS and monophasic SS. Conventional biphasic tumors are relatively easier to diagnose on cytology. This conforms to the findings of the other authors.[10]

Mathur, et al.[17] reported a somewhat lower concordance for low grade lesions and higher concordance for high grade lesions. Mathur, et al.[17] reported a 74% overall concordance in grades, Jones et al[10] 55%, whereas Weir, et al.[18] reported a much higher concordance of 92%. Our overall grading accuracy of 53.85% is lower to that achieved by Palmer, et al.[19], when only the spindle-cell sarcomas are taken into consideration.

Mallick, et al.[20] in their study on soft tissue sarcoma found that in the grade I cases, only 3/11 cases were graded correctly on cytology, 31 sarcomas were diagnosed correctly as grade II tumors and one case was under diagnosed, there was one case of grade III sarcoma on histopathology which was correctly graded. Weir, et al.[18] attempted grading of spindle cell type of STS and were able to correctly grade in 33 FNAC specimens from 36 patients, with one major non-correlation due to FNAC interpretation error and two minor non-correlations due to sampling errors. Palmer, et al.[19] attempted to subtype and grade 64 cases of STS by the proposed scheme of Weir, et al.[18] When they combined the grade II and III tumors as high grade, they were able to correctly grade 90% of STS and concluded that in majority of STS it is possible to grade on FNAC and Grade I STS is relatively difficult to grade than grade II STS. Mathur, et al.[17] stated that intralesional morphologic heterogeneity, a feature commonly seen in STS, can cause sampling errors and may account for the major non-correlation seen in some of cases. The current study suggests that cytologic grading of sarcomas is feasible and can accurately grade these sarcomas in a significant number of cases.

Conclusion

The findings of this study show that FNAC is a reliable method for recognizing subtyping synovial sarcoma. However, the limited experience of the cytopathologist with the relatively rare tumor and lack of definite guidelines/consensus regarding the cytological criteria required for their subtyping, coupled with overlapping morphologic appearances of reactive and neoplastic lesions, could limit its use as the diagnostic procedure of choice. Although accurate assessment of the grade of synovial sarcoma is difficult by FNAC, yet a significant percentage of accurate grading can be obtained by FNAC.

The recommendations based on the results obtained from the present study are that synovial sarcoma should

be evaluated using a multidisciplinary approach. Further correlative cytological-histological studies on a larger number of cases should be carried out to try and identify distinguishing cytological features for each type of STT and the scope of such studies can be enhanced by using ancillary studies.

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Competing Interests

None declared

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