Original Article

Immunohistochemical Expression of SOX-10 in Spindle Cell Neoplasms

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Abstract

Background: Spindle cell neoplasms may range from benign to malignant tumors. This heterogenous group of lesions includes those of neural, fibroblastic, myofibroblastic, myogenic, epithelial and vascular tumors. This study was conducted to evaluate the immunohistochemical expression of SOX-10 in spindle cell neoplasms.
Materials and Methods: The study comprised of total 50 cases of spindle cell neoplasm collected over a period of one year and evaluated for SOX-10 expression using the immunohistochemistry technique.
Results: Out of 50 cases of spindle cell neoplasms, 44% were benign and 56% were malignant. Patients' age ranged from 17 to 89 years with female predominance (male:female::2:3). Tumor size in maximum dimension varied from 0.3 to 15 cm with a mean diameter of 4.8 cm. SOX-10 positive immunohistochemical expression was seen in 38.0% cases. Nuclear staining of SOX-10 was evaluated according to the four-point system of Adams et al. SOX-10 expression was significantly associated with tissue/site, S100, SMA and benign spindle cell neoplasms, while no statistically significant association was seen with malignant spindle cell neoplasms.
Conclusion: The present study on spindle cell neoplasms highlights the importance of accurate diagnosis in guiding appropriate treatment.

Keywords: Spindle cell neoplasm; SOX-10; Immunohistochemistry; Benign; Malignant.

Introduction

Spindle cells are of mesenchymal origin and constitute a part of the body's connective tissue.[1] Spindle cell neoplasms are defined as neoplasms that consist of spindle-shaped cells in the histopathology and may range from benign to malignant tumors. These can occur in head and neck, skin, soft tissues of the scalp, orbit, and neck, and along the upper aerodigestive tract (UADT) mucosa.[2] The tissue of origin can be determined based on evidence of collagen, cartilage, bone, fat or myxomatous material formed by the tumour cells. Epithelial Mesenchymal Transition has been postulated as a versatile mechanism that facilitates cellular reconstitution during embryonic development and when incited later in life, contributes to various pathologic processes.[1]

The vast appearances and architectural patterns of the spindle cell tumours make the distinction from similar microscopic lesions quite enigmatic. The tissue of origin can determine the biologic potential of the lesions. With attention to the clinical scenario, it is very difficult to diagnose these neoplasms from routine hematoxylin and eosin sections of histopathology.[3] Thus, the use of one or more ancillary techniques like immunohistochemistry, and molecular pathology can be quite beneficial.[1]

SOX10 is a transcription factor encoded by the SOX10 gene located on the long arm of chromosome 22 at position 22q13.1 and encodes 446 amino acids. It plays a key role in the development of testes, oligodendrocytes, central nervous system and chondrocytes.[4] It participates in maintaining the pluripotency of progenitor cells via the specification and differentiation of cell lines and the formation of neural crest cells. The products of these cells include: neural and glial cells in the peripheral nervous system, skin melanocytes, thyroid gland, adrenal medulla and visceral sacroiliac cartilage.[5, 6, 7]

In our study, we attempted to assess the immunohistochemical expression of SOX-10 in spindle cell neoplasms.

Materials and Methods

Case selection: The present observational study was conducted on 50 cases of spindle cell neoplasms including tru-cut/excision biopsy and resected specimen received in the Department of Pathology, PGIMS, Rohtak during a period of one year. Exclusion criteria included all previous treated cases of spindle cell neoplasms.

Morphological evaluation: The tissue was fixed in 10% formalin, processed for histopathological examination and representative sections were stained with Haematoxylin and eosin (H&E).

Immunohistochemical analysis: Representative section from each case were subjected to immunohistochemical staining for SOX-10 (Biocare medical; clone: BC34; Dilution: 1:100); Antigen retrieval: Heat-Induced Epitope Retrieval (HIER) buffer: EDTA Buffer, pH 9.0.

SOX-10 staining interpretation: Nuclear brown staining was graded according to the four-point system of Adams et al. as follows:[8]

- **Strong (3+):** dark staining that is easily visible at low power and involves >50% of cells.
- **Moderate (2+):** focal darkly staining areas (<50% of cells) or moderate staining of >50% of cells.
- **Weak (1+):** focal moderate staining in <50% of cells or pale staining in any proportion of cells not easily seen at low power.
- **Negative (0+):** None of the above.

Skin tissue was used as positive control. Tonsillar tissue was used as negative control.

The SOX-10 expression was correlated with various clinicopathological parameters including age, sex, tumor size, tumor site and other IHC used for diagnosis of spindle cell neoplasms. Approval from the institutional ethics committee of the University of Health Sciences was obtained.

Statistical analysis: An observational study was carried out for 50 cases of spindle cell neoplasms. The collected data was analysed with the help of software package (SPSS version 24.0). Chi square test was used for qualitative variables. Correlations were assessed using spearmen test. A p-value <0.05 was taken as significant.

Results

Distribution of cases according to clinicopathological parameters: A total of 50 cases of spindle cell neoplasms were included in the present study. The age of patients varied from 17 to 89 years, with the majority of patients (26.0%) in the age group of 60-69 years. A higher incidence was seen in females, with a ratio of 2:3. Tumor sites were upper trunk, central nervous system, female reproductive system, lower body and gastrointestinal system. Maximum cases (34.0%) were seen on upper trunk. The tumor size ranged from 0.3 to 15 cm in maximum diameter with a mean size of 4.8 cm. Out of 50 cases, 44.0% were benign and 56.0% were malignant. Neurilemmoma (31.8%) comprised majority of the benign spindle cell neoplasms (Table 1) while malignant category was dominated by leiomyosarcoma, malignant mesenchymal tumor and synovial sarcoma group (Figure 1).

SOX-10 expression by immunohistochemistry: The SOX-10 expression was seen in the nucleus of tumor cells. Out of 50 cases of spindle cell neoplasms, S0X-10 was expressed in 19 (38.0%) cases while 31 (62.0%) cases were negative for S0X-10 expression. Positive cases were further graded according to four-point system of Adams et al.[8] (Figure 2). SOX-10 expression was significantly associated ($p<0.05$) with tissue site, S100, SMA and benign spindle cell neoplasms (Table 2).

Discussion

Spindle cell neoplasms are defined as neoplasms that consist of spindle-shaped cells in the histopathology. These can occur in head and neck, skin, in the soft tissues of scalp, orbit, and and along the upper aerodigestive tract (UADT) mucosa.[2]

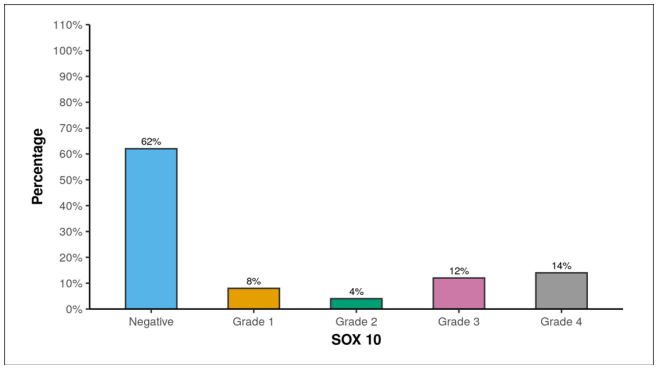

Figure 1: Distribution of the Cases in Terms of 'Malignant spindle cell neoplasms' (n=28)

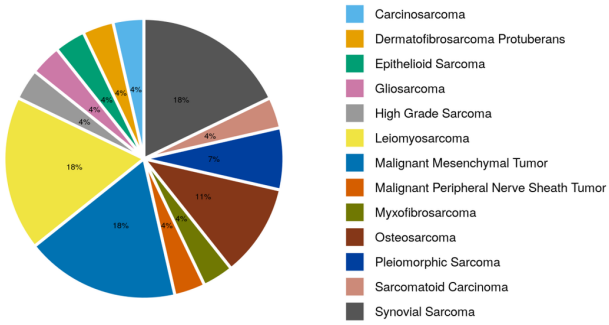

Figure 2: Case distribution as per "Grading of SOX-10 expression"

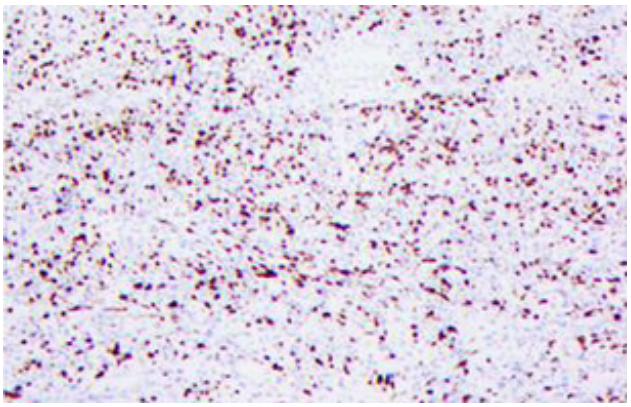

Figure 3: Photomicrographs of case1: Schwannoma (H&E, x100).

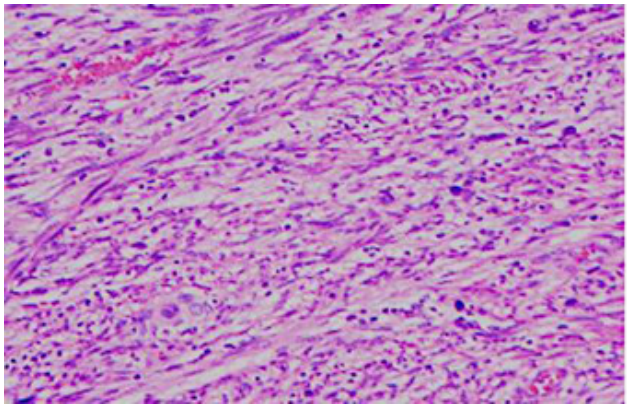

Figure 4: Photomicrographs of case1: Positive nuclear expression SOX-10 (IHC, x400).

Table 1: Distribution of cases in terms of benign spindle cell neoplasms. (n=22)

Benign Diagnosis	Frequency	Percentage	95% CI
Gastrointestinal Stromal Tumor	3	13.6%	3.6% - 36.0%
Leiomyoma	5	22.7%	8.7% - 45.8%
Neurilemoma	7	31.8%	14.7% - 54.9%
Neurofibroma	6	27.3%	11.6% - 50.4%
Pleomorphic Adenoma	1	4.5%	0.2% - 24.9%

Epithelial-Mesenchymal Transition has been postulated as a versatile mechanism that facilitates cellular reconstitution during embryonic development and when incited later in life, contributes to various pathologic processes.[1]

As the spindle cells contain both benign and malignant mimics, misclassification has the potential to result in either under or over-treatment of the patient. The tissue of origin can determine the biological potential of the lesions.[3] Thus, the use of histopathology alongwith one or more ancillary techniques like immunohistochemistry, and molecular pathology can be quite beneficial.[1]

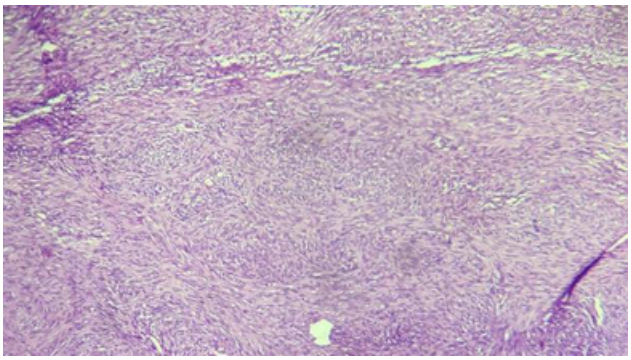

Figure 5: Photomicrographs of case2: Malignant peripheral nerve sheath tumor (H&E, x100).

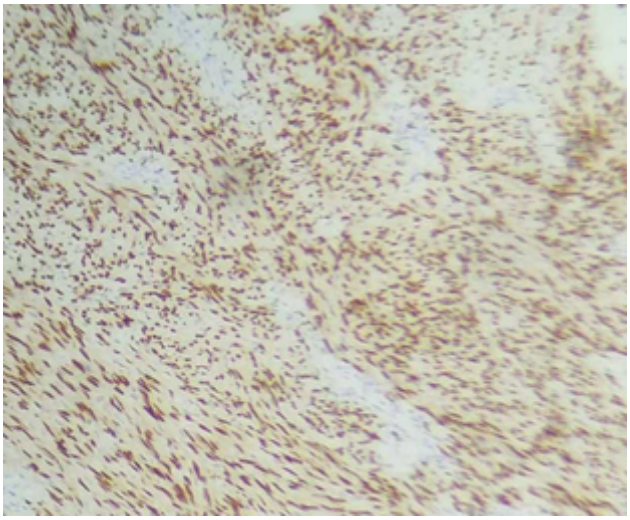

Figure 6: Positive nuclear expression of SOX-10 (IHC, x400).

SOX10 is a transcription factor encoded by the SOX10 gene located on the long arm of chromosome 22 at position 22q13.1 and encodes 446 amino acids. The regulation of SOX10 functions consists of binding this protein to promoters or enhancers of transcription in target genes, alone or in combination with other transcription factors.[9]

The present study was conducted in the Department of Pathology, Pt. B.D. Sharma Post Graduate Institute of Medical Sciences, Rohtak. Histopathologically confirmed spindle cell neoplasm cases were included in the study group. IHC expression of SOX-10 was evaluated and correlated with the clinicopathological parameters.

Age and sex distribution

The age of patients ranged from 17 to 89 years, with maximum cases (26.0%) in the age group of 60-69 years. These results were similar with study conducted by Lei Fang et al.[10] (most cases belonged to age group >64 years). The majority of patients were females (60%) with male to female ratio of 2:3. The gender distribution was consistent with the study by Gassert et al.[11], who also observed female predominance.

Site and Size distribution

In the study, tumor site distribution comprised of 17 (34%) cases from upper trunk, arms and forearm, 9 (18%) cases from lower trunk, 3 (6%) cases from CNS, 2 (4%) cases from GIT, 9 (18%) cases from reproductive system and 10 (20%) cases from other sites. These results were discordant with the findings of Gassert et al.[11], where most of the cases (46.09%) were from lower extremities. This difference could be attributed to geographical variation in the spindle cell neoplasms and case selection. Tumor size in the maximum dimension varied from 0.3 to 15 cm with a mean diameter of 4.8 cm.

Histological diagnosis of spindle cell neoplasms

Out of 50 cases, the study comprised 22 cases of benign spindle cell neoplasms and remaining 28 cases were malignant. The benign group included 3 cases of Gastrointestinal Stromal Tumors (13.6%), 5 Leiomyomas (22.7%), 7 Neurilemomas (31.8%), 6 Neurofibroma (27.3%) and 1 Pleomorphic Adenoma (4.5%). Distribution of cases were similar with the studies conducted by Nonaka et al.[12] and Miettinem M et al.[13].

The malignant group of spindle cell neoplasms were dominated by cases of leiomyosarcoma, malignant mesenchymal tumor and synovial sarcoma which constituted 53.7% of the total cases. In the studies by Nonaka et al.[12] and Miettinem M etal.[13], maximum cases were of malignant peripheral nerve sheath tumor, 31.42% and 10.99% respectively. While Kang et al.[14] observed maximum cases of synovial sarcoma (66.9%).

SOX-10 expression in spindle cell neoplasm

In the present study, Immunohistochemical expression of SOX-10 was studied and brown nuclear staining was evaluated according to the four-point system of Adams et al.[8]. Among the benign category, cases of Gastrointestinal stromal tumor

Table 2: Association between SOX-10 Expression and Clinicopathological Parameters (n=50)

Parameters	SOX-10 Expression	
	Positive (n=19)	**Negative (n=31)**
Age (Years)	49.05 ± 18.98	52.90 ± 19.27
Gender		
Male	7 (36.8%)	13 (41.9%)
Female	12 (63.2%)	18 (58.1%)
Tissue/Site		
Other	4 (21.1%)	6 (19.4%)
Upper Trunk	9 (47.4%)	8 (25.8%)
CNS	3 (15.8%)	0 (0.0%)
Female Reproductive System	1 (5.3%)	8 (25.8%)
Lower Body	2 (10.5%)	7 (22.6%)
GIT	0 (0.0%)	2 (6.5%)
Tumor size (maximum diameter) (cm)	4.20 ± 2.09	5.18 ± 3.92
SOX 10		
Negative	0 (0.0%)	31 (100.0%)
Grade 1	4 (21.1%)	0 (0.0%)
Grade 2	2 (10.5%)	0 (0.0%)
Grade 3	6 (31.6%)	0 (0.0%)
Grade 4	7 (36.8%)	0 (0.0%)
S100 (Positive)	12 (100.0%)	4 (50.0%)
SMA (Positive)	0 (0.0%)	10 (83.3%)
KI-67 (%)	13.12 ± 9.61	23.12 ± 17.21
Diagnosis Type		
Malignant	6 (31.6%)	22 (71.0%)
Benign	13 (68.4%)	9 (29.0%)
Benign Diagnosis		
Gastrointestinal Stromal Tumor	0 (0.0%)	3 (33.3%)
Leiomyoma	0 (0.0%)	5 (55.6%)
Neurilemoma	7 (53.8%)	0 (0.0%)
Neurofibroma	5 (38.5%)	1 (11.1%)
Pleiomorphic Adenoma	1 (7.7%)	0 (0.0%)
Malignant Diagnosis		
Carcinosarcoma	0 (0.0%)	1 (4.5%)
Dermatofibrosarcoma Protuberans	0 (0.0%)	1 (4.5%)
Epithelioid Sarcoma	0 (0.0%)	1 (4.5%)
Gliosarcoma	1 (16.7%)	0 (0.0%)
High Grade Sarcoma	0 (0.0%)	1 (4.5%)
Leiomyosarcoma	0 (0.0%)	5 (22.7%)
Malignant Mesenchymal Tumor	2 (33.3%)	3 (13.6%)
Malignant Peripheral Nerve Sheath Tumor	1 (16.7%)	0 (0.0%)
Myxofibrosarcoma	0 (0.0%)	1 (4.5%)
Osteosarcoma	1 (16.7%)	2 (9.1%)
Pleiomorphic Sarcoma	0 (0.0%)	2 (9.1%)
Sarcomatoid Carcinoma	0 (0.0%)	1 (4.5%)
Synovial Sarcoma	1 (16.7%)	4 (18.2%)

(0/3) and Leiomyoma (0/5) showed no positivity (0.0%). Whereas Neurilemmoma showed positivity in all 7 cases (7/7; 100%) and Neurofibroma showed positivity in 5 cases out of 6 (5/6; 83.33%). 1 case of Pleomorphic adenoma (1/1) with significant high spindle cell component also turned out to be positive for SOX-10 expression. Results of present study were compared with other studies (Table 3).

In the malignant spindle cell neoplasms, application of SOX-10 IHC in the Malignant mesenchymal tumor showed positivity in 2 cases (2/5; 40.0%) and Synovial sarcoma showed positivity in 1 case (1/4; 25.0%). 1 case each of osteosarcoma (1/2), Gliosarcoma (1/1), and Malignant peripheral nerve sheath tumor (1/1) were positive. Whereas carcinosarcoma (0/1), dermatofibrosarcoma protuberance (0/1), epitheliod sarcoma (0/1), high-grade sarcoma (0/1), leiomyosarcoma (0/5), myxofibrosarcoma (0/1), pleomorphic sarcoma (0/2) and sarcomatoid carcinoma (0/1) showed no positivity for SOX-10. Findings similar to our results for MPNST was seen in studies done by Miettinen M et al.[13], Kang Y et al.[15] and Nonaka et al.[12] showing 49% positivity (38/77), 67% positivity (32/48), and 47.7% positivity (31/65) respectively using SOX-10. In contrast, findings for synovial sarcoma in a study conducted by Karamchandani et al.[15], Nonaka et al.[12], and Miettinen et al.[13] showed no positivity whereas 25% synovial sarcoma cases showed positivity for SOX-10 in our study.

Table 3: SOX-10 expression in benign spindle cell neoplasms

Neoplasms	Study	No. of cases	SOX-10 Positive	Percentage
Gastrointestinal stromal tumor	Karamchandani et al.[15]	53	0/53	0.00%
	Nonaka et al.[12]	77	0/77	0.00%
	Miettinen et al.[13]	94	0/94	0.00%
	Present study	03	0/3	0.00%
Leiomyoma	Miettinen et al.[13]	72	0/72	0.00%
	Karamchandani et al.[15]	22	0/22	0.00%
	Present study	05	0/5	0.00%
Neurilemmoma	Nonaka et al.[12]	33	33	100%
	Boulagnon-Rombi et al.[16]	35	33	94.0%
	Miettinen et al.[13]	101	100	99.0%
	Tach D et al.[17]	28	28	100%
	Present study	07	7/7	100%
Neurofibroma	Miettinen et al.[13]	31	31	100%
	Nonaka et al.[12]	52	51	98.07%
	Boulagnon-Rombi et al.[16]	05	04	80.0%
	Present study	06	5/6	83.33%

This study revealed statistically significant correlation of SOX-10 expression with specific tissue/site distribution, S-100 and SMA expression, as well as benign spindle cell neoplasms, while showing no significant correlation with age, gender, tumor size and malignant spindle cell neoplasms.

Limitation: The present study has a few limitations. Due to small sample size and time-bound nature of our study, further researches are recommended on large scale to fully understand the role of SOX-10 in diagnosing spindle cell neoplasms.

Conclusion

Our study on spindle cell neoplasms highlighted the importance of accurate diagnosis in guiding appropriate treatment. Utilizing SOX-10 expression via immunohistochemistry showed promising results, particularly in diagnosing benign spindle cell neoplasms like Neurofibroma and Schwannoma. However, further research with larger sample sizes is warranted to establish robust outcomes, as variable results were observed in malignant spindle cell neoplasms. Additionally, correlations between SOX-10 and other markers like S-100 and SMA were statistically significant, indicating its potential diagnostic utility by using alone or in addition to above mentioned IHC markers.

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Competing Interests: There are no conflicts of interest in this study.

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