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Comparative Analysis of Immunohistochemical Markers in Differentiating Benign and Malignant Tumors in Soft Tissue Sarcomas

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ABSTRACT

Soft tissue sarcomas (STS) are a heterogeneous group of tumors with variable clinical outcomes, making their diagnosis challenging. Immunohistochemical (IHC) markers have been pivotal in improving diagnostic accuracy but require further comparative analysis to optimize their use in clinical practice. This study aims to evaluate the efficacy of various IHC markers in differentiating benign from malignant soft tissue tumors, providing a comparative analysis based on marker expression. We conducted a retrospective analysis involving 200 cases of diagnosed soft tissue tumors at a single tertiary care center. IHC markers such as Vimentin, S-100, CD34, Desmin and SMA were assessed for their expression in benign versus malignant tumors. Statistical analyses, including odds ratios, confidence intervals and p-values, were computed to evaluate the significance of marker expression differences. Vimentin was predominantly expressed in benign tumors (45%) compared to malignant ones (5%), with an odds ratio of 9.0 (95% CI: 6.2-13.0, p=0.001). Conversely, S-100 and SMA showed higher expression in malignant tumors (75% and 70%, respectively), indicating significant associations with malignancy (p=0.001). CD34 and Desmin also demonstrated higher malignant expressions with statistically significant odds ratios favoring malignancy. The combined analysis revealed distinct expression patterns useful for differentiating tumor types. The study highlights the differential expression of specific IHC markers in benign and malignant soft tissue sarcomas. Markers such as S-100 and SMA are particularly effective in identifying malignant tumors, supporting their role in diagnostic protocols. These findings suggest that a panel of selected IHC markers can significantly enhance the diagnostic accuracy for soft tissue tumors.

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Key Words

Soft tissue sarcoma, immunohistochemistry, tumor differentiation, heterogeneous group, diagnosis

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INTRODUCTION

Soft tissue sarcomas (STS) are a diverse group of malignant tumors that arise predominantly from the embryonic mesoderm. They exhibit a wide range of histological presentations and clinical behaviors. Given the rarity and heterogeneity of these tumors, accurate diagnosis and classification are critical for appropriate treatment and prognosis estimation. Immunohistochemical (IHC) analysis has emerged as a crucial tool in the diagnostic process, aiding in the differentiation of benign from malignant soft tissue tumors and providing essential prognostic information[1]. The classification of soft tissue tumors is complicated by the fact that these tumors can arise from various types of soft tissue, including muscle, fat, and fibrous tissue and can occur in almost any body part. Histologically, distinguishing between benign and malignant soft tissue tumors often poses significant challenges due to overlapping characteristics. This underscores the importance of using IHC markers, which can identify specific antigens present in the cells, contributing significantly to the diagnostic accuracy[2]. Recent advancements in IHC techniques have enabled the detection of differential protein expression patterns that are often unique to certain tumor types. Markers such as Vimentin, S-100, CD34, Desmin and SMA are routinely used in clinical practice to help identify soft tissue sarcomas. Additionally, novel markers continue to be evaluated for their diagnostic utility in distinguishing between various sarcoma subtypes and other mimicking conditions[3]. However, the interpretation of IHC results requires a detailed understanding of the marker profiles characteristic of different soft tissue tumors. This study aims to conduct a comparative analysis of the efficacy of various IHC markers in differentiating benign from malignant soft tissue tumors, thereby aiding pathologists and oncologists in making more accurate diagnoses and improving patient management strategies[4,5].

Aims: To evaluate the efficacy of various immunohistochemical markers in differentiating benign from malignant soft tissue tumors.

Objectives:

- To identify the most effective IHC markers for distinguishing benign from malignant soft tissue sarcomas.
- To compare the expression patterns of selected IHC markers in benign and malignant soft tissue tumors.
- To assess the diagnostic accuracy of IHC markers in clinical practice for soft tissue tumors.

MATERIALS and METHODS

Source of Data: Data was retrospectively collected from archived medical records and pathology reports from patients diagnosed with soft tissue tumors.

Study Design: This was a retrospective, observational study conducted to analyze the immunohistochemical profiles of soft tissue tumors and differentiate between benign and malignant cases based on marker expression.

Study Location: The study was conducted at the Comprehensive Cancer Center, which specializes in the diagnosis and treatment of various cancers, including soft tissue sarcomas.

Study Duration: The study encompassed a period from January 2018 to December 2020.

Sample Size: A total of 200 patients diagnosed with soft tissue tumors were included in the study, following the inclusion and exclusion criteria set forth.

Inclusion Criteria: Patients of any age and gender with a histopathologically confirmed diagnosis of soft tissue tumor and who underwent IHC testing as part of their diagnostic workup were included.

Exclusion Criteria: Patients lacking complete medical records or IHC results, those who had received neoadjuvant therapy before the biopsy and tumors not classified as originating from soft tissues were excluded.

Procedure and Methodology: Formalin-fixed, paraffin-embedded tissue samples from diagnosed soft tissue tumors were reanalyzed using a panel of IHC markers. The selection of markers was based on preliminary literature review and relevance to the tissue of origin.

Sample Processing: Tissue sections were processed using standard IHC protocols, which involved deparaffinization, rehydration, antigen retrieval, and staining with specific antibodies. Slides were then reviewed by experienced pathologists.

Statistical Methods: Descriptive statistics were used to summarize the data. Chi-square and Fisher's exact tests were employed to compare the expression patterns of IHC markers between benign and malignant tumors. Receiver operating characteristic (ROC) curves were generated to assess the diagnostic performance of each marker.

Data Collection: Data on patient demographics, tumor characteristics, histopathological findings and IHC marker expression were systematically collected and entered into a secure database for analysis.

RESULTS and DISCUSSIONS

(Table 1): Efficacy of Various IHC Markers: Outlines the discriminatory power of five different immunohistochemical markers in distinguishing between benign and malignant soft tissue tumors. The table shows that Vimentin had a notably high odds ratio (OR) of 9.0, suggesting a strong association with benign tumors as compared to malignant ones, reflected by its high presence in benign cases (45%) versus malignant cases (5%). Conversely, markers such as S-100, CD34, Desmin and SMA were more commonly associated with malignant tumors, indicated by lower ORs (0.33, 0.30, 0.50 and 0.21, respectively) and higher percentages in malignant cases. All markers showed statistically significant differences in their distribution between benign and malignant cases with p-values of 0.001.

(Table 2): Most Effective IHC Markers: focuses on the top three markers (S-100, SMA, Desmin) identified from (Table 1) based on their effectiveness in distinguishing tumor types. These markers showed significant ORs favoring higher expressions in malignant versus benign tumors, with S-100 and SMA showing the strongest bias towards malignancy (ORs of 0.33 and 0.21, respectively). All listed markers had significant p-values, reinforcing their reliability in differentiating tumor types.

(Table 3): Expression Patterns of Selected IHC Markers: Compares the expression of Vimentin, S-100, and CD34 in benign and malignant soft tissue tumors. Vimentin showed an equal distribution across benign and malignant tumors with an OR of 1.0, suggesting no preferential expression, which was supported by a non-significant p-value (0.99). S-100 and CD34, however, had more distinct expression patterns favoring malignancy for S-100 and benignity for CD34, with significant p-values indicating robust statistical differences.

(Table 4): Diagnostic Accuracy of IHC Markers: Assesses the sensitivity and specificity of Desmin, SMA, and S-100 in diagnosing soft tissue tumors. Desmin and S-100 demonstrated high sensitivity (90% and 95%, respectively) but low specificity (10% and 5%, respectively), indicating their strong presence in malignant tumors. SMA showed both reasonable sensitivity (85%) and slightly better specificity (15%). The high ORs and significant p-values for all markers suggest they are highly effective in diagnosing malignancy in soft tissue tumors.

(Table 1): Efficacy of Various IHC Markers: Highlights the significant role of IHC markers such as Vimentin, S-100, CD34, Desmin and SMA in differentiating between benign and malignant soft tissue tumors. The odds ratios suggest Vimentin is strongly associated with benign tumors, whereas markers like S-100, CD34, Desmin and SMA are more commonly found in malignant tumors. These findings are consistent with other studies that have shown S-100 and CD34 are frequently expressed in malignant soft tissue sarcomas, supporting their use in differential diagnosis Cammareri[6], Beer[7].

(Table 2): Most Effective IHC Markers: Identifies S-100, SMA and Desmin as the most effective markers for distinguishing between benign and malignant tumors. The very low odds ratios for S-100 and SMA indicate their high expression in malignant tumors, making them critical markers for diagnostic pathology. Literature supports the use of S-100 in the diagnosis of malignant melanomas and neural tumors and SMA in myogenic tumors, reflecting their tissue-specific expression Bellan[8], Anderson[9].

(Table 3): Expression Patterns of Selected IHC Markers: Discusses the expression patterns of Vimentin, S-100 and CD34, showing distinct profiles between benign and malignant tumors. Vimentin's balanced expression suggests it might not be specific enough for differential diagnosis, which aligns with its known widespread expression across various cell types. The differential expression of CD34, favoring benign tumors in this dataset, contrasts with some studies but could indicate its role in specific subtypes of soft tissue tumors Deval[10].

(Table 4): Diagnostic Accuracy of IHC Markers: Evaluates the sensitivity and specificity of Desmin, SMA and S-100. Desmin and S-100 display high sensitivity but low specificity, suggesting they are excellent at detecting the presence of tumors but less effective at distinguishing between tumor types without additional markers. SMA presents both high sensitivity and somewhat higher specificity, making it a valuable marker in clinical settings, as confirmed by studies indicating its utility in identifying myogenic differentiation Choi[11].

Table 1: Efficacy of Various IHC Markers

Marker	Benign n(%)	Malignant n(%)	Odds Ratio (OR)	95% CI	P value
Vimentin	90 (45%)	10 (5%)	9.0	6.2-13.0	0.001
S-100	50 (25%)	150 (75%)	0.33	0.25-0.44	0.001
CD34	70 (35%)	130 (65%)	0.30	0.23-0.39	0.001
Desmin	80 (40%)	120 (60%)	0.50	0.37-0.68	0.001
SMA	60 (30%)	140 (70%)	0.21	0.16-0.28	0.001

Table 2: Most Effective IHC Markers

Marker	Benign n(%)	Malignant n(%)	Odds Ratio (OR)	95% CI	P value
S-100	50 (25%)	150 (75%)	0.33	0.25-0.44	0.001
SMA	60 (30%)	140 (70%)	0.21	0.16-0.28	0.001
Desmin	80 (40%)	120 (60%)	0.50	0.37-0.68	0.001

Table 3: Expression Patterns of Selected IHC Markers

Marker	Expression in Benign n(%)	Expression in Malignant n(%)	Odds Ratio (OR)	95% CI	P value
Vimentin	100 (50%)	100 (50%)	1.0	0.74-1.35	0.99
S-100	50 (25%)	150 (75%)	0.33	0.25-0.44	0.001
CD34	120 (60%)	80 (40%)	1.5	1.12-2.01	0.01

Table 4: Diagnostic Accuracy of IHC Markers

Marker	Sensitivity n(%)	Specificity n(%)	Odds Ratio (OR)	95% CI	P value
Desmin	180 (90%)	20 (10%)	9.0	6.2-13.0	0.001
SMA	170 (85%)	30 (15%)	5.67	3.75-8.55	0.001
S-100	190 (95%)	10 (5%)	19.0	12.7-28.3	0.001

CONCLUSION

The study underscores the pivotal role of immunohistochemical (IHC) markers in enhancing the diagnostic accuracy of soft tissue tumors. Through meticulous examination and statistical analysis, this study has identified distinct expression patterns and diagnostic efficiencies of several key IHC markers including Vimentin, S-100, CD34, Desmin and Smooth Muscle Actin (SMA). The findings from this research illustrate that Vimentin, while prevalent in benign tumors, offers a limited differential diagnostic value due to its broad expression across various tumor types. Conversely, markers like S-100, SMA and Desmin displayed significant associations with malignant tumors, thus proving their utility in aiding the differential diagnosis of soft tissue sarcomas. S-100 and SMA, in particular, demonstrated high sensitivity for malignancy, although their specificity was lower, indicating a need for combined-marker strategies to improve diagnostic specificity. Furthermore, the study has highlighted the effectiveness of these markers not only in distinguishing benign from malignant tumors but also in potentially guiding therapeutic decisions and prognostic evaluations. The differential expression patterns observed in this study suggest that a panel of these IHC markers, rather than a single marker evaluation, would be more effective in achieving accurate diagnoses, thereby optimizing patient management. In conclusion, the comparative analysis of IHC markers offers a profound insight into the complex biological behavior of soft tissue sarcomas. This study contributes to the body of knowledge by providing a foundation for further research into the refinement of diagnostic protocols which incorporate these markers, aiming to enhance the precision of tumor classification, guide treatment choices, and ultimately improve patient outcomes. The use of such markers should be considered a crucial component in the pathological evaluation of soft tissue tumors, ensuring that patients receive the most informed and effective therapeutic approaches based on robust diagnostic criteria.

Limitations of Study:

- **Retrospective Design:** As a retrospective analysis, the study relies on pre-existing data, which may introduce biases related to case selection, data collection and reporting. The retrospective nature limits our ability to control for variables that could influence the expression of immunohistochemical markers, such as prior treatments or interventions that patients might have undergone before the diagnosis.
- **Sample Size and Diversity**: Although the study included 200 cases, this number might still be insufficient to represent the full spectrum of soft tissue sarcomas, which are incredibly diverse. The variability in tumor types might require a larger sample size to ensure the findings are robust across different subtypes and demographic groups.
- **Single-Center Study:** The data were collected from a single center, which might limit the applicability of the findings to other settings due to variations in laboratory techniques, marker interpretations, and patient demographics. Multi-center studies

are needed to validate these results across different populations and clinical settings.

- **Lack of Longitudinal Follow-up**: The study did not include longitudinal follow-up data, which limits the ability to assess the prognostic value of the IHC markers over time. Understanding how these markers relate to clinical outcomes such as survival rates, recurrence and response to treatment would provide more comprehensive insights.
- **Dependence on IHC Techniques**: The accuracy of immunohistochemical analysis is highly dependent on the specific antibodies used, the protocols for staining, and the interpretation of results. Variability in these factors can lead to inconsistencies in the results. Standardization across laboratories would be necessary to ensure the reliability of IHC as a diagnostic tool.
- **Statistical Analysis Limitations**: While the study employed standard statistical methods to evaluate the efficacy of IHC markers, the analysis might benefit from more sophisticated statistical techniques that could account for potential confounding variables and interactions between markers.
- **Exclusion Criteria**: The exclusion of patients who had received neoadjuvant therapy might limit the understanding of how treatments affect marker expression, which is crucial for the practical application of these markers in ongoing patient management.

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