UAR Publisher

UAR Journal of Arts, Humanities and Social Sciences (UARJAHSS)

ISSN: 3049-4362 (Online) | Published by UAR Publisher

IMPORTANCE OF IMMUNOHISTOCHEMISTRY IN THE DIFFERENTIAL DIAGNOSIS OF THORACIC NEOPLASMS

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Abstract

Introduction: Thoracic neoplasms present a significant diagnostic challenge due to the anatomical complexity of the thorax and the morphological overlap between pulmonary, pleural, mediastinal, and metastatic tumors. Although imaging techniques allow for adequate localization of lesions, their ability to establish tumor type is limited. In this context, immunohistochemistry (IHC) has become a key tool for differential diagnosis, enabling precise characterization with diagnostic, prognostic, and therapeutic impact. The objective of this study is to describe the utility of IHC in a case series of complex thoracic neoplasms. Methodology: A retrospective case series was conducted, including five patients evaluated over the past three years at a tertiary care institution in the city of Cúcuta. All cases were discussed in a multidisciplinary thoracic team. Histological samples were obtained via percutaneous biopsies, thoracoscopy or surgical resection. Specific immunohistochemical panels were applied according to the diagnostic suspicion, including epithelial, mesothelial, mesenchymal and cell proliferation markers. Results: Immunohistochemistry allowed definitive diagnosis in all cases where imaging and conventional morphology proved insufficient.

Article DNA

Article Type:
Research Paper

DOI:
10.5281/zenodo.18878570

Article History:
Received: 18-02-2026
Accepted: 26-02-2026
Published: 05-03-2026

Keywords:
Immunohistochemistry, Thoracic neoplasms, Malignant mesothelioma, Solitary fibrous tumor, Differential diagnosis

How to Cite

Marcel Leonardo Quintero Contreras, Anna Isabella Rojas Atencia , José Alexander Rubiano Pedroza. (2026). IMPORTANCE OF IMMUNOHISTOCHEMISTRY IN THE DIFFERENTIAL DIAGNOSIS OF THORACIC NEOPLASMS. *UAR Journal of Arts, Humanities & Social Sciences (UARJAHSS)*, 2(3), 1–6. https://zenodo.org/records/18753187

***Related declarations are provided in the final section of this article.*

The Ki-67 index provided relevant prognostic information, identifying malignant behavior in mesenchymal tumors. Correct immunohistochemical classification was associated with favorable clinical outcomes in resectable cases. Conclusion: Immunohistochemistry is an essential and highly effective tool in the differential diagnosis of thoracic neoplasms. Its systematic integration into clinical practice allows for precise tumor classification, guides multidisciplinary management, and optimizes therapeutic decisions, establishing itself as a fundamental pillar of modern thoracic oncology.

Introduction

The diagnosis of thoracic neoplasms represents one of the greatest challenges in current oncological and surgical practice, due to the anatomical complexity of the mediastinum and pleura, as well as the wide variety of pathologies that can coexist in these spaces. While imaging techniques such as computed tomography (CT) and magnetic resonance imaging (MRI) are fundamental for localizing masses, they often fail to accurately determine the etiology of the lesion. In this scenario, immunohistochemistry (IHC) is an indispensable tool for achieving a definitive classification, allowing differentiation between primary neoplasms of the lung parenchyma, tumors of pleural origin, and metastatic processes that mimic similar clinical presentations (Brenes, 2011).

The relevance of immunohistochemistry (IHC) is particularly evident in the management of malignant pleural mesothelioma (MPM), where diagnostic uncertainty arising from histological diversity necessitates the use of specific panels (Alia, 2025). The use of positive markers such as calretinin, Wilms tumor type 1 (WT-1), and cytokeratin five-sixths (Ohnishi, 2020), in conjunction with negative markers for adenocarcinoma (frequently of pulmonary origin) such as CEA, Ber-EP4, and MOC-31, allows for a precise diagnostic evaluation that cell morphology alone cannot guarantee. Furthermore, the IHC detection of BAP1 protein loss and MTAP expression has revolutionized the differential diagnosis between reactive mesothelial hyperplasia and diffuse mesothelioma (Hajj, 2021).

In the case of tumors of mesenchymal origin, such as solitary fibrous tumor (SFT), immunohistochemistry (IHC) allows the identification of specific cell lineages through the strong and diffuse expression of STAT6 and CD34 (Ortega, 2018). Likewise, the use of markers such as desmin is crucial to determine whether the tumor presents with primary pleural involvement or invasion of the lung parenchyma (Curi, 2008). On the other hand, neoplasms of the chest wall such as liposarcoma, nuclear reactivity for CDK4 and MDM2 is essential to

confirm the diagnosis of well-differentiated subtypes, distinguishing them from benign lipomatous lesions that, due to their large size, could lead to diagnostic confusion (Resag, 2022).

IHC not only fulfills a diagnostic function, but also a prognostic and biological one (Gomez, 2021). Measuring the cell proliferation index using the Ki-67 marker allows for estimating tumor aggressiveness and predicting potential malignant behavior, recurrence rates, and metastasis potential. Integrating histopathological findings with a robust immunohistochemical profile is the cornerstone of multidisciplinary and personalized management in thoracic oncology, optimizing therapeutic decisions and improving patient survival prospects.

The following presents a series of cases where immunohistochemical analysis (IMQ) was fundamental for the diagnosis and treatment of pulmonary oncological pathologies.

Methodology

Over the past three years, a case series of five patients with clinical outcomes based on immunohistochemistry and clinical relevance has been compiled. These patients attended the thoracic surgery board at a tertiary care institution in the city of Cúcuta.

Patient / Neoplasm	**Surgical Intervention**	**Immunohistochemistry (IHC)**	**Results Clinical Outcome**
Unilocular Thymic Cyst (Female, 55 years old)	Thoracoscopic resection following radiology-guided biopsy.	Reactive: CD31, CD34, and D240 (in vessels); Smooth Muscle Actin (in the wall). Negative: Calretinin and AE1/AE3	Favorable outcome; discharged on the third day with resolution of interscapular pain.
Malignant Solitary Fibrous Tumor (SFT) (Female, 73 years old).	Pleurectomy, decortication, and resection via thoracostomy. pulmonary hypertension.	Positive: Vimentin, STAT-6, CD99, and CD-34 (strong and diffuse expression). Ki-67: 4%.	Full recovery in 6 months; improvement of previous severe pulmonary hypertension.
Fluid Myopathies with Malignancy (Female, 58 years old)	Resection of a giant mass (2.2 kg) via thoracotomy.	Positive: CD34, STAT6, Desmin, and Ki-67 (5%). Negative: Calretinin, CK5/6, CK7, CK20, and CKAE1AE3.	Satisfactory progress at one month of follow-up; resolution of dyspnea on minimal exertion.
Epithelioid Pleural Mesothelioma (Male, 51 years old).	Diagnostic thoracoscopy with biopsy.	The diagnosis of epithelioid variant was confirmed by IHC (after a 40-year latency period due to exposure).	The patient was referred to oncology; he did not tolerate chemotherapy.

Well-differentiated liposarcoma (Female, 57 years old).	Resection of a 30x30 cm tumor with ligation of the vascular pedicle.	Positive: CDK4 and MDM2 (in nucleoli). Negative: p16.	No evidence of recurrence after 5 years; patient functional and asymptomatic.

Results

Immunohistochemistry (IHC) analysis in the five patients who required this technique demonstrates its effectiveness as a tool for resolving complex diagnoses where imaging and cell morphology are insufficient.

The technique applied in these patients was based on processing samples obtained through percutaneous biopsies (cores), cell blocks, or surgical specimens. The effectiveness of IHC lies in its ability to identify specific antigens using antibodies, allowing for accurate histological classification in the described scenarios.

STAT6 is described as the marker with the highest specificity for Solitary Fibrous Tumor, allowing for a definitive diagnosis even when CD34, which is sensitive but less specific, may fail (Toro, 2017). MTAP (Methylthioadenosine phosphorylase) is used as a surrogate marker for CDKN2A loss in mesotheliomas (Brune, 2025). Sources report a specificity of 96% and a sensitivity of 78% for this test. On the other hand, BAP1 loss by IHC has a high prevalence in the epithelioid subtype of mesothelioma (Panadero, 2015), being key to distinguishing it from benign mesothelial hyperplasia, and Ki-67 is not diagnostic of lineage, but prognostic (García, 2023). A proliferation index greater than 4-5% in TFS is a strong indicator of malignant behavior.

Conclusion

IHC proved highly effective in this case series for reclassifying tumors initially misdiagnosed based on imaging or morphology. Although the sources do not provide the negative predictive value (NPV) and positive predictive value (PPV) for each marker, they emphasize that the 96% specificity of tests such as MTAP and the strong reactivity of CDK4/MDM2 for liposarcomas are the cornerstones that validate the success of subsequent surgical and oncological treatment.

Article Publication Details

This article is published in the **UAR Journal of Arts, Humanities and Social Sciences (UARJAHSS)**, ISSN 3049-4362 (Online). In Volume 2 (2026), Issue 3 (March)

The journal is published and managed by **UAR Publisher**.

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