REVIEW ARTICLE

Comprehensive Overview of SMARCA4-Deficient Thoracic Neoplasms

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ABSTRACT
Recently, SMARCA4, an important part of the SWI/SNF chromatin remodeling complex, was found to play a major role in the development of some thoracic cancers. SMARCA4-deficient thoracic tumors are a special type of cancer because they don't produce SMARCA4 proteins. These tumors have been linked to aggressive behavior in patients and a unique histopathological profile. The goal of this review is to give a full picture of thoracic tumors that don't have SMARCA4, giving us clues about possible ways to target these tumors and make patient results better.

Keywords: SMARCA4 deficiency, thoracic tumors, who entity

INTRODUCTION
SMARCA4 deficient thoracic tumor is a new entity in who recent classification.[1] The SMARCA4 protein, which is also known as BRG1, is an important part of the SWI/SNF chromatin remodeling complex. This complex changes the structure of chromatin to make it easier for transcriptional machinery to reach it and control gene expression. Recently, new discoveries have shown that SMARCA4 genes play a big part in many types of cancer, such as those in the thorax, uterus, and intestines [2, 5]. Notably, thoracic tumors that don't have SMARCA4 are very aggressive and have unique clinical and histological features that make normal treatment methods more difficult [4, 6].

MOLECULAR PATHOGENESIS
Finding SMARCA4 as a tumor suppressor gene is very important for learning about the genetic processes that cause some types of cancer. Lack of SMARCA4 is often linked to changes in genetic and epigenetic regulation in thoracic cancers, which impacts important biological functions such as DNA repair, cell division, and differentiation [7,8]. Some changes in the BAF chromatin remodeling complex are what cause SMARCA4-deficient thoracic tumors to grow, especially aggressive thoracic sarcomas [7, 8].

CYTOLOGY
A close look at the cells of SMARCA4-deficient thoracic tumors, such as non-small cell lung carcinomas (SMARCA4-dNSCLCs) and thoracic sarcomas (SMARCA4-dTSs), shows that they are different in several ways [13, 24]:
1. SMARCA4-dNSCLCs are usually poorly differentiated carcinomas that have cohesive groups of large tumor cells with a lot of pale cytoplasm. This helps doctors tell them apart from other carcinomas[3].
2. There is a rhabdoid trait for SMARCA4-dTS. This means that tumor cells have perinuclear cytoplasmic condensations, which are often set against an inflammatory or necrotic background. Because of these factors, a high level of concern and the right extra tests are needed to make a correct diagnosis [13, 24].

CLINICAL AND HISTOLOGICAL FEATURES
SMARCA4-deficient thoracic sarcomas are highly aggressive, poorly differentiated tumors that often display rhabdoid features. They predominantly occur in male smokers, are large, and are typically located in the mediastinum, pleura, or lung. The median survival rate is about 6 months, underscoring their aggressive nature [9].
DIAGNOSIS
1. Immunohistochemical Profile: The "SMARCA4-DTS immunohistochemical signature" is very important for identification because it shows that both SMARCA4 and SMARC2A2 are missing at the same time, while SOX2 is overexpressed. This helps set these tumors apart from other intrathoracic cancers [10, 11, 14]. Also helpful are markers like CD34 and SALL4, especially in tough cases [9].
2. Cell Block Examination as a Diagnostic Tool: Cell block analysis is very important when regular biopsy samples are not enough. Along with immunohistochemical tests [24], it shows polyhedral to round tumor cells with unique nuclear and cytoplasmic traits.
3. Genetic and molecular insights: To prove SMARCA4 mutations, genetic testing is a must. Targeted therapies work best when this gene is turned off, which is a feature of these cancers [10,11].

THERAPEUTIC APPROACHES AND RESPONSE
Therapeutic Approaches and Response New ways of treating lung cancers that don’t have SMARCA4 show promise. Immunotherapy, like nivolumab, has been shown to work in recent case reports, especially when standard cytotoxic chemotherapy has not [16]. Drug combinations like atezolizumab with bevacizumab, paclitaxel, and carboplatin also seem to work, which suggests that targeted treatment might be possible [20, 21].

PROGNOSTIC OUTCOMES
Patients with SMARCA4-deficient thoracic tumors still have a bad outlook; the median survival time is often not more than a few months from the time of diagnosis. These tumors are very aggressive and spread quickly, which makes patient results much worse. Biomarkers that can predict and improve treatment effectiveness are the focus of ongoing studies [21, 22].

CONCLUSION
Due to their unique molecular and histological features, SMARCA4-deficient lung tumors are very challenging to treat. It is very important to get a correct evaluation and learn more about how their diseases work. To find better ways to treat this difficult type of cancer [15–19], researchers must keep working together on projects.

REFERENCES
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