Review of Screening, Molecular Mechanism and Clinical Application of Sebaceous Carcinoma

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Abstract: Sebaceous carcinoma (SC) is relative rarity and variable clinical presentation. It's difficult to diagnose. The screening of immunohistochemical markers, molecular mechanism analysis and clinical application of sebaceous carcinoma are the focus of current research. This paper aims to comprehensively comb and summarize the latest immunohistochemical markers, and deeply explore the molecular mechanisms and the treatment of sebaceous carcinoma. Through a review of the extensive literature, we found that immunohistochemical stains play an important role in the early diagnosis, formulation of individualed treatment plan and prognostic evaluation of sebaceous carcinoma.

***Keywords*:** sebaceous carcinoma; immunohistochemistry; molecular mechanism; clinical application; biomarker

1. Introduction

Globally, although the incidence of sebaceous cancer is less than other common cancer types, but its aggressive and poor prognosis makes it a significant focus in clinical research. Immunohistochemistry (IHC), as an important means of biomarker detection, has shown great potential in the early diagnosis and prognosis evaluation of cancer. IHC can not only detect biomarkers in fixed tissues, but also provide spatial information between the tumor and the surrounding tumor microenvironment (TME), providing key clues to understanding the mechanisms of disease onset and progression. For example, adipophilin(ADFP) and PRAME have proven useful in diagnosing sebaceous cell carcinoma.[1] P53 protein provides an important basis for distinguishing between benign and malignant sebaceous tissue, highlighting the value of IHC in the diagnosis of sebaceous cancer.[2]

2. Screening method for immunohistochemical markers of sebaceous glands

2.1 Application of immunohistochemistry technology in the study of sebaceous carcinoma

2.1.1 Diagnosis and differential diagnosis

IHC technology provides a powerful tool for the diagnosis and differential diagnosis of sebaceous cancers by detecting the expression of specific antigens. [3]Such as adipophilin (ADFP), which is observed as membranous vesicular staining is suggestive of intracellular lipids . It is useful in helping to differentiate squamous cell carcinoma and basal cell carcinoma . PRAME expression has been reported in sebaceous neoplasms. It is strong cytoplasmic staning in normal sebaceous gland, but weakly cytoplasmic staning in sebaceous carcinoma. [1, 4]P53 protein, its abnormal expression in sebaceous tumors, especially the specificity of nuclear staining, has become a key marker to distinguishing benign and malignant lesions. [5]

2.1.2 Prognostic evaluation and molecular subtyping

The application of IHC technology in prognostic evaluation is mainly reflected in predicting the aggressiveness of tumor and metastatic potential by detecting a series of molecular markers, such as apoptosis-related proteins such as Survivin, Bax and so on, and factors related to angiogenesis such as VE GF and HIF-1 α.[6]

2.1.3 Discovery and validation of therapeutic targets

Breakthroughs in modern cancer therapy often rely on the accurate identification and intervention of key molecular targets.[7] IHC technology plays an important role in this process, by visually displaying the expression pattern and localization of therapeutic targets in tissues, providing a visual basis for drug design and evaluation of treatment effects.[8]

2.1.4 Study on the accompanying diagnosis and the mechanism of drug resistance

Concomitant diagnosis refers to guiding the choice of medication by testing relevant biomarkers before specific drug treatment. IHC technology plays a key role in this field to detect specific markers of concomitant drug sensitivity, such as

HER2, PD-L1, and enabling personalized treatment.

2.2 The latest progress in the screening of sebaceous gland cancer markers

2.2.1 Application of high-throughput screening technology

High-throughput screening technologies, such as gene chips, proteomics and metabolomics, have become cutting-edge means for marker screening.[9] They are able to detect the expression of thousands of biomolecules simultaneously, significantly improving the efficiency and speed of screening.[10]

2.2.2 In-depth resolution of the molecular mechanisms

With the development of marker screening technology, the understanding of the molecular mechanism of sebaceous gland cancer has also deepened. Studies have revealed the role of multiple key signaling pathways in the development of sebaceous gland cancer, such as Wnt / β -catenin pathway, Notch pathway and Hedgehog pathway.[11]Aberrant activation or inhibition of these pathways, is often directly associated with the expression of specific markers. For example, hyperactivation of Wnt pathway.

2.2.3 Expansion of clinical application

The clinical application value of markers is increasingly prominent, not only playing a key role in early diagnosis and prognostic assessment, but also demonstrating their potential in guiding personalized therapy and monitoring disease progression.[12] For example, the detection results of p53 protein are able to predict the aggressiveness and prognosis of sebaceous cancers, guiding the choice of therapeutic strategies.[13] Latest studies have reported a subtye of sebaceous carcinoma.is expressing HER-2 revealed that it presence of hormonal receptors.Such as HR antagonists could be a well therapeutic option with ER.PR observed sebaceous carcinoma patients.[14] Some reserches have shown inhibition of PD-L1 may be a therapeutic option of sebaceous cancer.[15]

3. An expression and regulation of sebaceous gland cancer-related genes

The molecular mechanism of sebaceous cancer first focused on the expression and regulation of related genes. Abnormal regulation of gene expression is the core link in cancer development and progression. In addition to p53, other gens such as MLH1, MSH2,and MSH6,which lead to Muir–Torre syndrome,are related to sebaceous carcinoma.[1,16]

At the deep molecular level, abnormal expression and regulation of genes involved in signaling pathways are equally important in sebaceous cancer.The Hedgehog signaling pathway controls cell proliferation and differentiation. High expression of the Hedgehog pathway (including PTCH1, SMO, Gli1, and Gli2),.is found in sebaceous carcinoma. This suggests that aberrant Hedgehog signaling plays a promoting role in SC development, offering potential for targeted therapy.

4. Clinical application of immunohistochemical markers in sebaceous glands

4.1 Value of early diagnosis and differential diagnosis

Immunohistochemical markers of sebaceous glands have demonstrated significant value in the early diagnosis of cancer. The expression of specific antigens such as p53 protein, Ki-67, adipophilin(ADFP) , PRAME , etc. can provide important information about the state of cell proliferation and the degree of differentiation to distinguish between benign and malignant lesions. The membranous vesicular staining specificity of adipophilin(ADFP) protein in sebaceous gland hyperplasia has become an important basis for diagnosis, and its abnormal expression pattern contributes to the early identification of sebaceous gland tumors. The high expression level of Ki-67 is correlated with the aggressiveness and poor prognosis of the tumor, and it is a key indicator to evaluate the tumor proliferative activity.

4.2 Prognosis assessment and disease surveillance

Immunohistochemical markers also play a critical role in the prognostic evaluation of sebaceous cancers. The upregulation of epidermal growth factor receptor and vascular endothelial growth factor receptor may play a significant role in the development of sebaceous carcinoma.Moreover, the dynamic monitoring of markers, such as detecting changes in the expression of specific markers during the course of treatment, is important for evaluating treatment efficacy and predicting disease recurrence. This information helps doctors to adjust their treatment strategies and achieve more precise disease management.

4.3 The accompanying diagnosis and the formulation of personalized treatment plan

Concomitant diagnosis refers to predicting the efficacy of drugs by detecting specific markers before treatment and guiding the development of an individualized treatment plan. In sebaceous cancers, the application of IHC technology is able

to detect biomarkers associated with drug sensitivity, such as HER 2.PD-L1, providing a basis for targeted therapy.

5. Discussion

Through continuous technological innovation and the discovery of biomarkers, the clinical management of sebaceous gland cancer will be more precise and efficient, providing patients with more treatment options and hope for survival. With the deepening of research and the expansion of clinical applications, immunohistochemistry technology will continue to play an important role in precision medicine for sebaceous carcinoma promoting the continuous development of research in this field.

References

[1] Christopher K,Fahd Y,Roman S,et al. Current review of sebaceous cell carcinoma[J]. Current Opinion in Ophthalmology, 2018, 29:445–450DOI:10.1097/ICU.0000000000000505

[2] Cui Jiaojiao, Xia Heshun, Yang Chibing. Clinicopathological analysis of 7 cases of eyelid sebaceous gland carcinoma [J]. Journal of Practical Medical Technology, 2024,31(02):128-130+154.DOI:10.19522/j.cnki.1671-5098.2024.02.014.

[3] Wang Meihong, Ma Jianhui, Wang Tao, et al. Primary sebaceous carcinoma of the mandibular gingiva was reported and reviewed in the literature [J]. Cancer prevention and Treatment Research, 2019,46 (01): 93-95.

[4] Joanna K.M,Paul C.L,Chit Chow, et al. prame immunostain expression in seba source pathology so 2022 [J].Pathology,https://doi.org/10.1016/j.pathol.2022.03.003

[5] Fang Sangao, Ma Qiang, Wang Yuanyuan, et al. Clinicopathological analysis of sebaceous carcinoma of the eyelid [J]. Modern Medical Oncology, 2014,22 (07): 1557-1561.

[6] Liang Yuan, Yu Wenbo, Xiong Jianhui, et al. Progress in the molecular mechanism of aortic dissection [J]. Journal of Gannan Medical College, 2024,44 (04): 354-356 + 382.

[7] Wei Ruili. Evidence-based evaluation and study of molecular mechanism [D]. The Chinese Academy of Chinese Medical Sciences, 2023.DOI:10.27658/d.cnki.gzzyy. 2023.000044.

[8] He Jinwen. Anti-osteoporosis drug screening and Molecular Mechanism of targeting AXL [D]. Lanzhou University, 2023.DOI:10.27204/d.cnki.glzhu. 2023.000302.

[9] Doshi N ,Gond P ,Prasad T , et al.An unusual presentation of giant sebaceous cyst over the back: A case report.[J]. Clinical case reports,2024,12(4):e8714-e8714.

[10] Daniele T ,Rudolf H .Phacomatosis spilosebacea: A new name for a distinctive binary genodermatosis.[J].Journal of the American Academy of Dermatology,2023,89(4):764-773.

[11] Tarun K ,Prerna T ,Nisha K , et al.Cytomorphology of sebaceous arcinoma of the eyelid: A short series of three cases with literature review.[J].Diagnostic cytopathology,2022,50(12):E361-E366.

[12] Subhra D ,U A M ,Jaya J S , et al.Lynch syndrome: An unusal case of familial cancer unearthed.[J].Indian journal of pathology & microbiology,2022,65(2):465-467.

[13] Oscar T ,Carlos J C ,Pedro J R , et al.Benign follicular tumors.[J].Anais brasileiros de dermatologia,2015,90(6):780-96; quiz 797-8.

[14] Hee Young Na,Ji-Young Choe,Seon Ah Shin, et al. Proposal of a Provisional Classification of Sebaceous Carcinoma Based on Hormone [J]. Am J Surg Pathol 2016;40:1622–1630.

[15] Maelle S,Muhammad S,Rana El H, et al.PD-L1 expression in sebaceous carcinomas.[J]Cancer Immunology, Immunotherapy .https://doi.org/10.1007/s00262-020-02821-3

[16] Rachel L,Kimberly L,Eva A.Sebaceous Carcinoma: Review of the Literature.[J]Dermatol Surg 2015;41:1–15,DOI: 10.1097/DSS.0000000000000152.

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