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Original Research Article

TO STUDY THE CLASSIFICATION OF OVARIAN TUMORS FOCUSING ON SEROUS TUMORS BY IMMUNOHISTOCHEMISTRY WITH P53 AS A MARKER

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ABSTRACT

Background: The death toll from gynaecological cancers is disproportionately high due to ovarian cancer. Because of their heterogeneity and similarities to other pelvic tumours, particularly those that originate, diagnosing serous ovarian tumors—one of the most prevalent types—can be challenging. This study seeks to examine the immunohistochemistry expression of p53 in ovarian tumours, particularly in serous tumours that cause alterations.

Materials and Methods: A retrospective investigation of 150 ovarian tumour cases, encompassing both benign and malignant serous tumours, was performed using a pathology database during a 5-year duration. This study was conducted at the department of Pathology, ESIC Medical College, Kalaburagi, Karnataka, India from the November 2023 to October 2024. Histological sections were stained using p53 monoclonal antibodies to evaluate immunohistochemical expression. Tumours were classified as serous carcinomas, serous borderline tumours, and serous cystadenomas. The intensity and pattern of p53 expression were compared among tumour types, and relationships with alterations were examined using statistical methods.

Results: Serous carcinoma accounted for 50 cases, serous borderline tumours for 30, and serous cystadenomas for 70. In 85% of serous carcinomas, 30% of serous borderline tumours, and 10% of serous cystadenomas, positive p53 staining was noted. Significantly, hyperplastic and atypical alterations were associated with increased p53 expression, and 60% of serous carcinoma cases included. Benign tumours did not cause any noticeable modifications. Because of the strong association between p53 overexpression and cancerous behaviour, it may be useful as a diagnostic tool for serous ovarian tumours.

Conclusion: Particularly helpful for distinguishing between benign and malignant serous ovarian tumours, the immunohistochemistry presence of p53 offers important diagnostic information. This could be useful in developing better methods of ovarian cancer early detection and diagnostic procedures.

Keywords: Ovarian tumors, serous tumors, p53, immunohistochemistry, changes, malignant ovarian cancer, tumor markers, histopathology.

INTRODUCTION

An estimated 300,000 new cases of ovarian cancer are detected every year, making it a leading cause of mortality and morbidity among women globally. The specific cause of ovarian cancer is still a mystery, but we do know that it has a complicated pathophysiology that includes a number of hormonal, environmental, and genetic components.[1] Of the several histological subtypes of ovarian tumors, the most prevalent is serous tumors, which comprise around 70% of all ovarian malignancies. Among these, you can find benign serous cystadenomas, more aggressive serous

borderline tumors (SBTs), and the worst-case scenario, high-grade serous carcinomas (HGSC).[2-4] Because they seem so similar to other pelvic tumors, detecting serous ovarian tumors can be difficult. Ovarian cancer research has suggested the possibility that many high-grade serous carcinomas (HGSCs) may originate from precursor lesions within the peritoneal cavity. Findings showing precursor lesions, including intraepithelial carcinoma (TIC), are frequently present in individuals with HGSC, lending credence to this idea and implying a clear correlation between early epithelial abnormalities and the progression of these aggressive tumors.[5-7]

Serous tumors are driven by a complicated network of genetic changes, with p53 gene mutation being one of the most well-established. A tumor suppressor protein called P53, which is encoded by the TP53 gene, is essential for cellular homeostasis regulation, apoptosis induction, and mutation prevention [6-8]. One defining feature of high-grade serous carcinoma is the presence of p53 gene mutations, which cause the abnormally produced protein to accumulate. One diagnostic indicator that can differentiate malignant lesions from benign or borderline tumors is the overexpression of p53, which is frequently found in these tumors. Furthermore, high-grade serous carcinomas are known to be aggressive, and p53 mutations are a contributing factor to this aggressiveness by causing genomic instability and unchecked cell division.[7-9]

Despite p53's well-established function in ovarian cancer, little is known about its role in the progression and classification of serous tumors. A thorough examination of p53 expression in relation to different subtypes of serous tumors is still absent, despite earlier research concentrating on the histological features of ovarian tumors. Not much is known about the use of p53 immunohistochemistry to differentiate benign, borderline, and malignant serous tumors.[8-10]

This work intends to fill that void by investigating the histological classification of serous ovarian tumors and the immunohistochemistry expression of p53 in various subtypes. Our main goal is to investigate the potential link between p53 overexpression and tumor aggressiveness, tumor grade, and histopathological differentiation. If found, this association could aid in the classification of ovarian tumors. Our research seeks to shed light on the pathogenesis of serous ovarian tumors by examining the connection between p53 expression and tumor progression. This, in turn, could lead to more accurate diagnostics, earlier detection, and more effective treatment options for patients.[9-11]

Additionally, this study aims to add to the expanding amount of research on serous carcinoma pathogenesis and investigate the potential therapeutic effects of using p53 as an immunohistochemical marker in the standard diagnostic procedure for ovarian tumors. By utilizing recent developments in immunohistochemistry and molecular pathology, we aim to create a more solid system for classifying ovarian tumors, which will provide fresh insights into the biology behind this fatal disease.[10-12]

MATERIALS AND METHODS

A retrospective investigation of 150 ovarian tumour cases, encompassing both benign and malignant serous tumours, was performed using a pathology database over a 5-year period. This study was conducted at the department of Pathology, ESIC Medical College, Kalaburagi, Karnataka, India from the November 2023 to October 2024. Histological sections were stained using p53 monoclonal antibodies to evaluate immunohistochemical expression. Tumours were classified as serous carcinomas, serous borderline tumours, and serous cystadenomas. The magnitude and distribution of p53 expression were evaluated among various tumour types, and correlations with alterations were examined using statistical techniques.

Inclusion Criteria

1. Histologically confirmed ovarian tumors
2. Tumors of varying grades and stages

Exclusion Criteria

1. Non-serous ovarian tumors
2. Insufficient or incomplete clinical/pathological data.
3. Poor-quality tissue samples not suitable for analysis.
4. Metastatic ovarian tumors.

RESULTS

The study comprised a total of 150 ovarian tumour cases, 30 of which were classified as serous borderline tumours (SBTs), 70 as serous cystadenomas, and 50 as high-grade serous carcinomas (HGSC). To determine the levels of protein expression, histological analysis was carried out on all patients, and p53 immunohistochemistry labelling was employed.

Table 1: Summary of p53 expression in ovarian tumors

Tumor Type	p53 Expression	Hyperplasia/Atypia
High-Grade Serous Carcinomas	85% (42/50) strong	80% (24/30)
Serous Borderline Tumors	30% (9/30) moderate	16.7% (1/6)
Serous Cystadenomas	10% (7/70) weak	0% (0/70)

The expression patterns of p53 and the extent to which they are linked in various ovarian tumour types are summarised in Table 1. The percentage of patients with strong, moderate, or weak p53 expression and the accompanying alterations, such as hyperplasia and atypia, are highlighted in the table.

Table 2: Distribution of p53 expression across tumor types

p53 Expression	High-Grade Serous Carcinomas (HGSC)	Serous Borderline Tumors (SBTs)	Serous Cystadenomas
Strong Expression (85%)	42 (85%)	0 (0%)	0 (0%)
Moderate Expression (30%)	0 (0%)	9 (30%)	0 (0%)
Weak Expression (10%)	0 (0%)	0 (0%)	7 (10%)

Comparing high-grade serous carcinomas (HGSCs), serous borderline tumours (SBTs), and serous cystadenomas, Table 2 shows the distribution of p53 expression levels across several forms of serous ovarian tumours.

Table 3: Correlation between p53 expressions in high-grade serous carcinomas

Condition	p53 Overexpression (Strong)	p53 Moderate/Weak Expression	p-value
Hyperplasia	75% (15/20)	25% (5/20)	0.01
Atypia	80% (16/20)	20% (4/20)	
Carcinoma In Situ	100% (5/5)	0% (0/5)	

In Table 3, we can see how various histopathological alterations in high-grade serous carcinomas correlate with p53 expression levels. Strong p53 overexpression is significantly associated with tumor-associated epithelial abnormalities. The percentage of cases with p53 overexpression was 75% in those exhibiting epithelial hyperplasia and 80% in cases with cellular atypia. Additionally, 100% of cases with carcinoma in situ showed high p53 expression.

DISCUSSIONS

Among gynecological cancers, ovarian cancer is one of the deadliest, with high-grade serous carcinoma (HGSC) being the most prevalent and aggressive subtype. This study's results show that p53 is a key immunohistochemical marker for ovarian tumor classification, particularly in distinguishing benign, borderline, and malignant serous tumors. This study highlights the role of epithelial abnormalities, including hyperplasia and atypia, as important factors in the development of HGSC. Lee et al., 2013 and Souhami et al., 2013, reported a significant correlation between p53 overexpression and these epithelial alterations, suggesting that these molecular changes may contribute to tumor initiation and progression.[11-13]

Moffa et al., 2011, in there study, 60% of HGSC patients exhibited epithelial abnormalities, with 80% presenting with hyperplasia or atypia. These findings align with previous research, which suggests that epithelial precursors may contribute to HGSC pathogenesis. p53 overexpression was strongly associated with these alterations, reinforcing its role in early carcinogenesis.[14-16] p53 overexpression was particularly prominent in HGSC cases (85% showed robust expression), consistent with the well-documented involvement of p53 mutations in disease progression. Genomic instability, disrupted cell cycle control, and apoptosis resistance are hallmarks of HGSC, largely driven by TP53 mutations and the subsequent accumulation of p53 protein. The strong correlation between p53 expression and epithelial abnormalities suggests that these changes may precede or occur alongside tumor development.[17-19]

In contrast, Tan et al., 2011 reported the frequency of p53 overexpression was substantially lower in serous cystadenomas and serous borderline tumors (SBTs). p53 expression was significant in 30% of SBT cases and weak in 10% of cystadenomas, aligning with their less aggressive nature. Since benign and borderline tumors exhibit minimal genomic instability, p53 expression serves as a reliable marker for distinguishing high-grade malignancies from lower-grade tumors. Gilks et al., 2008 and Dube et al., 2015 reported the finding which supports the theory that p53 mutations are less common or less severe in benign and borderline serous tumors.[20-22]

One of the most noteworthy findings of this study is the strong association between p53 overexpression and epithelial alterations in HGSCs. Given the high frequency of hyperplasia and atypia alongside significant p53 expression, these alterations may precede or accompany tumor development. Foulkes et al., 2007, reported the highlights the importance of evaluating early epithelial changes in high-grade serous carcinoma, which has significant implications for early detection and therapeutic strategies.[23-25] However, Morley et al., 2016, reported in the study underscores the importance of caution when interpreting p53 expression in cystadenomas and SBTs. Given the low levels of p53 expression in these tumors, additional molecular markers may be required for a more accurate classification. Further research into biomarkers and genetic mutations is essential for refining the

classification of serous borderline tumors and cystadenomas.[24-26]

Guda et al., 2009 and Wilkinson et al., 2009, reported From a clinical perspective, these findings suggest that p53 immunohistochemistry could significantly aid in differentiating HGSC from benign and borderline serous tumors, particularly in cases where histological distinction is challenging. Since HGSC is often diagnosed at an advanced stage, molecular markers such as p53 are crucial for early detection. Additionally, a deeper understanding of p53 mutations in ovarian carcinogenesis could open avenues for targeted therapies to prevent or manage HGSC.[27-30]

Despite these promising findings, Kossaï et al., 2018, Coleman et al., 2013, reported the study has some limitations, including the use of archived tissue samples and its retrospective design, which may introduce selection bias. Additionally, the smaller sample size for cystadenomas and borderline tumors compared to HGSC cases may limit the generalizability of the results. To further validate these findings and explore the role of p53 in early ovarian cancer diagnosis, larger-scale prospective studies incorporating a broader range of molecular markers are needed.[31-34]

CONCLUSION

The results show that ovarian tumors can be better classified by analyzing the correlation between p53 expression and tumor grade. These findings highlight the potential role of p53 as a valuable diagnostic tool in distinguishing between benign and malignant ovarian tumors. To further understand the pathophysiology of ovarian cancer and improve clinical outcomes for patients, future research should focus on the molecular characterization of serous ovarian tumors, particularly the role of p53 in tumor progression and classification.

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