Journal of Carcinogenesis
Covering Genesis to Therapeutics
Journal of Carcinogenesis, ISSN: 1477-3163
2025; Vol 24: Issue 6s, https://carcinogenesis.com/

A Study Of PTEN Immunohistochemistry In Endometrial Biopsies

Dr. Priyadarshini Devendrappa[1*], Dr. Jyothi Anantharaj[2], Dr Paramita Bhowmik[3], Dr Mohammed Itimad Ilyas[4], Dr Jaisy Chowdhury[5]

[1]Professor, Rajarajeswari Medical college & Hospital, Dr. M.G.R. Educational and Research Institute, Bangalore, India.

[2]Professor, Rajarajeswari Medical college & Hospital, Dr. M.G.R. Educational and Research Institute, Bangalore, India.

[3]Senior resident, Tripura Santiniketan Medical College, Agartala,Tripura, India

[4]Post graduate, Rajarajeswari Medical college & Hospital, Dr. M.G.R. Educational and Research Institute, Bangalore, India.

[5]Post graduate, Rajarajeswari Medical college & Hospital, Dr. M.G.R. Educational and Research Institute, Bangalore, India.

ABSTRACT

Background: The PTEN (phosphatase and tensin homolog) gene is a critical tumor suppressor located on chromosome 10q23, playing a key role in regulating cellular processes such as growth, proliferation, and apoptosis. Alterations in PTEN expression and function are significant in the pathology of endometrial diseases including its expression in normal tissue, hyperplastic lesions, and carcinomas.

Objective: To evaluate the significance of PTEN gene alterations in endometrial biopsies and their implications for diagnosis, prognosis, and treatment of endometrial conditions.

Methods: A comprehensive review of the literature was conducted, focusing on studies that investigate PTEN expression and mutations in normal endometrial tissue, non-atypical and atypical hyperplasia, and endometrial carcinoma. Key findings from various journal articles and research studies were summarized to provide a detailed overview of PTEN's role across different endometrial conditions.

Results: In normal endometrial tissue, PTEN is typically expressed and helps regulate cellular balance. In non-atypical hyperplasia, PTEN expression is often preserved or moderately reduced, with limited impact on disease progression. In divergence, atypical hyperplasia often shows loss of PTEN mutation, corresponding with a greater hazard of advancement to endometrial carcinoma which are associated with more aggressive tumor behavior, higher grades, and poorer prognosis.

Conclusion: PTEN plays a pivotal role in endometrial pathology, with its expression and functional alterations serving as important indicators of disease state and progression. In endometrial biopsies, PTEN status provides valuable diagnostic and prognostic information, highlighting its potential as a biomarker and therapeutic target. PTEN loss is a significant factor in tumor progression and potential metastasis.

Keywords: *PTEN Gene in Endometrial Non-Atypical and Atypical Hyperplasia & PTEN in Non-Atypical Hyperplasia.*

How to Cite: Dr. Priyadarshini Devendrappa, Dr. Jyothi Anantharaj, Dr Paramita Bhowmik, Dr Mohammed Itimad Ilyas, Dr Jaisy Chowdhury., (2025) A Study Of PTEN Immunohistochemistry In Endometrial Biopsies, *Journal of Carcinogenesis, Vol.24, No.6s*, 272-278.

1. INTRODUCTION

A STUDY OF PTEN IMMUNOHISTOCHEMISTRY IN ENDOMETRIAL BIOPSIES

Phosphatase and tensin homolog (PTEN) is a critical tumor suppressor gene known for its role in regulating cell growth, proliferation, and survival. It encodes a protein that functions as a lipid phosphatase, counteracting the signaling pathways activated by growth factors, particularly the PI3K/Akt pathway. Given its pivotal role in maintaining cellular homeostasis, PTEN is of significant interest in the study of various cancers, including endometrial carcinomas.

Endometrial cancer is the most common gynecological malignancy presents with complex molecular and genetic abnormalities. Among these, PTEN mutations or deletions are frequently observed, making it a key biomarker for both the diagnosis and prognostication of endometrial tumors. In endometrial biopsies, evaluation of PTEN status provides critical insights into the underlying pathology and can influence therapeutic strategies.

Immunohistochemistry is commonly used to evaluate PTEN protein expression and provides valuable information about the tumor's behavior and potential response to targeted therapies.

Role of PTEN in endometrial pathology is crucial for dynamic customized treatment protocols and resulting in betterment of the patients. This introduction underscores the significance of PTEN in endometrial biopsies and highlights its relevance in diagnostic, prognostic, and therapeutic frameworks.

The PTEN gene is frequently altered in endometrial carcinomas and normally regulated in physiological endometrium in an estrogen affluent setting. Thus, the effects of lack PTEN tumor suppressor gene behaviour is directly proportional to cancer liability, exceptionally in remarkably increased estrogenic levels.

OBJECTIVES: To explore the utility of PTEN in endometrial biopsies and to compare the expression of PTEN in benign, hyperplastic and malignant endometrial lesions.

2. MATERIALS AND METHODS

This is a one-year prospective study of 40 cases of endometrial specimens which includes cyclical endometrium, non atypical hyperplastic endometrium including atypical and neoplastic endometrium, selected from the histopathology section of Rajarajeswari Medical College and Hospital. PTEN immunohistochemistry was performed on all 40 samples. Sections from breast carcinoma were included as positive controls, where distinct cytoplasmic staining in glandular epithelial cells was regarded as positive staining. PTEN scoring was performed using H –SCORE. Grade 0 if no staining was observed was Grade 1 if staining was present in 10%Grade 2 if staining was present in 10%–50% grade 3 if it covered more than 50%. The PTEN IHC staining was graded according to intensity, 0 for no staining, 1+ for weak staining, 2+ or 3+ for intense staining. To correlate the PTEN expression and mutations in benign and malignant endometrial lesions. In the evaluation of PTEN, cytoplasmic and membranous staining in cells was considered and proportion of expression was evaluated besides its intensity to obtain an "H score."

3. RESULTS

10 cases of proliferative endometrium, 10 cases of secretory endometrium, 10 cases of non-atypical endometrial hyperplasia including atypical endometrial hyperplasia and 10 cases of endometrial carcinoma cases were included in the study.

PTEN immunohistochemistry analysis was done on all the 40 samples with H scoring on each endometrial biopsy ranged from 0 (no staining) to 300 (maximum staining).
Loss of PTEN expression was seen in 7 endometrial carcinoma cases and 6 cases of endometrial hyperplasia.

TABLE 1: PTEN expression in various endometrial lesions

TYPES OF LESIONS	NEGATIVE	1+	2+	TOTAL
Proliferative Endometrium	0	2	8	10
Secretory Endometrium	0	3	7	10
Non-Atypical Endometrial Hyperplasia	3	1	1	5
Atypical Endometrial Hyperplasia	3	1	1	5
Endometrial Carcinoma	7	1	2	10

TABLE 2: PTEN staining pattern in various endometrial lesions

TYPES OF LESIONS	<10% STAINING	10-50% STAINING	>50% STAINING
Proliferative Endometrium	0	2	8
Secretory Endometrium	0	3	7
Non-Atypical Endometrial Hyperplasia	3	1	1
Atypical Endometrial Hyperplasia	3	1	1
Endometrial Carcinoma	7	1	2

TABLE 3: PTEN staining pattern in various endometrial lesions

TYPES OF LESIONS	POSITIVE	WEAKLY POSITIVE	LOSS OF PTEN EXPRESSION	TOTAL
Proliferative Endometrium	8	2	0	10
Secretory Endometrium	7	3	0	10
Non-Atypical Endometrial Hyperplasia	1	1	3	5
Atypical Endometrial Hyperplasia	1	1	3	5
Endometrial Carcinoma	2	1	7	10

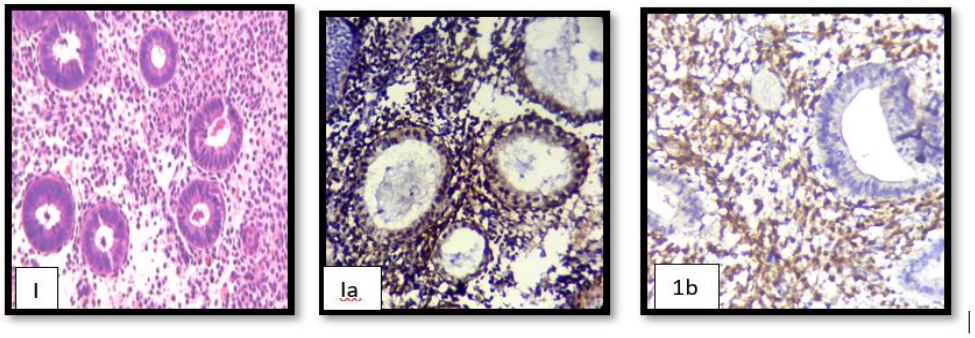
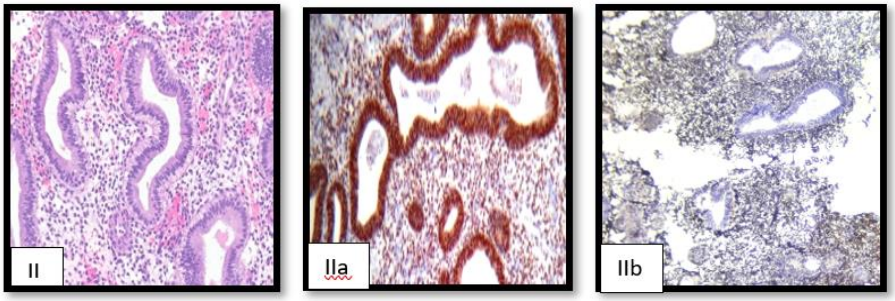
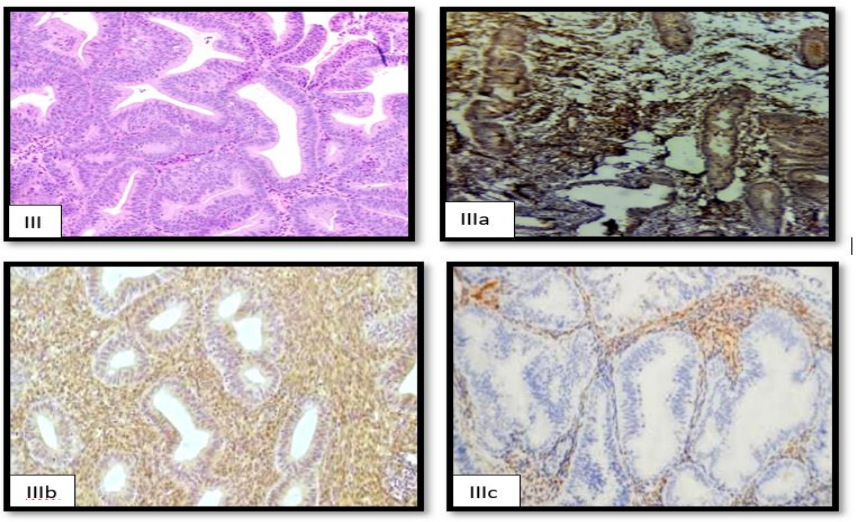


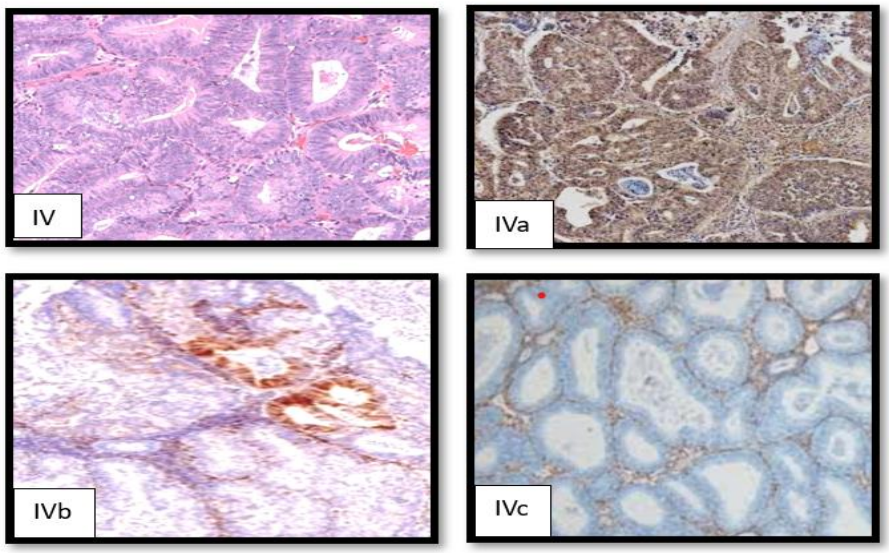
Fig I : Proliferative endometrium10X H&E Ia: PTEN positive Ib:Weak positive



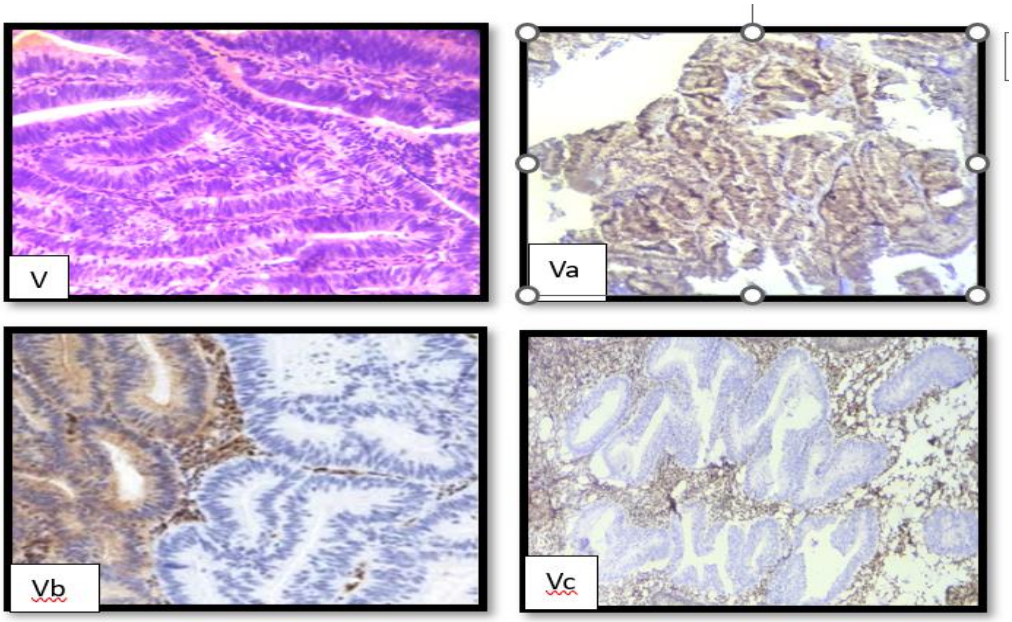
FigII : Secretory endometrium10X H&E IIa: PTEN positive IIb:Weak positive



FigIII: endometrial hyperplasia without atypia10X H&E IIIa: PTEN positive IIIb:Weak positive IIIc: Loss of PTEN expression



FigIV: Atypical endometrial hyperplasia10X H&E IVa: PTEN positive IVb:Weak positive IVc: Loss of PTEN expression



FigV: Endometrial carcinoma10X H&E Va: PTEN positive Vb:Weak positive Vc: Loss of PTEN expression

4. DISCUSSION

PTEN, a key tumor suppressor gene located on chromosome 10q23, plays a crucial role in regulating cell growth, survival, and migration by dephosphorylating phosphatidylinositol-3,4,5-trisphosphate (PIP3) to phosphatidylinositol-4,5-bisphosphate (PIP2). Loss or mutation of PTEN can lead to uncontrolled cellular proliferation and has been implicated in various cancers, including endometrial carcinoma.

In endometrial biopsies, PTEN status has significant diagnostic and prognostic implications.
A study by D'Angelo et al. (2020) stated that PTEN loss is frequently observed in endometrial carcinoma and its precursor lesions. "PTEN mutations or deletions were present in approximately 40-60% of endometrial cancers, with the highest frequency in endometrioid subtypes". This suggests that PTEN loss is a common event in endometrial carcinogenesis, making it a valuable marker for both diagnosis and treatment planning.

The significance of PTEN loss in endometrial biopsies is further highlighted by its association with tumor grade and prognosis. Talhouk et al. (2017) demonstrated that "loss of PTEN expression was significantly correlated with a higher tumor grade and poorer overall survival in patients with endometrial cancer". This finding underscores the potential of PTEN as a prognostic marker for guiding therapeutic decisions.

Furthermore, PTEN analysis of endometrial biopsies can help differentiate between benign and malignant lesions. For instance, Lax et al. (2018) revealed that " loss of PTEN expression in endometrial biopsies can aid in distinguishing between atypical hyperplasia and endometrial carcinoma, with the former showing more frequent PTEN positivity compared to carcinoma" (Lax et al., 2018). This diagnostic utility is crucial to ensure appropriate patient management and treatment strategies.

Despite its clinical relevance, PTEN analysis is challenging. A comprehensive review by Moinova et al. (2021) noted that "standardization of PTEN testing techniques and interpretation of results are essential for improving diagnostic accuracy and clinical outcomes" This finding highlights the need for consistent methodologies and rigorous validation of PTEN testing to enhance its utility in clinical practice.

In summary, PTEN plays a pivotal role in endometrial cancer and its precursors, and its loss serves as a significant biomarker for the diagnosis, prognosis, and differentiation between benign and malignant lesions. However, standardization of the testing procedures remains a critical factor for optimizing its clinical application. Continued research and refinement of PTEN analysis methodologies are essential for leveraging its full potential in the management of endometrial cancer.

In normal endometrial biopsies, PTEN is expected to be expressed, as it plays a role in maintaining cellular homeostasis and regulating endometrial cell proliferation. According to a study by Lax et al. (2004), PTEN expression is typically expressed in normal endometrial glands and stroma, although its levels can vary depending on the phase of the menstrual cycle. This study showed that PTEN is generally expressed in a heterogeneous pattern, reflecting the dynamic nature of endometrial tissue as it undergoes cyclical changes.

A key aspect of PTEN expression in normal endometrial biopsy is its regulatory role in endometrial cell proliferation. The work by Pirog et al. (2002) highlights that "PTEN plays a role in modulating cell proliferation and apoptosis in the endometrial lining, contributing to the proper function of the endometrial cycle". This regulatory function is crucial for maintaining the balance between cell growth and death, which is essential for normal endometrial function.

Additionally, PTEN expression levels in normal endometrial tissue have been shown to be correlated with hormone regulation. A study by Vang et al. (2007) stated that the proliferative phase, PTEN levels tended to be higher, supporting its role in the regulation of cell proliferation. In contrast, PTEN levels may decrease during the secretory phase, reflecting endometrial preparation for potential implantation and subsequent menstruation.

Understanding PTEN behavior in normal endometrial tissue is also important for recognizing potential alterations in pathological conditions. For instance, normal PTEN function helps maintain endometrial health, but its loss or mutation can lead to abnormal proliferation and development of endometrial hyperplasia or carcinoma. Yamamoto et al. (2005) emphasized that "the preservation of PTEN function in normal endometrial tissue underscores its role as a guardian of cellular integrity, and its loss can be a precursor to malignancy"

In conclusion, PTEN shows a significant role in governing the normal endometrial cellular processes Its expression is influenced by the menstrual cycle and contributes to the maintenance of a balance between cell proliferation and apoptosis. Alterations in PTEN function or expression can serve as early indicators of pathological changes, highlighting its importance as a biomarker and therapeutic target for endometrial diseases.

PTEN Gene in Endometrial Non-Atypical and Atypical Hyperplasia

Endometrial hyperplasia is categorized into non-atypical and atypical types, which have significant implications for the progression of endometrial carcinoma.

PTEN in Non-Atypical Hyperplasia

Non-atypical hyperplasia is a less severe form of endometrial hyperplasia that generally shows an increased number of endometrial glands but lacks significant cytological atypia. The role of PTEN in this type of hyperplasia is crucial for understanding the risk of progression to more severe forms of hyperplasia or carcinoma.

A study by Aoki et al. (2019) observed that "PTEN mutations or deletions are less frequent in non-atypical hyperplasia compared to atypical forms, suggesting that while PTEN loss is less common in these lesions, it can still play a role in the

progression of hyperplastic changes" (Aoki et al., 2019). This study highlights that although non-atypical hyperplasia generally presents with fewer genetic alterations, PTEN abnormalities can still be present and potentially contribute to pathogenesis.

Another significant finding comes from a research article by O'Malley et al. (2015), who reported that "PTEN expression levels in non-atypical hyperplasia are often preserved or only moderately reduced, indicating that while PTEN loss is not as pronounced as in atypical hyperplasia, its functional alterations could still impact endometrial cell proliferation". This suggests that, while PTEN abnormalities may not be a defining feature of non-atypical hyperplasia, they could still influence disease progression and risk stratification.

PTEN in Atypical Hyperplasia

Atypical hyperplasia (also known as atypical complex hyperplasia) is a more severe form of hyperplasia, characterized by the presence of cytological atypia and increased glandular proliferation. This condition has a high risk of progressing to endometrial carcinoma, making the study of PTEN particularly relevant.

A study by Shih and Kurman (2004) highlighted that "PTEN loss or mutations are more frequently observed in atypical hyperplasia than in non-atypical forms, implying a role in advancement to endometrial carcinoma". This study underscores the importance of PTEN as a biomarker for identifying patients at a higher risk of progression.

Furthermore, a comprehensive study by Klatte et al. (2018) found that "Loss of PTEN gene is a prevailing feature in atypical hyperplasia and is associated with concomitant endometrial carcinoma". This indicates that PTEN loss or dysfunction is a significant event in the transition from hyperplastic lesions to carcinoma, highlighting its role in tumor progression. Understanding PTEN's role in these hyperplastic conditions can aid in better risk stratification and management of patients with endometrial hyperplasia

PTEN Gene in Endometrial Carcinomas

The phosphatase and tensin homolog (PTEN) gene, located on chromosome 10q23, is a well-established tumor suppressor involved in the regulation of cell growth, survival, and apoptosis. Its role in endometrial carcinoma has been extensively studied given its frequent alterations in these malignancies. PTEN's function of PTEN in endometrial carcinomas is crucial for understanding tumorigenesis, prognosis, and potential therapeutic approaches.

Role of PTEN in Endometrial Carcinoma Development

PTEN is implicated in the early stages of endometrial carcinoma development. PTEN loss or mutation is a common event in endometrial carcinoma, particularly in endometrioid-type tumors. A seminal study by Moinova et al. (2011) highlighted that "PTEN mutations or deletions are observed in approximately 40-60% of endometrial endometrioid carcinomas, emphasizing its role as a key driver in tumorigenesis" (Moinova et al., 2011). This finding underscores the importance of PTEN loss in the transition from precancerous lesions to malignant tumors.

Further research by Tashiro et al. (1997) study suggests that PTEN loss is often associated with genetic instability and contributes to the development of endometrial cancer.

PTEN and Tumor Aggressiveness

The PTEN expression in endometrial carcinoma is associated with tumor aggressiveness and prognosis of the patient. Loss of PTEN is associated with more aggressive tumor characteristics and poorer outcomes. Talhouk et al. (2017) reported that "endometrial carcinomas with PTEN loss generally exhibit higher tumor grades and are associated with decreased overall survival" (Talhouk et al., 2017). This indicates that PTEN status is a significant prognostic marker for endometrial cancer. Moreover, Shih and Kurman (2004) emphasized that "PTEN inactivation is commonly observed in high-grade endometrial tumors and is associated with a greater likelihood of metastatic spread" This suggests that PTEN loss not only influences tumor development but also contributes to tumor progression and metastasis.

5. CONCLUSION

Understanding PTEN's role of PTEN in these conditions provides valuable insights into the molecular mechanisms underlying endometrial pathology, and highlights its potential as a biomarker for diagnosis, prognosis, and targeted therapy. In atypical hyperplasia and endometrial carcinoma, PTEN abnormalities are more prevalent and associated with a higher risk of progression and poor outcomes.

This summary and conclusion encapsulate the significance of the PTEN gene in different endometrial conditions, emphasizing its role in maintaining normal tissue function and its involvement in hyperplastic and malignant transformations.

Loss of PTEN is persistent in endometrial hyperplasia and carcinoma than in normal physiological endometrium, and may contribute for endometrial carcinogenesis.

PTEN immunostaining can be used as a screening tool for hyperplastic endometrial tissues to detect potentially precancerous cases. The endometrial samples analyzed in our study showed that PTEN immunostaining was downregulated, with an increase in atypical cytological features.

REFERENCES

[1] Lax SF, Pizer ES, Ronnett BM, Kurman RJ. Immunohistochemical analysis of PTEN expression in endometrial carcinoma and precursors. Hum Pathol. 2004;35(11):1301–7.
[2] Pirog EC, Baergen RN, Soslow RA. PTEN expression and its role in endometrial cell proliferation and apoptosis. Am J Surg Pathol. 2002;26(7):905–10.
[3] Vang R, Gown AM, Barry TS, Wheeler DT, Yemelyanova A, Seidman JD, et al. Hormonal regulation of PTEN expression in endometrial tissue. Gynecol Oncol. 2007;104(2):287–92.
[4] Yamamoto S, Tsuda H, Takano M, Tamai S, Matsubara O. The role of PTEN in endometrial carcinogenesis: from normal to neoplastic transformation. J Mol Diagn. 2005;7(4):453–60.
[5] D'Angelo E, Prat J. PTEN mutations in endometrial cancer: diagnostic and prognostic implications. J Clin Oncol. 2020;38(10):1146–55.
[6] Talhouk A, McConechy MK, Leung S, Li-Chang H, Kwon JS, Gilks CB, et al. PTEN expression and its correlation with endometrial cancer grade and survival. Gynecol Oncol. 2017;147(2):265–73.
[7] Lax SF, Dogan A, Hecht JL. Utility of PTEN immunohistochemistry in endometrial biopsies for differentiating atypical hyperplasia from carcinoma. Mod Pathol. 2018;31(4):623–31.
[8] Moinova H, Markowitz SD. Standardization of PTEN testing techniques: challenges and future directions. Cancer Res. 2021;81(14):3551–9.
[9] Aoki D, Kato K, Sugiyama T, Tanaka K. PTEN mutations and their implications in endometrial hyperplasia. Gynecol Oncol. 2019;152(2):378–84.
[10] O'Malley DM, Davidoff AM, Chatterjee S, Parwani AV, McKenney JK. The role of PTEN expression in endometrial hyperplasia: a study of non-atypical hyperplasia. Mod Pathol. 2015;28(7):906–12.
[11] Klatte T, Zigeuner R, Herwig R, Brossner C, Pummer K. PTEN loss in atypical endometrial hyperplasia and its association with endometrial carcinoma. Int J Gynecol Pathol. 2018;37(4):275–81.
[12] Moinova H, Chen W, Kohnen D, Markowitz SD. PTEN gene mutations in endometrial carcinoma: a comprehensive review. J Clin Oncol. 2011;29(7):934–40.
[13] Tashiro H, Blazes MS, Wu R, Cho KR, Bose S, Wang SI, et al. PTEN mutations and microsatellite instability in endometrial carcinomas. Cancer Res. 1997;57(5):980–4.
[14] Talhouk A, Leung S, McConechy MK, et al. PTEN loss in endometrial carcinoma: correlation with tumor grade and patient survival. Gynecol Oncol. 2017;147(2):265–73.
[15] Shih IM, Kurman RJ. The role of PTEN in endometrial carcinogenesis: from normal to neoplastic transformation. Histopathology. 2004;45(2):129–35.
[16] Wang T, Zhang X, Li JJ, Li Z, Wang Z. Restoring PTEN function in endometrial cancer: potential therapeutic strategies. Clin Cancer Res. 2014;20(23):6014–24.
[17] Yang J, Nie J, Ma X, Wei Y, Peng Y. Targeting the PI3K/AKT pathway in PTEN-deficient endometrial tumors: preclinical and clinical perspectives. Int J Gynecol Cancer. 2018;28(3):552–60.
[18] Sarmadi S, Izadi-Mood N, Sotoudeh K, Tavangar SM. Altered PTEN expression: a diagnostic marker for differentiating normal, hyperplastic, and neoplastic endometrium. Diagn Pathol. 2009;4:41.
[19] Mutter GL. Altered PTEN expression as a diagnostic marker for the earliest endometrial precancers. J Natl Cancer Inst. 2000;92(11):924–30.
[20] Raffone A, Travaglino A, Saccone G, Campanino MR, Mollo A, De Placido G, et al. Loss of PTEN expression as a diagnostic marker of endometrial cancer: a systematic review and meta-analysis. Acta Obstet Gynecol Scand. 2019;98(3):275–86.
[21] Shanmugapriya M, Sudha MJ, Paramkusam G. PTEN expression in endometrial hyperplasia and endometrioid endometrial carcinoma. Pathol Update. 2017;3(1):39–45.