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Coexistence of Chronic Endometritis in Adenomyosis: A Histopathological Study

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KEYWORDS

Adenomyosis, Chronic Endometritis, CD138, Immunohistochemistry

ABSTRACT:

Background: Adenomyosis with chronic endometritis are common yet underdiagnosed gynecological conditions with overlapping clinical features and their potential coexistence and pathophysiological relationship remain inadequately explored.

Objective: To determine the prevalence of chronic endometritis among patients with adenomyosis and to examine its underlying etiology and histopathological characteristics.

Methods: This retrospective study was conducted in the Department of Pathology at Sri Ramachandra Institute of Higher Education and Research over a six-year period, from January 2018 to April 2024.

Results: Of the 52 cases of chronic endometritis identified using CD138 immunostaining, 12 cases (23.1%) showed coexisting adenomyosis. The mean age of affected patients was 47.75 years, with most cases occurring between 44 and 50 years. All patients presented with abnormal uterine bleeding and many had reported dysmenorrhea with pelvic pain. Histopathology showed proliferative endometrium with chronic inflammatory changes and plasma cell infiltration confirmed by immunohistochemistry CD138. Adenomyosis was identified by the presence of endometrial glands and stroma within the myometrium and coexisting leiomyomas were noted in some cases, indicating overlapping uterine pathology in this symptomatic patient group.

Conclusion: Chronic endometritis was identified in a significant proportion of adenomyosis cases, indicating a potential pathological association. Recognizing this coexistence may aid in better clinical management and understanding of disease mechanisms.

Introduction

Adenomyosis is a prevalent but often underrecognized benign gynecological condition, defined histologically by the presence of endometrial glands and stroma within the myometrium, typically surrounded by reactive smooth muscle hyperplasia.(1) It represents a form of benign invasion of the endometrial tissue into the myometrial wall and is considered a significant contributor to various gynecological symptoms, including dysmenorrhea, menorrhagia and chronic pelvic pain.(2) Despite its clinical relevance, adenomyosis remains poorly understood in terms of pathogenesis and is frequently underdiagnosed, particularly in premenopausal women.(3, 4)

Endometritis refers to inflammation of the endometrium, the inner lining of the uterus, and can be classified into acute and chronic forms. Acute endometritis, typically associated with postpartum or postabortion infections, presents with acute neutrophilic infiltrates and is usually of short duration.(5) In contrast, chronic endometritis is characterized by persistent inflammation, often lasting over 30 days and is defined histologically by the presence of plasma cells in the endometrial stroma,(6) along with lymphocytes and stromal changes.(7) Unlike acute endometritis, chronic endometritis is frequently

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asymptomatic but may manifest as abnormal uterine bleeding, dyspareunia, pelvic pain, or infertility. It has been increasingly implicated in reproductive disorders such as recurrent pregnancy loss and implantation failure in assisted reproductive technology.(8)

The coexistence of adenomyosis and chronic endometritis has not been extensively investigated, despite their overlapping clinical features and shared association with pelvic pain and abnormal uterine bleeding. Given that adenomyosis alters uterine architecture and local immune responses, it may predispose patients to chronic endometrial inflammation.(9, 10) Similarly, chronic endometritis may promote local immune dysregulation that could influence myometrial invasion by endometrial glands.(11) Understanding this potential interplay may offer new insights into the pathophysiology of both conditions and improve diagnostic accuracy and therapeutic strategies in women presenting with chronic pelvic complaints. Against this background, the objectives of the study were to determine the prevalence of chronic endometritis among patients with adenomyosis and to examine its underlying etiology and histopathological characteristics.

Methods

This retrospective study was conducted in the Department of Pathology at Sri Ramachandra Institute of Higher Education and Research over a six-year period, from January 2018 to April 2024. Ethical clearance for the study was obtained from the institutional ethics committee (Ref. CSP-MED/25/JUN/117/143 dated 16/7/2025), and patient anonymity was maintained throughout. As this was a retrospective analysis of archived histopathological data, individual informed consent was waived. All endometrial biopsy and hysterectomy specimens received during the study period were reviewed. The inclusion criteria comprised cases that were histologically confirmed as chronic endometritis through the identification of plasma cells in the endometrial stroma using immunohistochemical staining with the CD138 marker (Master Diagnostics). Only those cases in which the CD138 stain showed definitive positive nuclear membrane staining in plasma cells were included. Cases with equivocal staining, inadequate tissue sampling, or extensive tissue autolysis were excluded from the study.

Chronic endometritis was diagnosed based on both histological examination and immunohistochemistry. Hematoxylin and eosin (H&E)-stained sections were initially screened for stromal edema, spindled stromal cells and the presence of lymphoplasmacytic infiltrates. CD138 immunostaining was subsequently performed to confirm the presence of plasma cells. A minimum of one CD138-positive plasma cell per high-power field was considered diagnostic for chronic endometritis. Diagnosis of adenomyosis was made based on conventional histopathological criteria in hysterectomy specimens. Sections of the uterus were evaluated for the presence of endometrial glands and stroma located at least one low-power field (approximately 2.5 mm) beneath the endomyometrial junction within the myometrium. Associated findings such as leiomyoma, glandular crowding, and hemorrhage were also documented. All data were entered into Microsoft Excel and analyzed using descriptive statistical methods.

Results

The study included 52 confirmed cases of chronic endometritis identified using the CD138 immunohistochemical marker. Of these, 12 cases (23.1%) were found to be associated with adenomyosis. Among the 12 cases with coexisting adenomyosis and chronic endometritis, the mean age of the patients was 47.75 years. The most common age group affected was between 44 and 50 years, accounting for the majority of cases. The least affected age group was between 39 and 44 years.

Clinically, all 12 patients with adenomyosis and chronic endometritis presented with abnormal uterine bleeding. Other frequently reported symptoms included dysmenorrhea and pelvic pain, indicating the symptomatic burden in this patient subset.

Histopathological examination revealed a proliferative pattern of the endometrium with chronic inflammatory changes. The endometrial stroma showed increased plasma cell infiltrates, confirmed by positive CD138 staining. In the myometrial layer, features of adenomyosis were evident, characterized by the presence of endometrial glands and stroma within the myometrium. Additionally, leiomyoma was observed in some sections, indicating coexistent uterine pathology. These findings highlight the significant overlap between

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chronic endometritis and adenomyosis, both clinically and histologically.

Discussion

The present study identified a prevalence of 23.1% for chronic endometritis among patients diagnosed with adenomyosis over a six-year period at a tertiary care pathology department. These findings underscore a potentially underrecognized association between the two pathologies, both of which share overlapping clinical presentations such as abnormal uterine bleeding, dysmenorrhea and chronic pelvic pain. Importantly, this study adds to the growing body of literature suggesting that chronic endometrial inflammation may play a contributory role in the pathogenesis or exacerbation of adenomyosis.

Chronic endometritis is a persistent inflammatory condition of the endometrium, often resulting from low-grade microbial colonization without concurrent cervical or vaginal infection.(5, 12) It is histologically characterized by the presence of endometrial stromal plasma cells (ESPCs), which are best identified via CD138 immunostaining, along with other features such as stromal edema, polyps and asynchronous endometrial maturation.(7, 13, 14) Cytokine imbalances, including elevated interleukin-1β and tumor necrosis factor-α levels, have been reported in patients with chronic endometritis, leading to local inflammatory responses and increased estrogen biosynthesis in endometrial glands.(15) This local estrogen excess may be implicated in endometrial hyperactivity and may partially explain the presence of polyps and aberrant tissue remodeling frequently observed in these patients.(16)

The pathogenesis of adenomyosis involves the presence of endometrial glands and stroma within the myometrium, typically surrounded by reactive smooth muscle hyperplasia.(17) The most widely accepted theory attributes the development of adenomyosis to the invagination of the endometrial basalis layer into the underlying myometrium through the disrupted endometrial-myometrial interface, also referred to as the junctional zone.(18) This disruption may be spontaneous or associated with iatrogenic or mechanical trauma, such as childbirth, curettage, or uterine surgeries.(19)

Recent immunopathological studies have shown that immune cell populations, particularly B cells and plasma cells accumulate in endometrium in cases of adenomyosis and chronic endometritis.(20) These findings suggest a possible immunological overlap or continuum between chronic inflammation of the endometrium and the aberrant migration of endometrial tissue into the myometrium. Chronic inflammation at the endometrial-myometrial interface could thus facilitate or perpetuate the basal endometrium's invagination, thereby contributing to the development of adenomyosis.(21)

The present study found that all 12 patients with coexisting adenomyosis and chronic endometritis presented with abnormal uterine bleeding, while dysmenorrhea and pelvic pain were also commonly reported. These findings are consistent with earlier reports indicating that both conditions contribute independently and synergistically to menstrual irregularities and chronic pain syndromes in women.(22) Histopathologically, chronic endometritis in these cases demonstrated typical features, including increased stromal plasma cells, as confirmed by CD138 positivity, and proliferative endometrial patterns. The myometrial sections confirmed adenomyosis, with some also demonstrating coexisting leiomyoma, further complicating clinical symptomatology. Given the immunological and structural interplay observed in this study, it is plausible to postulate a pathophysiological link between chronic endometritis and adenomyosis. Chronic inflammation could alter the local immune environment, disrupt tissue barriers, and promote abnormal tissue remodeling—factors that may contribute to the presence of endometrial elements in the myometrium. However, due to the retrospective nature of this study and the limited sample size, causality cannot be inferred. Prospective studies with larger cohorts and molecular profiling are required to elucidate the mechanistic relationship between these two conditions.

Conclusion

This study demonstrated that chronic endometritis was present in 23.1% of histologically confirmed adenomyosis cases, suggesting a potential association between chronic endometrial inflammation and the development or progression of adenomyosis. The overlapping clinical presentations and histopathological features underscore the importance of routine evaluation for chronic endometritis in patients with adenomyosis. Early identification and targeted management of

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coexisting chronic endometritis may have implications for improving symptom control and reproductive outcomes in affected women. Further prospective studies are warranted to explore the underlying immunopathological mechanisms linking these two conditions.

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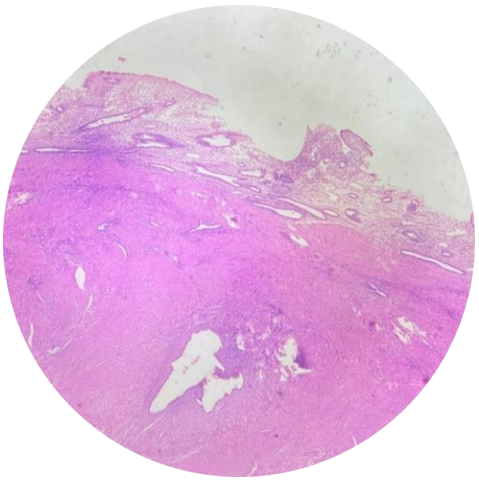
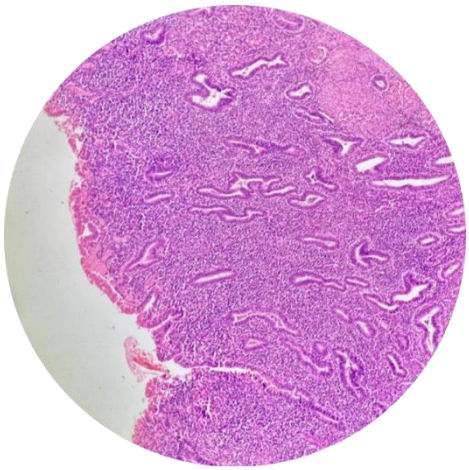
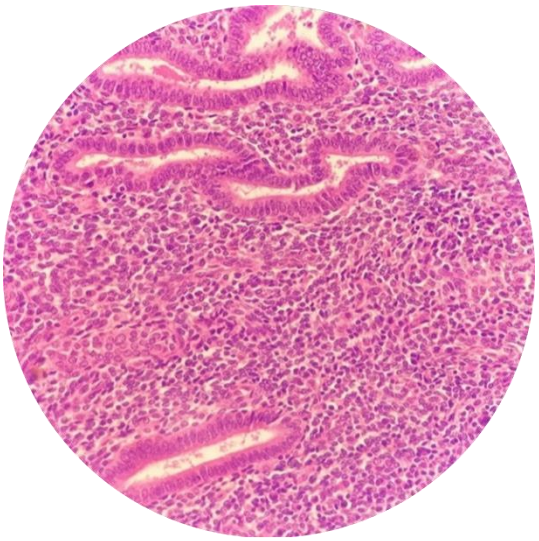
a. H&E image showing endometrium – myometrium junction (40x)



b. H&E image showing lymphoid aggregates and plasma cells (100x)



c. H&E image showing lymphoid aggregates and plasma cells (400x)



d. H&E image showing coexistent adenomyosis (100x)

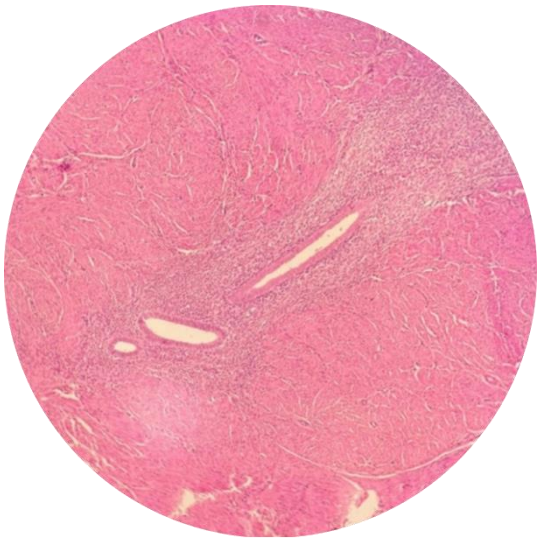


Figure 1: Histopathological Features of Chronic Endometritis with Coexistent Adenomyosis

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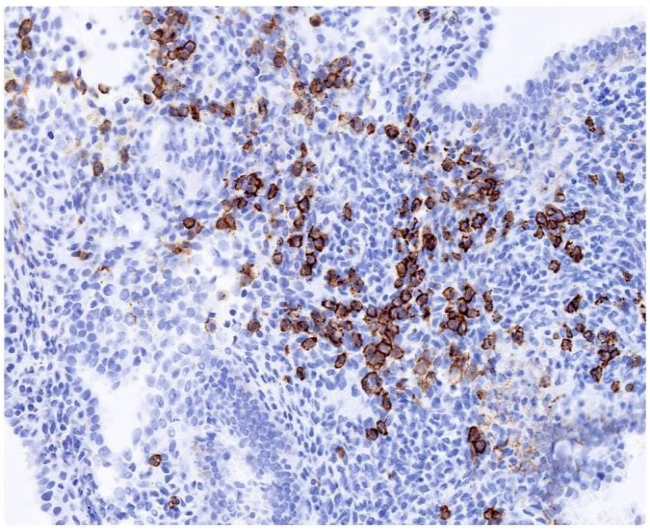

Figure 2: Immunohistochemical Staining CD138 Highlighting Plasma Cells in Chronic Endometritis (200x)

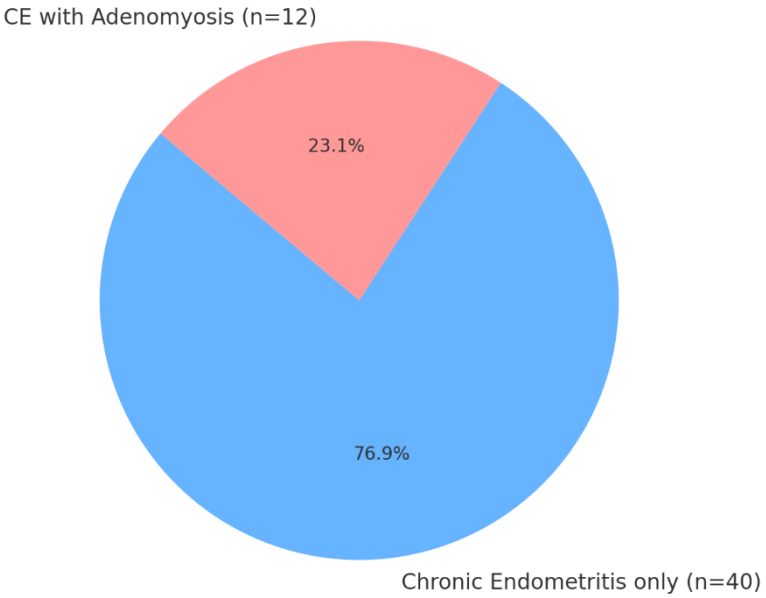

Figure 3: Prevalence of adenomyosis among confirmed chronic endometritis cases (N=52)