FOUR-YEAR GLUTEN-FREE DIET RESOLVES ENDOMETRIOSIS: A CASE REPORT

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Keywords:

Endometriosis, Endometrioma, Gluten-Free, Diet, CA-125

ABSTRACT

Introduction: Ectopic endometrial tissue and persistent inflammation are characteristic features of endometriosis which is a chronic illness. Due to the limited efficacy of standard treatments such hormone therapy, analgesics, and surgery, patients are increasingly turning to alternative methods. The following case presents interesting information about the influence of controlling diet in management of recurrent endometriosis by shedding light on the improvement experienced by a 44-year-old woman struggling with endometriosis, after being on a gluten-free diet.
Case Presentation: A 44-year-old multiparous woman with chief complaint of dyschezia and constant pelvic pain worsening during menstruations, was found to have increased CA-125 levels. Imaging revealed bilateral hemorrhagic ovarian cysts diagnosed as endometriosis. Initially, oral contraceptives led to minor relief, but the pain recurred after termination of usage. The patient then decided to opt for another solution by strictly adhering to a gluten-free diet. Over the course of four years, it was noted that her pelvic pain had disappeared and her CA-125 levels returned to normal. Recent imaging showed that the left ovary's cyst had shrunk in size and the right ovary's cyst had resolved.
Conclusion: This case suggests a potential role for dietary interventions, especially a gluten-free diet, in the management of endometriosis. Although preliminary data points to its advantages, randomized trials have to be undertaken to validate these results and investigate the mechanisms relating diet to the development of disease.

Introduction

Endometriosis is a devastating condition that affects women of reproductive age and is characterised by endometrial tissues outside the uterine cavity which cause a state of continuous inflammation.[1] While there is no known cure for this condition, analgesics, mainly anti-inflammatory drugs, hormonal therapies, and surgery aimed at removing the ectopic tissue, are typically employed for managing endometriosis.[1, 2] Recurrence and treatment dissatisfaction continue to be major issues despite the enhancements in medical and surgical care, often causing patients to look for alternative solutions.

We report a unique case of endometriosis in a 44-year-old woman whose symptoms and ovarian cysts whose condition significantly improved after adopting a gluten-free diet. Moreover, her pelvic pain dramatically reduced and her CA-125 levels were back to normal range. In addition to offering important insights into the role of lifestyle factors in controlling endometriosis, this case highlights the potential of dietary changes as a supplemental therapy.

Case Description

A 44-year-old female patient, para 2, first presented to the outpatient clinic complaining of severe pelvic and lower abdominal pain persisting for several months. The pain was constant, with the most intense exacerbation occurring during menstruation. It was associated with dyschezia and reduced appetite. Her medical and surgical history was unremarkable, except for two caesarean sections, with the last being eight years prior. Her family history was non-contributory, being irrelevant for any similar conditions or malignancies.

On examination, her overall physical and systemic assessments were normal. The per vaginum examination indicated a bulky anteverted uterus with tenderness in bilateral fornices. She was initially diagnosed as a case of uterine infection and was prescribed a one-week course of antibiotics, which failed to resolve her pain.

Subsequent pelvic ultrasound (US) demonstrated a 79 x 65 x 70 mm anteverted uterus, with no sac or retained products of conception (RPOC) observed. A posterior wall subserosal fibroid measuring 48.7 x 43 mm with calcification foci was identified. The endometrium appeared centrally located with a thickness of approximately 8 mm. Additionally, a single ovarian cyst with dense internal echoes measuring 52 x 51 mm was noted in the right ovary (61 x 58 mm), while the left ovary (32 x 19.5 mm) showed no cystic or mass lesions. The ultrasound impression indicated a calcified intramural uterine fibroid and a right ovarian cyst. Laboratory studies demonstrated a normal full blood count and inflammatory markers; however, the CA-125 level was elevated at 160.40 U/mL, as shown in Table 1.

An MRI was performed which confirmed the diagnosis of endometriosis and revealed bilateral ovarian cysts, with an increase in size of the right ovarian cyst. The report indicated a normal-sized anteverted uterus with a posterior wall irregularity consistent with previous intramural haemorrhage. Bilateral haemorrhagic ovarian cysts were identified, measuring 68 x 68 x 61 mm on the right and 46 x 43 x 39 mm, as seen in Figure 1.

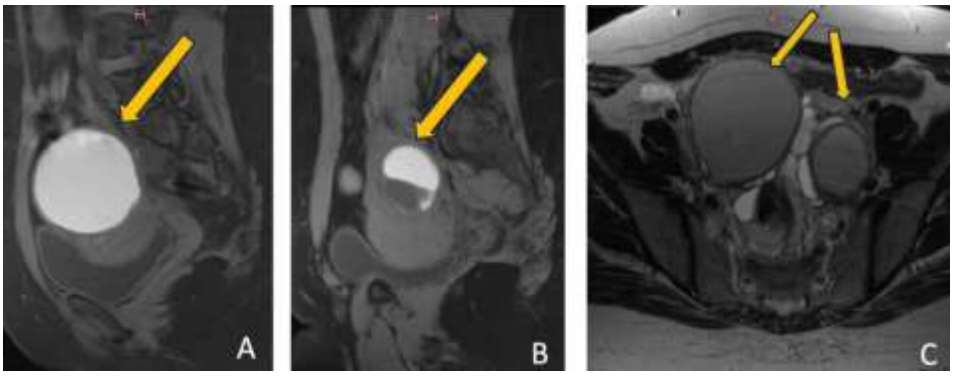

Figure 1. MRI revealed bilateral ovarian cysts containing fluid with high T1 signal intensity in sagittal T1WI with fat saturation (right "image A", left "image B") and T2 signal drop, consistent with the T2 shading sign (axial T2WI "image C"), consistent with blood content and suggestive of endometriomas.

Following consultation with obstetric and gynaecological specialists, the patient was advised to undergo surgical excision of the ovarian cysts and was placed on a nine-month regimen of daily progesterone-only oral contraceptive pills (POPs) to induce amenorrhea followed by a one-month interval then repeating similar cycle until menopause. The patient reported significant pain relief within one month of starting the POPs. However, she was not satisfied by the long-term nature of the treatment. Hence, she stopped the medication, and the symptoms recurred. She subsequently consulted multiple specialists, pursued alternative therapies, and experimented with various home remedies.

One year later, a repeat pelvic US revealed that both ovarian cysts had enlarged. The right ovary measured 97 x 76 x 87 mm, with the cyst increasing to 83 x 65 x 81 mm. The left ovary showed two complicated cysts: the larger measuring 59 x 29 x 49mm and a new cyst measuring 36 x 24 mm. Furthermore, the CA-125 levels rose to 740 U/mL [Table 1].

In response, she decided to adopt a strict gluten free diet. Her diet was based on lentils, pulses, vegetables, fruits, and similar whole foods. In addition, she adhered to consistent meditation every day for an hour before sleeping at night.

Four years into the strict gluten-free diet, the patient, still in the premenopausal period, underwent another pelvic US and CA-125 serum studies. The US showed a normal-sized anteverted uterus with a central endometrium with a normal thickness of 7.6 mm and with no irregularities, fibroid, sac, or RPOC. A total of three ovarian cysts were noted: two in the right ovary and one in the left. The sizes of the previous right and left ovarian cysts had decreased to 51.2 x 45.8 mm and
48.1 x 42.4 mm, respectively, while a new right ovarian cyst measured 30.2 x 26.9 mm. Interestingly, her CA-125 levels have fallen to reach 34.10 U/mL back to the normal range [Table 1].

Table 1: The CA-125 marker test of the patient throughout the timeline.

Timeline	Description/Intervention?	CA-125 TEST value	Reference Range
2017	Patient presents	160.4 U/mL	0-35
2018	1 year after stopping OCPs	740.0 U/mL	
2022	4 years into gluten free diet	34.10 U/mL	

Six years later, the patient had her most recent pelvic ultrasound while still following the gluten-free diet and menstruating, as shown in Figure 2. The results showed an anteverted uterus with a central endometrium that was 13.3 mm thick. and no irregularities, fibroids, sacs, or RPOC. Notably, the right ovarian cysts had completely resolved, while the left cyst had reduced to 20.4 x 22.8 mm. The patient has noted that her pelvic pain had resolved completely **[Figure 2].**

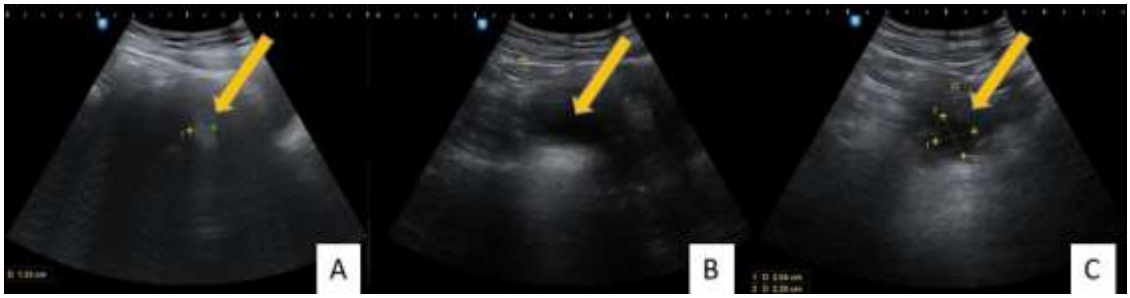

Figure 2. The latest pelvic US of the patient, six-years into a strict gluten-free diet. The uterus is anteverted normal in size with average endometrial thickness of 13.3 mm (arrows "image A"). The right ovary is normal in size with no cysts (arrows "image B"). The left ovary is normal in size with a single simple cyst 2.04 x 2.28 cm in sized (arrows "image C").

Discussion and Conclusion

Traditionally, endometriosis is managed by analgesics and anti-inflammatory drugs such as nonsteroidal anti-inflammatory drugs (NSAIDs), hormonal therapies in the form of oral contraceptives, and conservative surgery in extreme cases.[1, 2] The objective of these treatments is to provide symptomatic relief not cure. However, in recent years interplay between dietary habits and various diseases has been a subject of increasing interest and endometriosis is not an exception. Since endometriosis is characterised by an increased inflammatory response, several studies have hypothesised about the influence of different dietary components on its development and progression.[3, 4] Of particular interest for this case, the potential impact of gluten consumption on the course of endometriosis has been explored in few experimental studies.[5]

To begin, this patient reported decreased levels of pelvic pain after adhering to a gluten free diet for four years. This has also been reported in previous research. In a study with over two hundred patients who suffered from severe pain caused by endometriosis, adhering to a gluten free diet for 12 months caused significant reduction in pain levels in at least three fourths of the study participants.[6] It is hypothesised that the inflammatory response triggered by gluten in genetically susceptible individuals contributes to the exacerbation of endometriosis leading to higher levels of pain.[7]

The return of CA-125 levels to normal after adhering to gluten-free diet for four years is another noteworthy feature of this case. CA-125 is a glycoprotein biomarker CA-125 which is frequently used to gauge the severity of endometriosis. The higher the levels of CA-125, the worse the stage of endometriosis in terms of adhesions and lesion sizes.[8] Although the precise pathway by which a gluten-free diet may affect CA-125 levels is unknown, the normalisation of CA-125 levels is likely due to the reduction in systemic inflammation. Because gluten is a known trigger for immunologic reactions in genetically predisposed individuals, eliminating it from the diet may also contribute to the reduction of the chronic inflammatory state secondary to endometriosis, which in turn may cause a drop in CA-125 levels.[9]

In addition, one of the most prominent findings of this case is the marked reduction in the size of the ovarian cysts in this patient following the adoption of gluten-free diet. This finding is of crucial importance because endometriomas, or ovarian cysts caused by endometriosis, are often implicated in infertility.[10] The shrinkage of the ovarian cysts seen in this patient may be explained by the reduction in the baseline inflammatory state. However, the precise relationship between dietary factors and the formation and growth of endometrioma is not described in the literature.

This case highlights the potential role of adopting gluten-free diet as a treatment approach to endometriosis especially for patients who prefer natural, non-invasive approaches to manage their condition. While the role of diet in managing endometriosis seems promising, it is important to consider the limitations of drawing broad conclusions from a single case report. Furthermore, it must be kept in mind that existing literature provides only preliminary evidence in support of dietary modifications to manage such a debilitating condition. Genetic, environmental, and immunological factors likely contribute to individual responses to gluten free diets - and other dietary changes - employed to manage endometriosis.[7] Therefore, randomised clinical trials are required to further our understanding of the impact of dietary interventions, such as gluten free diets, on the pathogenesis and progression of endometriosis, the significance of clinical outcomes for patients who adhere to such diets, as well as any potential adverse effects. In addition, research is also needed to understand the exact pathophysiology of the condition to identify potential biomarkers that aid in predicting which patients will likely benefit from dietary interventions.

Acknowledgments
We would like to extend our gratitude to esteemed Dr. Maher Abdulrahim Ghazawi from Department of Radiology, Al-Noor Specialist Hospital, Ministry of Health, Makkah, SAU for his guidance with the radiological images.

Statements and declarations

Authors' Contribution: The authors contributed equally to the article and shared the first authorship position.

Ethical considerations
Not applicable.

Consent to participate
Written informed consent was obtained from the patient described in this case report and is available upon request at any time.

Consent for publication
Written informed consent was obtained from the patient described in this case report and is available upon request at any time.

Declaration of conflicting interest
The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article

Funding statement
The author(s) received no financial support for the research, authorship, and/or publication of this article.

Data availability
The required data will be made available upon contacting the corresponding author.

References
1. Brown J, Crawford TJ, Allen C, et al. Nonsteroidal anti-inflammatory drugs for pain in women with endometriosis. Cochrane Database of Systematic Reviews 2017. https://doi.org/10.1002/14651858.CD004753.pub4
2. Brown J, Crawford TJ, Datta S, et al. Oral contraceptives for pain associated with endometriosis. Cochrane Database of Systematic Reviews 2018. https://doi.org/10.1002/14651858.CD001019.pub3
3. Arab A, Karimi E, Vingrys K, et al. Food groups and nutrients consumption and risk of endometriosis: a systematic review and meta-analysis of observational studies. Nutrition journal 2022; 21: 58. https://doi.org/10.1186/s12937-022-00812-x
4. Markowska A, Antoszczak M, Markowska J, et al. The role of selected dietary factors in the development and course of endometriosis. Nutrients 2023; 15: 2773. https://doi.org/10.3390/nu15122773
5. Nirgianakis K, Egger K, Kalaitzopoulos DR, et al. Effectiveness of dietary interventions in the treatment of endometriosis: a systematic review. Reproductive sciences 2022: 1-17. https://doi.org/10.1007/s43032-020-00418-w
6. Marziali M, Venza M, Lazzaro S, et al. Gluten-free diet: a new strategy for management of painful endometriosis related symptoms? Minerva chirurgica 2012; 67: 499-504. https://pubmed.ncbi.nlm.nih.gov/23334113/
7. Brouns F, Van Haaps A, Keszthelyi D, et al. Diet associations in endometriosis: a critical narrative assessment with special reference to gluten. Frontiers in nutrition 2023; 10: 1166929. https://doi.org/10.3389/fnut.2023.1166929
8. Karimi-Zarchi M, Dehshiri-Zadeh N, Sekhavat L, et al. Correlation of CA-125 serum level and clinico-pathological characteristic of patients with endometriosis. International journal of reproductive biomedicine 2016; 14: 713. https://pmc.ncbi.nlm.nih.gov/articles/PMC5153578/
9. Lerner A, Benzvi C and Vojdani A. Gluten is a Proinflammatory Inducer of Autoimmunity. Journal of Translational Gastroenterology 2024; 2: 109-124. https://dx.doi.org/10.14218/JTG.2023.00060
10. Jiang D and Nie X. Effect of endometrioma and its surgical excision on fertility. Experimental and therapeutic medicine 2020; 20: 1-1. https://doi.org/10.3892/etm.2020.9242