



Adenomyosis of the Uterus with Abnormally high CA-125 Managed Conservatively with GnRH Analogues Followed by Levonorgestrel Intrauterine System (LNG-IUS)

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Abstract

40 years old Para 2, history of Normal vaginal deliveries presented in January 2022 with menorrhagia and severe dysmenorrhea. On investigation patient was found to have mild anemia, CA-125 was abnormally high with a value of 1935 U/ml. Ultrasound pelvis showed an enlarged uterus with thickened posterior myometrium with heterogenous echotexture of myometrium of uterus.-Likely adenomyosis. Small anterior wall fibroid. MRI pelvis reveal enlarged uterus with thickened fundal posterior myometrial wall, suggesting changes of adenomyosis with adenomyoma in the fundal posterior uterine wall.

She was managed conservatively with GnRH analogue Injections for 2 months. Follow up CA-125 after 2 months drastically reduced to 222 U/ml. Patient had secondary amenorrhea and was asymptomatic. Next follow up after 3rd month - CA-125 - 36.5 U/ml. Patient was taken for diagnostic hysteroscopy, endometrial biopsy and LNG-IUS (MIRENA).

Post LNG-IUS insertion follow up after 5 months patient was symptomatically better. CA-125 was 347 IU/ml. Patient has average flow in periods and has 75% relief in her menstrual pains. Her quality of life improved with conservative management.

Conclusions: *Unexpectedly high CA-125 over 1000 IU/ml can be seen in benign gynecologic conditions such as severe adenomyosis. The high CA-125 level is positively correlated to the uterine size in severe adenomyosis.*

Key words: *Severe, Adenomyosis, High CA-125*

Abnormal uterine bleeding (AUB) accounts for 33% of outpatient referrals and 69% of referrals in the peri-menopausal and postmenopausal ages [1, 2]. AUB is a common cause of iron deficiency anemia (IDA), especially in the reproductive age group [3]. Polyps, adenomyosis, leiomyoma, malignancy and hyperplasia are the structural causes of AUB [3]. Endometrial biopsy is an important step in the assessment of AUB to rule out endometrial carcinoma, so that medical treatment can be offered, and unnecessary radical surgery can be avoided [1, 2].

Hysterectomy is the definitive, widely accepted treatment for fibroids, adenomyosis not responding to medical treatment and/or associated with endometrial hyperplasia [3, 4].

This case report represents a rare case of a perimenopausal woman who presented with severe abdominal pain to emergency and having history of progressive dysmenorrhea and enlarged uterus in pelvic scan and MRI with adenomyosis / adneomyoma and high CA-125 to highlight that unexpectedly high CA-125 over 1000 IU/ml can be seen in benign gynecologic conditions other than malignancy.

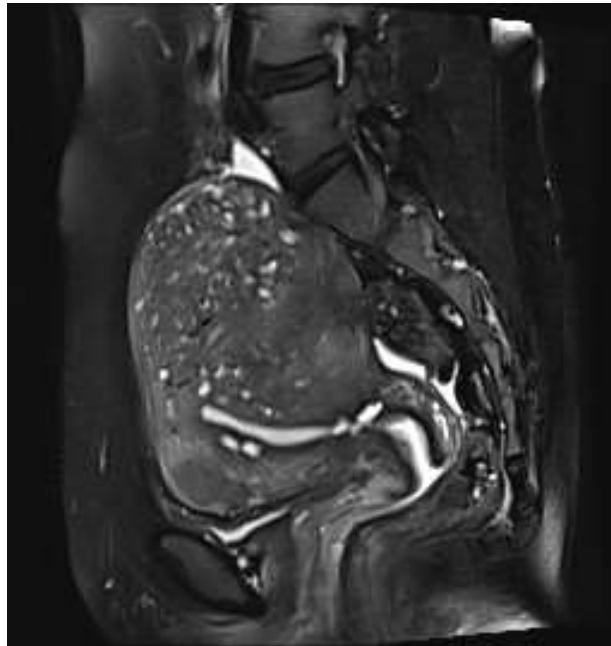
Case Report

40 years old Para 2, history of Normal vaginal deliveries presented in January 2022 with menorrhagia and severe dysmenorrhea. On investigation patient was found to have mild anemia, hemoglobin was 11.2 gm/dl, CA-125 was abnormally high with a value of 1935 U/ml. She was unable to carry out her routine work due to pain. Pain score 8/10 during periods and 4/10 without periods. Ultrasound pelvis showed an enlarged uterus with thickened posterior myometrium with heterogenous echotexture of myometrium of uterus.-Likely adenomyosis. Small anterior wall fibroid.

MRI pelvis was done which showed a uterus measures 11.2 x 11 x 9 cm. Contrast MRI pelvis findings reveal enlarged uterus with thickened fundal posterior myometrial wall. An ill-defined mass with multiple T1/T2 hyperintense cystic areas noted in the fundal posterior uterine wall. Features are likely to suggest changes of adenomyosis with adenomyoma in the fundal posterior uterine wall. An anterior wall intramural uterine fibroid noted.

Management done – Two injections of GnRH analogues, Triptorelin 3.75 mg intramuscular given every 28 days for 2 months. Follow up CA-125 after 2months drastically reduced to 222 U/ml. Patient had secondary amenorrhea and was asymptomatic. Next follow up after 3rd month – CA-125 – 36.5 U/ml. Patient was taken for diagnostic hysteroscopy, endometrial biopsy and LNG-IUS (MIRENA). Hysteroscopy findings - Uterus was bulky 10-12 weeks firm fornices free, uterocervical length 9 cms, Uterine cavity appeared normal, both ostia visualised. MIRENA intrauterine device inserted.

Post LNG-IUS insertion follow up after 5 months patient was symptomatically better. CA-125 was 347 IU/ml. Patient has average flow in periods and has 75 % relief in her menstrual pains. Her quality of life improved with conservative management.



Discussion

Adenomyosis is a common pathology detected in hysterectomy specimens, characterized by the presence of endometrial glands and stroma within the myometrium [3]. Patients with adenomyosis uterus typically present with abnormal uterine bleeding, dysmenorrhea, pelvic pain and backache at pre- or perimenopausal age.

Recognise that heavy menstrual bleeding (HMB) has a major impact on a woman's quality of life, and ensure that any intervention aims to improve this rather than focusing on blood loss. [NICE 2007]

Uterine adenomyosis is a commonly encountered estrogen-dependent disease in reproductive-age women, causing heavy menstrual bleeding, intense pelvic pain, and infertility. Although adenomyosis was previously considered a disease of multiparous women, it is becoming increasingly evident that it also affects younger nulliparous women and may compromise their fertility potential.

The sensitivity and specificity of transabdominal ultrasound in diagnosing adenomyosis are 32-63% and 95-97%, respectively, while MRI has 78-88% sensitivity and 67-93% specificity in diagnosing adenomyosis [3]. MRI findings of adenomyosis include diffuse uterine wall enlargement with hyperintense foci, cystically dilated glands and sites of microhemorrhages [10].

Uterine adenomyosis is a chronic estrogen-dependent condition affecting approximately 20% of gynecology patients [1]. Its most common symptoms include heavy menstrual bleeding, intense pelvic pain, and infertility. Despite the high prevalence and severe symptoms of the disease, its pathogenesis is not yet fully understood [1,2]. A lack of critical information on the origin of the disease and the absence of a universal classification system create a kind of therapeutic anarchy, with approximately 82% of adenomyosis patients eventually resorting to hysterectomy, a somewhat extreme way to deal with the disease [3,4,5].

It is clear that hysterectomy, the standard approach to definitively manage the disease, is not an option for patients wishing to preserve their fertility, so there is an urgent need to develop novel conservative strategies. We searched the current literature for available methods for conservative management of adenomyosis, including both pharmacological and surgical approaches. There is no existing drug that can cure adenomyosis at present, but some off-label treatment options may be used to tackle disease symptoms and improve fertility outcomes. Adenomyosis in patients wishing to conceive can be 'treated' by conservative surgery, though these procedures require highly experienced surgeons and pose a considerable risk of uterine rupture during subsequent pregnancies. While currently available options for conservative management of adenomyosis do have some capacity for alleviating symptoms and enhancing patient fertility perspectives, more effective new options are needed, with gonadotropin-releasing hormone antagonists and Levonorgestrel releasing intrauterine system (LNG-IUS) are showing encouraging results in preliminary studies. The choice of suitable therapy depends on individual patient age, severity of symptoms, and reproductive status, and can vary from full-scale hysterectomy to medical management of clinical symptoms and infertility.

A retrospective study was conducted by Rizvi et al. on hysterectomy specimens of patients with abnormal uterine bleeding, and they concluded that adenomyosis was the most common cause of abnormal uterine bleeding in perimenopausal age (46.34% [38/82]) [3].

Cancer antigen 125 (CA-125) is a high-molecular weight glycoprotein, traditionally associated with ovarian cancers, and it can be elevated in other benign conditions [11]. Kojima et al. reported elevated CA-125 (256 IU/l) in a case of adenomyosis uterus with mosaic Turner syndrome [10].

Ghaemmaghmi et al. reported 3 cases scheduled for laparotomy as ovarian cancer and leiomyosarcoma due to high levels of CA-125 (>1,000 IU/ml), and the histologic results after laparotomy showed uterine myoma in two patients and endometrioma in the third patient [12]. Ghaemmaghmi et al. concluded that high levels of CA-125 (> 1,000 IU/ml) can be seen in benign gynecological condition other than malignancy [12].

Zhou et al. found that women with adenomyosis had a higher CA-125 positive rate than normal controls or those with leiomyoma and the CA-125 levels were positively correlated with uterine size [13]. In addition, Zhou et al. found that the mean CA-125 level decreased significantly one week after surgery [13].

Fifty women having uterine enlargement of > 12 weeks' size due to severe adenomyosis and raised CA-125 were studied by Sheth and Ray, and they concluded that the greater the enlargement of the uterus over 240 cm³ volume or > 12 weeks' uterine size due to severe adenomyosis, the greater was the rise of CA-125 levels [14].

We searched the following bibliographic databases: MEDLINE via PubMed, SCOPUS, Web of Science, Cochrane Central Register of Controlled Trials (CENTRAL), EMBASE and Google Scholar for the relevant studies which used LNG-IUS in management of patients with clinically or ultrasonographic diagnosed adenomyosis. The main outcome measures are pain score at the end of follow-up, bleeding, symptomatic relief, uterine volume (mL), endometrial thickness (mm) and/or hemoglobin level.

Ten prospective studies (patients n = 551) were included. The overall effect estimates showed that the LNG-IUS led to significant reductions in pain score after 12 months (standardized mean difference [SMD] -3.87, 95% confidence interval [CI] -5.51 to -2.23, P < .001), 24 months (SMD -5.56, 95% CI -9.80 to -1.32, P = .01) and 36 months of insertion (SMD -3.81, 95% CI -4.27 to -3.36, P < .001). Similarly, the Pictorial Blood Assessment Chart (PBAC) showed significant reduction up to 36 months after LNG-IUS insertion (SMD -2.32, 95% CI -2.91 to -1.73, P < .001). The LNG-IUS led to significant reductions in the uterine volume 12 months (SMD -.60, 95% CI -0.88 to -.31, P < .001) and 36 months after insertion (SMD -0.42, 95% CI -0.69 to -0.14, P = .003).

This case report presents a rare case of a 40 years old parous woman with 2 normal vaginal deliveries and no history of any predisposing factor for adenomyosis, who presented with acute abdomen and enlarged uterus due to severe adenomyosis and high CA-125 to highlight that unexpectedly high CA-125 over 1000 IU/ml can be seen in benign gynecologic conditions other than malignancy.

Conclusion

Unexpectedly high CA-125 over 1000 IU/ml can be seen in benign gynecologic conditions such as severe adenomyosis. The high CA-125 level is positively correlated with the uterine size in severe adenomyosis.

LNG-IUS is a promising and effective option for the management of adenomyosis. Its use effectively reduced the severity of symptoms, uterine volume and endometrial thickness, and improved laboratory outcomes.

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