Clinical Practice

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Uterine adenomyosis:

an update for GPs

Box 1. Case

Jo is 42. They came to the GP with increasingly heavy, painful periods. They are not on HRT or hormonal contraception. A colleague arranged a pelvic USS, which suggests possible adenomyosis, with no other worrying features. They have come to see you to ask what this means and what could happen next.

BACKGROUND

Adenomyosis is the presence of endometriallike tissue and stroma within the myometrium. Historically, the diagnosis of adenomyosis was made on the basis of histopathology following hysterectomy, meaning the community prevalence of adenomyosis and prevalence in younger women are unknown.^{1,2}

The likelihood of identifying adenomyosis following hysterectomy varies widely, with reports ranging from 8.8% to 61.5%.² There is no unified histological diagnostic definition of adenomyosis.¹ Rates are likely influenced by care setting variables, for example, access to or indications for surgery. The evolution of alternative treatments to hysterectomy, including less invasive surgery (for example, endometrial ablation techniques) and hormonal coil treatments, influence hysterectomy rates,³ which in turn will impact on histology-based adenomyosis diagnoses.^{2,4}

Diagnosis without surgery has become possible through imaging (transvaginal ultrasound (TVUS) or MRI). Changes compatible with possible adenomyosis are increasingly described radiologically, but are dependent on the specialist performing the scan.² As with histology, there is no standardised radiological diagnostic criterion for adenomyosis.¹ Adenomyosis prevalence on TVUS in specialist clinics is estimated at 20.9% to 34%.²

Little is known about how often adenomyosis is documented, encountered, or managed in GP settings.

The aetiology of adenomyosis is unclear. It was originally thought to develop after disruption of the endometrium-myometrium junction (for example, during uterine surgery, pregnancy, or labour) allowing endometrial cells to invade the myometrium.² However, imaging identifies the condition in younger and nulliparous women, suggesting additional mechanisms. It is likely that factors associated with endometriosis development may also apply to adenomyosis, including genetic contributions, oestrogen dependence, and metaplasia of Müllerian remnants.⁵

ASSOCIATED SYMPTOMS

Adenomyosis can contribute to heavy menstrual bleeding, intermenstrual bleeding, painful periods, and pelvic pain.^{1,2,5} The uterus may feel enlarged or bulky to the patient or identified during examination.4 While it is often cited that approximately one-third of patients with adenomyosis have no associated symptoms, 1,4,5 this figure is uncertain.² It derives from retrospective reviews of hysterectomy indication, whereby a hysterectomy performed for prolapse was categorised as asymptomatic, although the patient may have experienced relevant undocumented symptoms. Newer evidence suggests that most patients with adenomyosis experience symptoms.²

Adenomyosis can be identified alongside or coexist with other gynaecological conditions, including endometriosis and fibroids.¹ Approximately 35%–55% of patients with adenomyosis also have fibroids⁴ and 16%– 62% of women having surgery for fibroids are reported to have adenomyosis.² These associations complicate understanding possible relationships between symptoms and adenomyosis,⁶ and may reflect aetiological or symptomatic overlap, or access to diagnoses.²

In patients with endometriosis having surgery, 15%–31% also have adenomyosis with higher rates of coexistence reported in patients with endometriosis and symptoms of subfertility or pelvic pain.² Conversely, in patients having surgery for adenomyosis, a case-series reports coexistent endometriosis in 28.6% of cases.⁷ A US population study

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REFERENCES

- Dason ES, Maxim M, Sanders A, et al. Guideline No. 437: diagnosis and management of adenomyosis. J Obstet Gynaecol Can 2023; 45(6): 417–429.e1.
- Upson K, Missmer SA. Epidemiology of adenomyosis. Semin Reprod Med 2020; 38(2-03): 89–107.
- Hammer A, Rositch AF, Kahlert J, et al. Global epidemiology of hysterectomy: possible impact on gynecological cancer rates. Am J Obstet Gynecol 2015; 213(1): 23–29.
- Peric H, Fraser IS. The symptomatology of adenomyosis. Best Pract Res Clin Obstet Gynaecol 2006; 20(4): 547–555.
- Vannuccini S, Tosti C, Carmona F, et al. Pathogenesis of adenomyosis: an update on molecular mechanisms. *Reprod Biomed Online* 2017; 35(5): 592–601.
- Gordts S, Grimbizis G, Campo R. Symptoms and classification of uterine adenomyosis, including the place of hysteroscopy in diagnosis. *Fertil Steril* 2018; 109(3): 380–388.e1.
- Naphatthalung W, Cheewadhanaraks S. Prevalence of endometriosis among patients with adenomyosis and/or myoma uteri scheduled for a hysterectomy. *J Med Assoc Thai* 2012; **95(9):** 1136–1140.
- Yu O, Schulze-Rath R, Grafton J, et al. Adenomyosis incidence, prevalence and treatment: United States population-based study 2006-2015. Am J Obstet Gynecol 2020; 223(1): 94.e1-94.e10.
- Mishra I, Melo P, Easter C, et al. Prevalence of adenomyosis in women with subfertility: systematic review and meta analysis. Ultrasound Obstet Gynecol 2023; 62(1): 23–41.
- Kapczuk K, Friebe Z, Iwaniec K, Kędzia W. Obstructive Müllerian anomalies in menstruating adolescent girls: a report of 22 cases. J Pediatr Adolesc Gynecol 2018; **31(3):** 252–257.
- Itam SP 2nd, Ayensu-Coker L, Sanchez J, et al. Adenomyosis in the adolescent population: a case report and review of the literature. J Pediatr Adolesc Gynecol 2009; 22 (5): e146–e147.
- Youm J, Lee HJ, Kim SK, et al. Factors affecting the spontaneous expulsion of the levonorgestrelreleasing intrauterine system. Int J Gynaecol Obstet 2014; 126(2): 165–169.
- 13. NICE. Heavy menstrual bleeding: assessment and management. NG88. 2018.

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Competing interests

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including 333 693 patients with adenomyosis found that 18% had a concurrent endometriosis diagnosis.⁸

Despite their similarity and potential overlap, endometriosis and adenomyosis are considered different conditions that can coexist or occur independently. It is important to be aware of their potential coexistence when counselling about treatments for symptoms, including careful safety netting, encouraging patients to report the impact of trials of hormonal treatment for symptomatic benefit including returning for review if these are not adequately tolerated or effective.

Although adenomyosis was considered an association of multiparity, the advent of imaging diagnosis highlights growing awareness of a potential association with subfertility. A 2023 systematic review reported that approximately 10% of patients assigned female at birth with subfertility had adenomyosis alone (without coexistent fibroids or endometriosis).⁹

Findings that may look like adenomyosis can be reported in adolescents with menstrual pain or heavy bleeding.^{10,11} Any adolescent with atypical ultrasound scan appearances should be referred for specialist assessment.

In general practice, as in the scenario (Box 1), an ultrasound scan is typically arranged in the context of a clinically relevant concern, with subsequent management in line with symptoms and the patient's priorities. However, possible adenomyosis may be encountered incidentally in the context of imaging done for another reason. This offers an opportunity to proactively ask about symptoms and consider support options.

MANAGEMENT IN PRIMARY CARE

Trials of empirical treatment are a mainstay of primary care for adenomyosis. These need to be supported by shared decision making, including acknowledging uncertainty and possible next steps. Ensuring patients know when to come back and the importance of this is central to adenomyosis care. Proactively arranging or enabling routes for follow-up and continuity of care may help.

Guidance about how to manage adenomyosis is usually embedded in symptom-focused pathways (for example, heavymenstrualbleedingordysmenorrhoea), rather than guidance specific to adenomyosis.

Offering treatments that mitigate against pain and bleeding are typically first line, tailored against patient preferences, medical context, and previous experiences. While not trialled specifically in adenomyosis, a trial of NSAIDs or medications to reduce menstrual flow (tranexamic acid, hormonal contraception) is appropriate if not

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contraindicated.¹ Medications that alter menstrual bleeding (contraceptive or noncontraceptive hormonal therapies) can be beneficial if acceptable and tolerated. The hormonal IUS is well studied in adenomyosis and is a first-line recommendation for heavy pain and bleeding, if acceptable or tolerable to the patient.¹ Rates of IUS expulsion are reported to be higher in patients with adenomyosis or fibroids.¹²

If any symptoms (pelvic pain, dysmenorrhoea, heavy bleeding) are not managed effectively or adequately with a primary care trial of treatment, or there are ongoing concerns, referral for specialist evaluation is appropriate. This is in part because of the potential overlap between adenomyosis and endometriosis but is equally applicable for anyone experiencing intractable or difficult symptoms. This includes adolescents, and those concerned about fertility.

The presence of adenomyosis can complicate interpreting ultrasound reports about the endometrium in patients with irregular bleeding. If there is any uncertainty in primary care, especially if perimenopausal or menopausal, referring for specialist assessment is appropriate.

SUPPORT FROM SPECIALIST CARE

If patients are referred on, subsequent treatment will be guided by further assessment, which may include further imaging (MRI), laparoscopy, or hysteroscopy and biopsy.

Gynaecology services may advise using non-contraceptive hormonal treatment (for example, non-contraceptive dose norethisterone or medroxyprogesterone acetate) or GnRHa treatment before or while waiting for specialist review. In this case, asking for guidance that includes duration of treatment and any monitoring or addback therapy advised is important. Other specialist medications trialled in adenomyosis include danazol and SERMs,¹ although their use is less widespread.

Specialist centres may offer multidisciplinary support for pelvic pain (including physiotherapy and psychological input). Trials of treatment may include supervised use of GnRH analogues. Specialist surgical treatments may include hysterectomy with or without oophorectomy depending on the patient's age. Hysterectomy is the only curative treatment for adenomyosis.

NICE identifies the long-term outcomes of pharmacological or uterine-sparing treatments for heavy menstrual bleeding associated with adenomyosis as a research priority evidence gap.¹³

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