Endometrial adenocarcinoma in association with a levonorgestrel-releasing intrauterine system (Mirena®)

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Surgical treatment was by total abdominal hysterectomy with bilateral salpingo-oophorectomy and pelvic lymphadenectomy. At the outset of the operation the peritoneal cavity was flushed with saline, which was then aspirated for cytological examination that proved negative for malignant cells. Histology revealed a moderately differentiated (Grade 2) endometrioid adenocarcinoma confined to the uterus with tumour invading the outer half of the myometrium but not extending to the peritoneal surface (FIGO Stage 1C).

Discussion
The LNG-IUS releases approximately 20 µg levonorgestrel into the uterine cavity daily. This causes the endometrial glands to become inactive and the stroma to become decidualised.1 There is a reduction in the duration and the volume of menstrual blood loss over time. A reduction in menstrual blood loss of 94% was identified at 3 months in a randomised trial2 and up to 97% at 12 months in a non-comparative study.3

The LNG-IUS has been used to protect the endometrium from undergoing hyperplastic and neoplastic change in women using oestrogen replacement therapy4 and it is now licensed for such use. The LNG-IUS has also been shown to have a protective action against the uterine effects of tamoxifen5 and it has been used effectively for primary treatment of early endometrial carcinoma.6 Therefore the LNG-IUS might reasonably be expected to protect women not being treated with oestrogen or tamoxifen against development of endometrial cancer. However, Jones et al.7 have reported the occurrence of endometrial carcinoma in two women following the insertion of a LNG-IUS. One of them, a 54-year-old multiparous woman, had an ultrasound scan and endometrial biopsy and then received cyclical combined oestrogen and progestogen hormone replacement therapy (HRT) for an unstated period of time before the LNG-IUS was inserted. It is open to speculation whether the HRT was implicated in the pathogenesis of adenocarcinoma following a negative endometrial biopsy. Alternatively, the biopsy may have yielded a false-negative result in the presence of an existing carcinoma low down in the uterine cavity, which was later rendered asymptomatic for a year by the insertion of the LNG-IUS.

The second case reported by Jones et al.7 was remarkably similar to the present case. A 48-year-old multiparous woman had presented with a 6-month history of irregular, heavy vaginal bleeding. A LNG-IUS had been inserted 3 years previously to treat menorrhagia, without prior endometrial sampling. The LNG-IUS was removed at hysterectomy and curettage, which identified moderately differentiated invasive adenocarcinoma of the endometrium. In this case, as in the present case, the patient may already have had the carcinoma before the LNG-IUS was inserted, and without prior endometrial sampling it is impossible to know if this was indeed the case. If in these cases the malignancy antedated the insertion of the LNG-IUS then it is possible that the levonorgestrel released into the uterine cavity suppressed the symptoms of carcinoma. But Jones et al.’s case was found to have inoperable metastatic pelvic lymph nodes, and metastatic endometrial carcinoma would not be expected to be inhibited by the LNG-IUS.7
CASE REPORT

These cases emphasise the importance of following the guidelines issued by the Faculty of Family Planning and Reproductive Health Care (FFPRHC)\(^8\) and the Royal College of Obstetricians and Gynaecologists (RCOG).\(^9,10\) The RCOG evidence-based guideline on the initial management of menorrhagia\(^9\) does not identify the LNG-IUS as a primary treatment option unless contraception is also required. The FFPRHC Clinical Effectiveness Unit (CEU) recommends that the LNG-IUS can be offered to women as a first-line treatment option for menorrhagia and supports the use of the LNG-IUS even if contraception is not required.\(^8\) The CEU asserts that endometrial assessment (biopsy or ultrasound scan) is not routinely required prior to LNG-IUS insertion for the management of menorrhagia. However, the caveat is added that women considering the LNG-IUS as a treatment for menorrhagia should be managed according to RCOG guidelines on the initial management of menorrhagia\(^9\) and the management of menorrhagia in secondary care.\(^10\) Practitioners working in general practice or in family planning and reproductive health care are more likely to be familiar with FFPRHC than with RCOG guidance.\(^8\) Whereas the RCOG guideline on initial management\(^9\) does not recommend endometrial assessment by transvaginal ultrasound scan or endometrial biopsy, the guideline on management in secondary care\(^10\) states that the uterine cavity should initially be investigated by transvaginal ultrasound and that an endometrial biopsy should be considered for all women with persistent menorrhagia. The CEU Guidance\(^8\) emphasises that women who present with persistent menorrhagia, despite LNG-IUS use, should be advised to return for further assessment of the uterine cavity (biopsy or ultrasound scan) to exclude pathology.

Carcinoma of the endometrium continues to be the most common gynaecological malignancy affecting Western women.\(^11\) Although relatively rare before the age of 40 years, the age-specific incidence increases steeply after the age of 44 years but then remains more or less static from age 55 years onwards.\(^11\) We conclude that the presented case and the two previously reported cases of endometrial carcinoma in association with a LNG-IUS provide compelling grounds for routine endometrial assessment by ultrasonography before insertion of a LNG-IUS for treatment of menorrhagia in perimenopausal women and for the thorough investigation of women in this age group who develop abnormal bleeding with a LNG-IUS in place.

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**References**


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