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Recurrent extended-spectrum beta-lactamase-producing *Escherichia coli* urinary tract infection due to an infected intrauterine device

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ABSTRACT The use of intrauterine devices (IUDs) have been widespread since the 1960s. In 2002, the World Health Organization estimated that approximately 160 million women worldwide use IUDs. However, IUDs are associated with short-term complications such as vaginal bleeding, pelvic discomfort, dyspareunia and pelvic infection. Herein, we report the case of a woman who had recurrent urinary tract infection (UTI) due to the use of an IUD, even after treatment. The patient developed four episodes of UTI within a seven-month period after IUD insertion. During each episode of UTI, extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli* (*E. coli*) was cultured from the patient's midstream urine. The IUD was finally removed, and culture of the removed IUD was positive for ESBL-producing *E. coli*. An infected IUD as a source of recurrent UTI should be considered in women with IUD *in situ* who develop recurrent UTI even after treatment.

Keywords: extended-spectrum beta-lactamase-producing Escherichia coli, intrauterine device, urinary tract infection

INTRODUCTION

Intrauterine devices (IUDs) have been widely used since the 1960s.[1] In 2002, the World Health Organization estimated that approximately 160 million women worldwide use IUDs.[1] IUDs are a popular method of contraception because other than being long-acting and rapidly reversible, they do not affect the spontaneity of sex. However, IUDs are associated with short-term complications such as vaginal bleeding, pelvic discomfort, dyspareunia and pelvic infection.[2] Herein, we report the case of a perimenopausal woman who had recurrent urinary tract infection (UTI) following the insertion of an IUD, in spite of antibiotic treatment.

CASE REPORT

A 44-year-old Chinese woman who was previously in good health presented with a six-month history of menorrhagia that was severe enough to cause iron deficiency anaemia. Her blood parameters on presentation were as follows: haemoglobin 8.4 (normal range [NR] 11.5–15.5) g/dL, mean corpuscular haemoglobin 23.1 (NR 27.0–35.0) pg and mean corpuscular volume 72 (NR 81–96) fL. The patient had low serum iron (4.8 [NR 6.6–30.4] umol/L), low serum ferritin (1 [NR 4–204] ng/mL) and high serum total iron binding capacity (98 [NR 44–80] umol/L). Faecal occult blood test was negative and the patient had no abdominal symptoms.

The patient underwent hysteroscopy and uterine curettage for investigation of menorrhagia. An IUD (Mirena®; Bayer Pharmaceuticals, Wayne, NJ, USA) was inserted during the procedure. The thread of the IUD was cut at 3 cm from the cervical os. The patient remained well after the insertion of the IUD and her menorrhagia resolved. She remained asymptomatic until four months after the insertion of the IUD, at which she presented with urinary frequency, dysuria and haematuria. Culture of her midstream urine grew extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli* (*E. coli*), with a bacterial count of 10^5 colony-forming units (CFUs)/mL. The patient was treated with intravenous meropenem and amikacin for ten days. Repeat midstream urinary culture ten days after completion of the antibiotic course was negative.

However, one month later, the patient presented again with recurrent urinary frequency, dysuria and haematuria. ESBL-producing *E. coli* was once again cultured from the patient's midstream urine, with a bacterial count of 10^4 CFUs/mL. Computed tomography (CT) urography and intravenous pyelography were unremarkable. Ultrasonography of the pelvis showed an IUD *in situ*. A high vaginal swab was taken for culture, and the results were negative. The patient was treated with intravenous meropenem and amikacin for 14 days. Her symptoms and bacteriuria resolved with the antibiotic therapy and she was discharged well. Microscopy and culture of midstream urine collected three weeks after discharge were unremarkable. To decrease the risk of post sexual intercourse-associated UTI, the patient was advised to practise early postcoital voiding and double voiding. She was also recommended liberal fluid and cranberry juice intake.

The patient presented again two months later with similar symptoms. Midstream urine was once again found to be positive for ESBL-producing *E. coli*, with a bacterial count of $> 10^5$ CFUs/mL. Further workup was performed to determine the cause of recurrent ESBL-producing *E. coli* UTI. However,

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Table I. Antibiotic sensitivity/susceptibility of the extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli* (*E. coli*) cultured from the patient's urine during the four episodes of urinary tract infection (UTI) and from the removed intrauterine device (IUD).

Antibiotic	Sensitivity/susceptibility of the ESBL-producing *E. coli* cultured from:				
	First UTI	Second UTI	Third UTI	Fourth UTI	Removed IUD
Ampicillin	R	R	R	R	R
Ampicillin/clavulanate	I	I	R	R	R
Cefuroxime	R	R	R	R	R
Cotrimoxazole	R	R	R	R	R
Ciprofloxacin	R	R	R	R	R
Levofloxacin	R	R	R	R	R
Ceftazidime	R	R	R	R	R
Cefotaxime	R	R	R	R	R
Ertapenem	S	S	S	S	S
Imipenem	S	S	S	S	S
Amikacin	S	S	S	S	S

I: intermediate; R: resistant; S: sensitive

low-dose CT of the thorax, upper endoscopy, colonoscopy and cystoscopy were all unremarkable. The patient, who was discharged after another 14-day course of intravenous meropenem and amikacin, remained asymptomatic for three months. Monthly urine microscopy and culture were unremarkable.

She presented once more with urinary frequency, dysuria and fever. Her midstream urine was again positive for ESBL-producing *E. coli*, with a bacterial count of > 10^5 CFUs/mL. As this was the fourth episode of UTI by the same organism in the previous seven months, and we were unable to determine any occult source for the infection, it was decided that the IUD be removed. Culture of the removed IUD showed heavy growth of ESBL-producing *E. coli*. The results of the antibiotic sensitivity testing of all ESBL-producing *E. coli* strains isolated from the patient's urinary cultures during all four episodes of UTI, and from the removed IUD, are shown in Table I. No other interventions, such as commencement of oestrogen-based oral contraceptive pills or topical oestrogen, were undertaken following the removal of the IUD. The patient attended follow-up sessions for 12 months, with midstream urinary cultures performed monthly. She did not develop another episode of UTI during the 12-month period following the removal of the IUD.

DISCUSSION

Although IUDs are safe and highly effective contraceptive devices, there is concern that the use or insertion of IUDs in women who have sexually transmitted infections will increase their risk of developing pelvic inflammatory disease.[3] This is because sexually transmitted organisms that are present in the endocervical canal can be transported into the uterine cavity when an IUD is inserted.[3] This 'fear' increased in the 1980s with the publication of a series of reports detailing *Actinomyces* spp. infection among women with IUDs *in situ*.[4,5]

While *Actinomyces* spp. are not part of the normal vaginal bacterial flora, they have been found to colonise the genital tracts of 2.8%–25% of women with an IUD *in situ*.[5,6] As *Actinomyces* spp. usually colonise plastic devices, *Actinomyces* spp. infection usually resolves when the plastic device is replaced by a copper-containing IUD.[7] Indeed, in a recent review on IUD use and the risk of pelvic inflammatory disease among women with sexually transmitted infection, Mohllajee et al found this risk to be low with the use of copper-containing IUDs.[8] However, the use or presence of copper-containing IUDs can alter the normal bacterial flora of the female genital tract.[6] This change in the ecological system, which occurs in the presence of an IUD, may have long-term sequelae in terms of the development of infection. A study by Charonis and Larsson found that the use of an IUD for more than five years increases the risk of tubo-ovarian abscess.[9] The authors also reported that *E. coli* was the most common pathogenic organism causing tubo-ovarian abscess; they postulated that the increased risk of tubo-ovarian abscess was probably due to a high incidence of bacterial vaginosis.[9] In addition to an increased incidence of bacterial vaginosis, IUDs are also associated with congestion of the bladder trigone.[10-12] This congestion can contribute to the development of UTI, accounting for the increased risk of UTI among IUD users.[10-12]

In the present case, as the IUD inserted in our patient was a hormone-releasing plastic IUD, it is possible that the recurrent episodes of UTI were not related to bacterial vaginosis,[10-12] but instead, were caused by the formation of a biofilm on the plastic IUD during an episode of infection. Release of bacteria from the biofilm on the plastic IUD may have caused the subsequent episodes of UTI in our patient. Other than that, one possible cause that should be considered for the recurrent UTI seen in our perimenopausal 44-year-old patient with menorrhagia is the onset of vaginal atrophy. Vaginal atrophy can result in structural changes in the vagina, as well as changes

in the flora of the genital tract, thereby resulting in heavy colonisation by ESBL-producing *E. coli*. It is possible that such vaginal colonisation may have been the source of the recurrent UTI seen in our patient and the colonisation, or even contamination, of the IUD during its removal. For this reason, a limitation of the present study is that bacterial molecular typing of the four strains of ESBL-producing *E. coli* cultured from the patient's urine to the ESBL-producing *E. coli* isolated from the culture of the removed IUD, using pulsed-field gel electrophoresis, was not performed. However, as our patient did not develop another episode of UTI following the removal of the IUD, it was apparent that removal alone was sufficient to prevent further recurrence of UTI in our patient.

In conclusion, although the association of UTI with IUD use is not a novel finding, physicians should keep in mind that recurrent UTI can occur among IUD users even after treatment. An infected IUD should be considered as a source of recurrent UTI in women with IUD *in situ* who develop recurrent UTI despite receiving appropriate therapy.

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