

Bladder endometriosis, a remarkable resemblance in a monozygotic twin

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Abstract It is known for many years that heritability plays a role in the development of endometriosis in many patients. Deep endometriosis of the bladder is a rare presentation of the disease and bladder endometriosis was not reported in monozygotic twin studies so far. Since monozygotic twins share the same genes, concordance and differences in presentation of endometriosis may help to discriminate between genetic and environmental determinants. The remarkable resemblance in the presentation of bladder endometriosis in this monozygotic twin seems to indicate that genetic factors are of importance in the arising of deep endometriosis in the bladder too.

Keywords Endometriosis · Bladder · Laparoscopy · Heritability · Twin

Introduction

Endometriosis affects 6–10% of women in their reproductive years and affects up to 35–50% of women with pain or infertility [1]. Urogenital tract is superficially involved in about 10–15% of cases but deep endometriosis of the bladder is estimated to be present in 1–2% of the patients only [2–5]. Bladder endometriosis is frequently accompanied by other forms of pelvic endometriosis [4]. Frequency, urgency, suprapubic pain and dysuria [3, 6, 7] are the most frequent symptoms of bladder endometriosis and a positive

correlation between severity of dysuria and lesion diameter has been described [7]. Haematuria seems to be a less frequent symptom in 20–35% of patients [2, 3, 6].

Heritability of endometriosis is well known from twin studies for many years, but this concerned mainly the increased risk to develop endometriosis and deep bladder endometriosis was not mentioned [8–11]. Despite the rare occurrence of bladder endometriosis, a monozygotic twin presented at our clinic with similar complaints and remarkable resemblance in the presentation of disease.

Case report

A 33-year-old Caucasian woman, G0P0, was referred to our department for relapse of endometriosis after previous surgery and hormonal treatment elsewhere. Although she did not have a relation at the moment, she wanted to preserve fertility. Dysmenorrhoea was acceptable with a levonorgestrel containing IUD in situ, but dysuria was increasing. Four years ago, she had a first laparoscopic local excision of endometriosis. Two years later, a re-excision took place followed by treatment with LHRH analogue for half a year. She was heterozygote for factor V Leiden without a history of thrombosis or embolism. Recto-vaginal examination revealed an enlarged and somewhat irregular painful uterus without vaginal or rectal involvement. IUD was in situ. At transvaginal ultrasound a round-shaped mass of about 1.5 cm was protruding from the uterus into the roof of the bladder. The ovaries had a normal appearance. There was no haematuria and urine culture was negative. Since the placement of the progesterone containing IUD a year before, the Ca 125 level decreased from 266 to a level varying from 97 to 116 kU/l. IVP showed a dimple in the roof of the bladder and excluded an

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Fig. 1 Laparoscopic view of patient 1. Firm adhesions around an adenomyotic uterus

obstruction of the ureters. The magnetic resonance imaging (MRI) scan showed an adenomyotic uterus with one lesion protruding in the backside of the bladder. The recto-vaginal septum was not involved and ovaries were normal. To plan surgery, an examination under general anaesthesia was scheduled. At cystoscopy, the protruding lesion was seen in the top of the bladder covered with endothelium and well away from the ureters. At laparoscopy (Fig. 1), the bladder attached densely to the adenomyotic uterus and superficial endometriosis was visible at the backside of the uterus. Further, there were no peritoneal implants, and the ovaries were normal.

Some months later, her monozygotic G0 twin sister presented with dysuria and dyschezia during bleeding periods. As a monozygotic twin sister, she was heterozygote factor V Leiden too without a history of thrombosis or embolism. She never had child wish and she had a levonorgestrel containing IUD 1 year earlier in life. She hardly suffered from dysmenorrhoea. At recto-vaginal examination, a firm nodule was palpable at the right sacro-uterine ligament; the uterus was of normal size and mobility. Haematuria was absent and Ca 125 was 50 kU/l. MRI scan (Fig. 2) revealed a normal uterus with a single nodule protruding in the backside of the bladder likewise as her sister. At the backside of the cervix, superficial endometriosis was visible but recto-vaginal septum was free of disease. Further, there were no plaques of endometriosis. At cystoscopy a nodule was seen at exact the same position as seen in her sister (Fig. 3). At laparoscopy, the uterus was normal, but the bladder was attached to the uterus with an implant of endometriosis present at the backside of the cervix comparable to the picture of her sister. There were no other spots of endometriosis intra-abdominally.

Because of the predominant complaint of dysuria, both sisters were planned for laparoscopic excision of the bladder nodule by partial cystectomy and excision of the lesion at the backside of the cervix. After excision, the

bladder was closed with a running suture vicryl 3×0. Complete closure of the bladder was tested with instillation of 150 ml methylene blue dye solution into the bladder at the end of the procedure. Since the sister with adenomyosis wanted to preserve fertility, her uterus was left in situ. The uterus of the sister without child wish was normal. Levonorgestrel IUD remained in situ in both. Prophylactic antibiotics were given for 24 h. Postoperative course was uneventful in both sisters. They were discharged the day after surgery with indwelling catheter. The bladder catheter was removed after a week and micturation proved normal afterwards. Histology confirmed in both cases an adenomyotic lesion through the bladder wall covered with normal bladder endothelium.

At follow-up visit after 6 weeks, dysuria had disappeared in both. At follow-up so far, the sister with the adenomyosis has some dysmenorrhoea still but bearable without pain medication. Her sister has no more complaints at all.

Discussion

Dysmenorrhoea, cyclic dysuria and suprapubic pain are the most frequent reported symptoms related to bladder endometriosis in literature [2, 3, 6]. In both our patients, dysuria was the predominant complaint with dysmenorrhoea as a second complaint. The dyschezia reported by one of the sisters was probably due to the nodule behind the cervix. Although the bowel was not involved, the complaint had disappeared after resection. The fact that the endometriotic lesions of both sisters were still covered with urothelium will explain the absence of haematuria. This is in agreement with the literature [2, 5].

Ultrasound is the simplest first step in diagnosis of endometriosis. Combination of abdominal, transvaginal and



Fig. 2 MRI scan of patient 2. Endometriosis nodule protruding in the top of the bladder and a second lesion behind the cervix

Fig. 3 Bladder nodule of patient 1 (*left*) and of patient 2 (*right*), localised in the roof of the bladder



transrectal ultrasound, depending on the complaints, may reveal endometriosis in infrequent sites [12]. In urogenital endometriosis, the bladder is the most frequent involved organ and superficial endometriosis of the bladder is often part of more extended endometriosis [13]. Ultrasound may also be used as a first step to exclude obstruction of the ureters. Although a dimple in the bladder was clear, an IVP is not the first choice to diagnose bladder disease. In case of suspicion of obstruction, however, it may help to localise the place and extent of the obstruction. MRI scanning is more sensitive to diagnose preoperatively the extent of endometriosis especially for retroperitoneal disease and bowel involvement [5, 14]. Cystoscopy and laparoscopy are required for definitive diagnosis [15].

The pathogenesis of bladder endometriosis has not been clarified. Donnez et al. proposed metaplasia from müllerian remnants [13], but the histological evidence of müllerian remnants in the urothelium of the bladder has been doubted [4]. Transplantation theory considers the extension of adenomyotic lesions and transport through blood and lymphatic vessels [16]. Finally, post surgery implantation, mainly after Caesarean, may be responsible in a part of the cases [13, 16]. Both twin sisters of this study had adenomyotic lesions of the bladder but only one of the sisters had further adenomyosis.

Urogenital endometriosis is much more frequent than deep bladder endometriosis [17]. Bladder endometriosis is frequently accompanied by other forms of endometriosis but bladder endometriosis and ureter endometriosis are not associated [4, 18]. Patients with ureter endometriosis usually have more advanced disease [5, 17, 18]. Therefore, the deep endometriosis of the bladder seems to be a different entity within advanced endometriosis.

Genetic factors play a part in the development of endometriosis but inheritance is complex. It is well known that family members of patients with endometriosis have an increased risk to develop endometriosis [10, 19]. The UK–Australian twin examination estimated 51% of the expression to be attributable to genetic factors [11]. The risks between monozygotic twins have been estimated as high as

75–87% [8, 9]. However, this concerned the change of endometriosis for relatives and a correlation in severity, but the localization of the endometriosis often differed between the twin pairs and bladder endometriosis was not described. Bladder endometriosis was mentioned neither in the large genome wide linkage study [11] nor in the genetic studies of Bischoff [19]. The lesions in the bladder and behind the cervix in the monozygotic twin described here were identical and there were no further peritoneal implants.

The development of endometriosis is multi-factorial and the presentation depends on genetic and extrinsic factors [19]. Apart from resemblance, our twin sisters showed discrepancies too. One of them had fewer complaints, had not been operated on before and had no further adenomyosis. She never had child wish and the levonorgestrel-releasing IUD had been placed about 1 year earlier in her life. It seems unlikely that the short time difference in the placement of the progesterone containing IUD explains the difference in adenomyosis between the sisters. The IUD had not prevented the progression of the bladder and the retro-cervical endometriosis in either of them. Evidence for a beneficial effect of a levonorgestrel-releasing IUD is still limited at this moment [20]. The sister with adenomyosis had been operated on incompletely twice. If this may cause extension of the adenomyosis is unlikely, but no other differences between the sisters is available from their medical histories. Inheritance is complex [1, 10, 19]. Presumably, different genes may influence the development in different ways as by influencing retrograde menstruation, cell differentiation, hormonal misbalance and by detoxification processes [1, 19]. Although this may explain the wide variation in expression of endometriosis, it cannot explain differences in our monozygotic twin.

Symptomatic lesions can be treated hormonally or by surgery. Hormonal treatment for pain will postpone child wish and overall does not improve fertility. It may have different side effects dependant of the medication chosen [21]. For small lesions and in women near menopause hormonal treatment may be considered. For larger and deeper lesions (>5 mm) surgery is recommended generally

[2, 3, 17]. Hormonal treatment resulted in temporary relief of symptoms only and previous surgery proved to be inadequate in the first of the twin sisters presented here. In the second sister, the levonorgestrel IUD controlled dysmenorrhoea reasonably but dysuria and dyschezia increased. Radical excision of the lesions relieved all her symptoms. Especially in younger women, surgical treatment of bladder endometriosis should be first choice treatment.

Conflicts of interest There are no conflicts of interest to disclose.

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