

# The menstruating bladder, an unusual cause of haematuria

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## Abstract

A 39 year old lady presented with flank pain and haematuria. Radiological investigations showed unilateral hydronephrosis and a serum creatinine of  $102\mu\text{mol/l}$ . At cystoscopy, a soft tissue mass was found in the region of the left ureteric orifice and was causing obstruction of the ureter. A resection biopsy of this lesion was taken.

A CT scan and DTPA renogram showed a non-functioning left kidney secondary to chronic obstruction by a soft tissue mass at the left vesico-ureteric junction. Histological analysis of the endoscopic resection specimen showed that the mass contained tubal-type epithelium compatible with a diagnosis of endosalpingiosis (a rare variant of Mullerianosis of the urinary tract).

In view of persistent symptoms, it was decided to proceed to surgery. A hysterectomy, bilateral salpingo-oophorectomy and partial cystectomy were performed. The patient has recovered well and is currently asymptomatic. Formal histology of the resection specimen showed the presence of endometriosis.

## Keywords

Haematuria, ureteral obstruction, endosalpingiosis, mullerianosis, endometriosis

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## Case report

A 39 year old lady presented with a long standing history of left flank pain and this was associated with episodes of haematuria during the time of menstruation. There were no symptoms of fever, dysuria, chronic pelvic pain or dyspareunia. Physical examination was unremarkable.

Initial investigations showed a normal full blood count, eGFR of  $56\text{ ml/min/1.73m}^2$ , normal serum creatinine and liver function. Urine analysis, microscopy and cultures were normal.

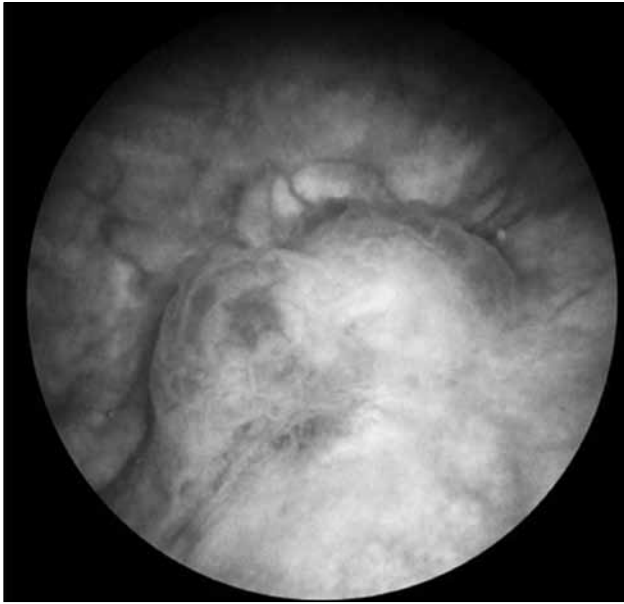
Ultrasound of the renal tract showed severe left sided hydronephrosis and hydroureter and parenchymal thinning (Figure 1). There was a normal right kidney. The CT scan revealed a solid mass at the left vesico-ureteric junction as the cause of the obstruction of the left ureter. The marked parenchymal loss was suggestive of long-standing obstruction of the left kidney. A DTPA renogram confirmed non-function of the left kidney and normal function of the right kidney with compensatory hypertrophy.

At cystoscopy, a soft tissue mass was identified in the region of the left ureteric orifice (Figure 2). The intravesical component of this mass was resected endoscopically. On resection of the lesion, there was a small collection of old blood within the mass itself, however the ureteric lumen could not be identified despite deep resection. Histology revealed the presence of tubal type epithelium, compatible with a diagnosis of endosalpingiosis (Figures 3 and 4).

In view of the on-going symptoms of pain and haematuria, the gynaecological opinion was to proceed to surgery. At operation, the macroscopic extent of endometriosis was limited



**Figure 1:** Ultrasound scan of the left kidney showing gross hydronephrosis and severe parenchymal atrophy



**Figure 2:** Endoscopic view of soft tissue mass in the region of the left vesico-ureteric junction

to the perivesical region without the heavy disease burden one usually expects in these cases. There was a soft tissue mass measuring about 3cm in diameter in the region of the distal left ureter and lateral bladder wall. A total abdominal hysterectomy, bilateral oophorectomy and partial cystectomy were performed, with excision of the mass together with the distal left ureter and a cuff of adjacent bladder wall (Figure 5). The patient had an uncomplicated postoperative recovery.

Histological assessment of the resection specimen showed predominantly endometriosis of the bladder wall, a minor component of tubal-type epithelium, with only focal adenomyosis of the uterus and normal adenexae.

## Discussion

### Background

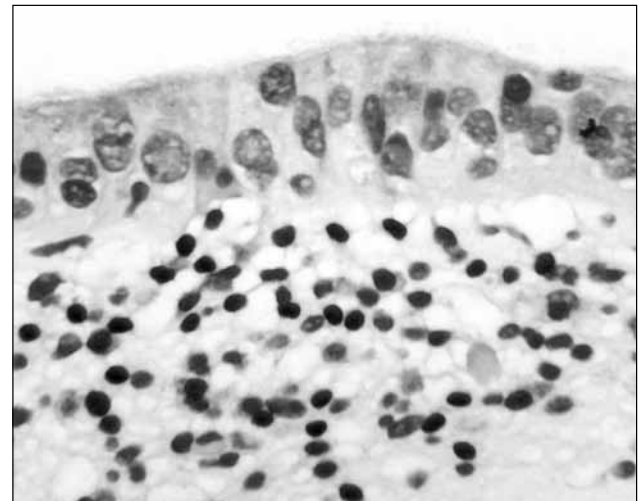
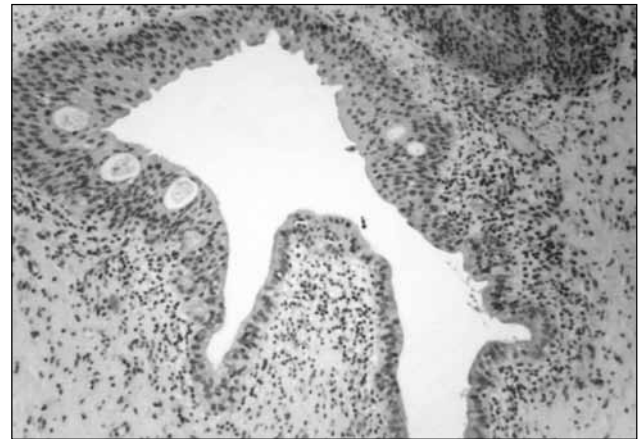
A variety of hyperplastic, metaplastic and neoplastic glandular lesions can occur in the urinary bladder.<sup>1</sup> Mullerianosis of the bladder is one such condition in which an admixture of endocervicosis, endosalpingiosis and endometriosis is found in the lamina propria and muscularis propria. Endocervicosis is usually more common than endosalpingiosis<sup>2</sup>, but overall, Mullerianosis is an extremely rare condition with fewer than 20 cases having been reported in the literature to date.

### History

In 1992, Clement and Young reported the finding of tumour-like glandular lesions in the urinary bladder in six women. The clinicopathological features of these cases were also presented. These glandular lesions were shown to have mucinous, endocervical-type of epithelium on histological examination.<sup>3</sup>

The investigators suggested that the lesion was most probably of Mullerian origin and proposed the term endocervicosis of the urinary bladder for this entity. Support for this explanation

was based on the fact that there was histological similarity to endocervical glands. Furthermore, the location, the occurrence in women, the association with endometriosis in some cases and the history of Caesarean section in others also supported this argument. Subsequently, Clement and Young coined the term Mullerianosis to encompass a spectrum of pathological lesions which are thought to have a Mullerian origin, including endocervicosis, endosalpingiosis and the commoner endometriosis.



**Figure 3&4:** Low and medium power views of endoscopic resection specimen showing ciliated columnar tubal-type epithelium



**Figure 5:** Resection specimen: ligated distal left ureter with vesico-ureteric junction and cuff of adjacent bladder wall

## Pathogenesis

Despite the fact that Sampson's theory of retrograde menstruation and implantation is still the most popular and accepted pathogenic mechanism of endometriosis, several clinical and experimental evidence seems to contradict this hypothesis.<sup>4</sup> Firstly, there is no evidence that endometrial cells present in the peritoneal fluid during menstruation can actually attach and invade the peritoneal surface and furthermore, it has been shown that endometrial cells are not commonly present in peritoneal fluid.<sup>5</sup> Sampson's theory also fails to explain the presence of endometriosis in such remote areas as the lungs, skin, lymph nodes and breasts.

An alternative hypothesis proposes that these lesions are of Mullerian origin and arise from Mullerian nests after their differentiation into mature endocervical, uterine or fallopian tissue. When the immunohistological phenotype of a case of Mullerianosis was compared with that of four other normal uterine endocervices, the endocervicosis glands displayed a stronger expression of antibodies reactive to endocervical glands such as HBME-1, oestrogen receptor and progesterone receptor.<sup>6</sup> These findings constituted further arguments for the Mullerian origin hypothesis.

The third, and oldest, concept in the pathogenesis of endometriosis was developed by Ridley in 1968. In this competing theory, metaplasia of peritoneal and ovarian tissue is thought to give rise to endometriotic deposits outside the uterine cavity.

These hypotheses are not however mutually exclusive, and several authors argue that more than one mechanism may play a role in the origin of Mullerianosis in the individual patient.

## Histopathology

Microscopic examination typically reveals extensive involvement of the bladder wall. In endocervicosis there is evidence of irregularly disposed benign appearing or mildly atypical endocervical-type glands some of which are cystically dilated.<sup>8</sup> In endosalpingiosis, there is evidence of ciliated cells and glands lined by non-specific cuboidal or flattened cells with eosinophilic cytoplasm (as was the case with this patient). Often one also finds some endometriotic stroma, indicating a relationship of these lesions with endometriosis.

## Urinary tract endometriosis

Endometriosis often dominates the clinical picture in Mullerianosis of the urinary tract. Urinary tract involvement by endometriosis is uncommon, and occurs in 1-5% of cases.<sup>9</sup> The process of endometriosis most commonly affects the bladder (85%), however the ureter, kidney and urethra can also be involved (10%, 4% and 2% of cases respectively).<sup>10</sup> When the bladder is involved, the lesion is usually situated in the posterior wall or at the dome, but endometrial lesions can rarely involve the bladder base. Ureteral endometriosis usually occurs below the pelvic brim and can be classified as being intrinsic or extrinsic with a 1:4 ratio respectively.

Involvement of the ureter may lead to urinary tract obstruction. Involvement can be unilateral (the left ureter being more commonly affected than the right), or bilateral (particularly in patients with extensive pelvic endometriosis).<sup>11</sup> Ureteral endometriosis is usually diagnosed in women aged between 30 and 35 years. It is uncommon (and therefore even more likely to remain undiagnosed) in postmenopausal women. Pathologic and clinical studies report that most patients with involvement of the ureter by endometriosis will have hydronephrosis, and a third of these cases will also have evidence of pyelonephritis. As many as 25-50% of nephrons are lost when ureteral endometriosis is present. Rare cases of renal failure caused by bilateral obstruction have been reported, but the true incidence of end-stage renal failure caused by endometriosis is unknown.

## Clinical presentation of ureteral endometriosis

With intrinsic involvement the disease is clinically silent in most cases, with only one third of patients having symptoms (cyclical flank pain, dysuria, frequency, urinary tract infections or haematuria).<sup>12</sup> With extrinsic disease, the symptoms are usually less specific and can be mistaken for the symptoms of post-operative adhesions, interstitial cystitis, irritable bowel syndrome, acute appendicitis or other gynaecological pathology.

It is rare for a patient to present with acute renal failure, but about a third of patients are found to have reduced renal function at diagnosis. The silent loss of one renal unit is not infrequent and often, the non-functioning kidney is discovered incidentally.

## Diagnosis

The diagnosis of such a rare entity is a difficult one. Ureteral endometriosis, and the rarer variants of endosalpingiosis and endocervicosis, should be considered in women with renal obstruction that is not caused by urolithiasis, particularly in premenopausal women with severe menstrual related symptoms.

Because a large percentage of patients with ureteral obstruction do not present with flank pain, imaging of the upper urinary tract in all patients with pelvic endometriosis is recommended.<sup>13</sup> Ultrasound is the initial modality of choice to exclude hydronephrosis.<sup>14</sup> ACT scan may help define the exact volume and location of the disease.

Ureteroscopy is particularly useful in the diagnosis of intrinsic endometriosis. It offers the possibility of biopsy for histological diagnosis of the ureteral lesion. Laparoscopy allows direct localisation of endometrial tissue around the ureter. Its role in intrinsic endometriosis is thus limited. In extrinsic endometriosis, its role is primarily to identify the sites and the extent of the disease.

## Outcome and prognosis

The prognosis depends on the time of diagnosis. In cases of early diagnosis, timely medical or surgical intervention may prevent renal deterioration, although recurrence is a distinct possibility.<sup>15</sup>

Unfortunately in the majority of cases of ureteral endometriosis, patients present late and already have evidence of long standing obstruction (with shrunken kidneys or dilated kidneys with extremely thin cortices). In bilateral obstruction there can be severe renal impairment which might require renal replacement therapy.

## Treatment

Medical therapy aims to induce quiescence of active endometrial deep lesions. Progestins should be considered as first-line medical treatment for temporary pain relief. Hormone therapy, in the form of Danazol or GNRH analogues, should be offered to patients of child bearing age who have early stage disease and wish to have children.<sup>13</sup>

Ureteral lesions that cause obstruction can be treated by ureteric stenting. However, in cases of more extensive involvement, the surgical management might include ureteroneocystostomy, ureterolysis with end-to-end anastomosis, or even autotransplantation.<sup>16</sup>

Traditionally, the procedures are done by open surgery, however, laparoscopic surgical correction is increasingly becoming more important in those centres with specialist experience.<sup>17</sup> It is still being debated which of the two options (whether either segmental resection and anastomosis or ureterolysis) is preferable.<sup>18</sup> Recent studies suggest that laparoscopic ureterolysis can be an effective treatment option, although there is a high recurrence rate. In more extensive disease, ureteric reimplantation onto a psoas hitch is preferable.<sup>19,20</sup> In symptomatic patients with long standing obstruction and irreversible renal dysfunction, laparoscopic nephrectomy can be offered to relieve pain.

## Conclusion

Urinary tract endometriosis is an uncommon problem and can be a silent cause of unilateral or bilateral ureteric obstruction. Mullerianosis represents an exceedingly rare variant of this disease. Clinicians caring for patients suffering from endometriosis should have a high index of suspicion for ureteric involvement and are advised to regularly monitor renal function and perform ultrasound examination of the renal tract. This is particularly important in patients who have undergone previous pelvic surgery or who have more extensive disease. In the more severe cases, open surgery is the treatment of choice, with conservative laparoscopic surgery being a safe and feasible option. Hormonal therapy is appropriate as adjuvant treatment.

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