Review Article

Immediate ureterovaginal fistula following oocyte retrieval: A case and systematic review of the literature

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Abstract

The aim of this study is to report a case of acute ureterovaginal fistula (UVF) formation with immediate symptomatic presentation after transvaginal ultrasound-guided oocyte retrieval (TVOR) for *in vitro* fertilization (IVF) and to perform a systematic literature review of ureteral injuries during TVOR. A 33-year-old woman with a history of anovulatory infertility presented with severe abdominal pain and vaginal leakage immediately following TVOR for IVF. We systematically reviewed the current literature regarding ureteral injury resulting from TVOR and present a case of timely identification and management of a UVF followed by a successful pregnancy. Computed tomography cystogram with intravenous contrast and left retrograde pyelogram confirmed the diagnosis of UVF which was managed by placement of the left ureteral stent. The IVF cycle was converted to a freeze-all cycle. The ureteral stent was removed 4 weeks later, and a subsequent frozen embryo transfer cycle resulted in pregnancy. We present the 13th case of ureteral injury and the fourth case of UVF following TVOR. UVF formation is a rare complication after TVOR and may result in serious long-term morbidity if it is not identified and treated promptly. Clinicians must exercise a high degree of suspicion and prompt evaluation for potential ureteral injuries in women presenting with abdominal pain, urinary symptoms, or vaginal leakage following TVOR.

Key Words: Complication, *in vitro* fertilization, transvaginal oocyte retrieval, ureteral injury, urinary fistula

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INTRODUCTION

Transvaginal ultrasound-guided oocyte retrieval (TVOR) is standard of care for a couple undergoing *in vitro* fertilization (IVF), with >100,000 retrievals performed annually in the US.[1] Its minimally invasive nature, high efficacy, low complication rates, and the added advantage of not requiring general anesthesia have made it the preferred approach.[2,3] Complication rates are low, with most studies citing a <5% complication rate.[4] The most common complications include severe abdominal pain (3%), vaginal

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bleeding (3%–8%), mild pelvic infections (~1%), and pelvic abscesses (0%–0.6%).[5,6] Injury to pelvic viscera including the ureter and bladder are far less common, and ureteral injury has been reported in only 13 prior cases.[2-5,7-15] Such ureteral injuries have been associated with a wide range of complications, including three cases of delayed ureterovaginal fistula (UVF).[3,9,12]

We report the first case of UVF as an acute postoperative complication of TVOR in which the patient presented with severe flank pain and copious leakage of fluid per vagina immediately following the procedure.

CASE REPORT

A 33-year-old woman with a history of primary, anovulatory infertility underwent TVOR for planned IVF. The patient had a history of Class II obesity (body mass index [BMI] 35.6 kg/m^2) and sleep apnea. She had a history of a dilation and curettage and was also previously diagnosed with endometrial intraepithelial neoplasia (EIN) and was treated with megestrol acetate for 3 months. She had a negative endometrial biopsy before initiating treatment. After failing numerous ovulation induction cycles, the decision was made to proceed with IVF. She underwent a GnRH agonist down-regulation gonadotropin stimulation protocol and was triggered on stimulation day 10.

TVOR was performed under monitored anesthesia care during which both ovaries were easily visualized and multiple preovulatory follicles were observed. The patient's co-morbidities required minimized depth of anesthesia resulting in patient movement complicating the retrieval. Follicular aspiration was particularly challenging on the left side but ultimately resulted in recovery of 19 oocytes.

On emergence from anesthesia, the patient reported immediate and significant sharp, predominantly left-sided lower abdominal and back pain. After an hour, her pain was controlled and she was discharged. She presented to a local emergency room (ER) while en route home due to recurrent severe lower abdominal pain, emesis, and copious leakage of vaginal fluid.

In the ER, her vital signs were stable. She described flank pain and sharp left lower quadrant abdominal pain with exacerbations, followed by increased vaginal leakage and back pain. Her abdominal examination demonstrated a diffusely tender and moderately distended abdomen without rebound or peritoneal signs. She received intravenous (IV) analgesics and antiemetics, which moderately improved her pain and resolved her recurrent emesis. Her white blood cell count was elevated to 15.1 g/dL, and the remainder of her laboratories were normal. Of note, she also had a normal urinalysis without hematuria. A transvaginal ultrasound to rule out ovarian torsion demonstrated enlarged, heterogeneous ovaries with adequate blood flow bilaterally and was otherwise normal. She was admitted for pain control and further evaluation. The IVF cycle was converted to a freeze-all embryo cycle.

On admission, a computed tomography (CT) scan of the abdomen/pelvis with IV contrast was obtained on admission and demonstrated bilaterally enlarged ovaries with no evidence of ascites, hematoma, abscess, infection, or hydronephrosis. On hospital day 1, pelvic examination was performed to determine the etiology of the vaginal leakage. No fistula was visualized; however, fluid was noted to be pooling in the vagina. A sample of the fluid was sent for measurement of creatinine and returned 82.6 mg/dL confirming the presence of urine. An IV indigo carmine tampon test demonstrated blue dye in the vagina. An indwelling Foley catheter was placed but did not mitigate the amount of vaginal drainage.

Urology was consulted on hospital day 2 and recommended CT urogram of the abdomen/pelvis with IV contrast to include a delayed phase to evaluate the urinary tract, which demonstrated a small fistula extending from the distal left ureter to the vagina consistent with a UVF [Figure 1]. Cystoscopy demonstrated intact bladder urothelium and cystogram confirmed no evidence of bladder injury. Right retrograde pyelogram was normal; however, the left side revealed a small amount of contrast extravasation from the distal ureter without associated hydroureteronephrosis [Figure 2]. She subsequently underwent successful placement of a left double-J ureteral stent. Her Foley catheter was uneventfully removed 2 weeks later, and the left ureteral stent was removed 4 weeks later in the operating room after a the left retrograde pyelogram demonstrated resolution of the UVF.

Figure 1: Computed tomography cystogram with intravenous contrast demonstrates the (a) left ureter proximal to fistula; (b) a slight narrowing of the distal left ureter; (c) a small fistula extending from the distal left ureter to the vagina; (d) extravasation of contrast

Eight weeks later, the patient elected to undergo a frozen embryo transfer of a single 5-day blastocyst. At the time of publication, the patient had an ongoing clinical pregnancy at <28 weeks of gestation.

MATERIALS AND METHODS

The preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines were utilized in the design and execution of this study. We performed a systematic literature review of the National Library of Medicine PubMed database on March 1, 2016 for all articles published before this date related to ureteral injuries during TVOR. The database was searched using the following keywords: Transvaginal oocyte retrieval, oocyte retrieval, oocyte recovery, ureteral injury, ureteral trauma, ureteral obstruction, UVF, and ureteral hemorrhage. The search was limited to English language articles. The reference lists of all primary and review articles were thoroughly searched to ensure a comprehensive inclusion of all relevant articles. After a preliminary screen was performed of all titles and abstracts, the full texts of the potentially eligible studies were obtained. These articles were then reviewed and studies were selected that included cases of any type of iatrogenic ureteral injury, which resulted from TVOR for IVF. Thirteen articles were identified including twelve case reports of ureteral injury during TVOR and one prospective review of complications following TVOR that included a single case of ureteral injury. The thirteen articles were included in the systematic review on ureteral injury following TVOR [Figure 3]. Data were extracted from all studies independently by the primary authors.

DISCUSSION

TVOR is a safe, simple, and efficacious procedure.[16] Ureteral injury is exceedingly rare but can lead to significant urologic morbidity. We report the fourth case of UVF formation following TVOR and the first case in which a patient presented with acute symptoms immediately following the procedure.

To review, the ureter passes anterolaterally over the anterior fornix of the vagina and therefore lies in the direct path of the aspiration needle during TVOR. Given its anatomic position, ureteral injury is surprisingly rare.[3] Anatomic distortion can be caused by both the pressure of the transvaginal ultrasound probe and conditions commonly associated with female infertility such as endometriosis, pelvic inflammatory disease, and prior gynecologic surgery. Such distortion may increase the risk of ureteral injury.[8]

There are 13 previous reports in the literature of ureteral injury at the time of oocyte retrieval with a wide range of clinical presentations [Table 1].[2-5,7-15] Patients were between the ages of 26–37 and presented between 2 h to a few months with pelvic pain, fever, dysuria, nausea, emesis, continuous leakage per vagina, and gross hematuria.[10,14] Four out of 13 patients had ureteral obstruction, two of which were managed with ureteral stent placement, one required ureteral re-implantation, and one patient ultimately required nephrectomy secondary to renal failure.[11,13-15] Two out of 13 patients presented with gross hematuria and clot retention, one immediately postoperatively and one patient 4 days later, both of whom were ultimately managed with ureteral stent placement.[2,4] One patient was diagnosed with uroretroperitoneum and a second with a ureteral perforation; both injuries were managed with ureteral stenting.[8,10] Two patients presented with unspecified ureteral lesions, one patient had clear vaginal leakage and was treated with ureteral stenting,[7] whereas the other patient's management was not reported.[5] Finally, three patients presented with

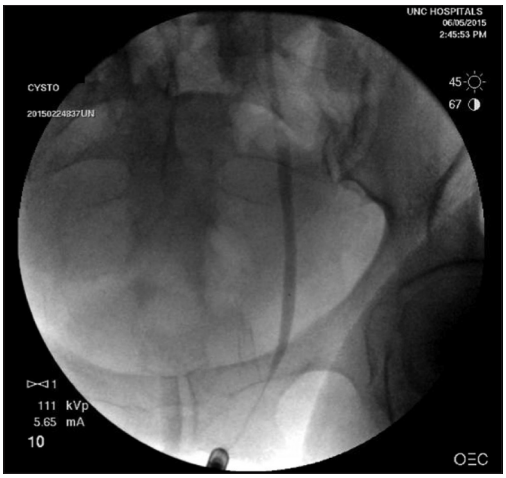

Figure 2: Intra-operative fluoroscopy demonstrates left retrograde pyelogram with a small amount of extravasation of contrast from the left distal ureter

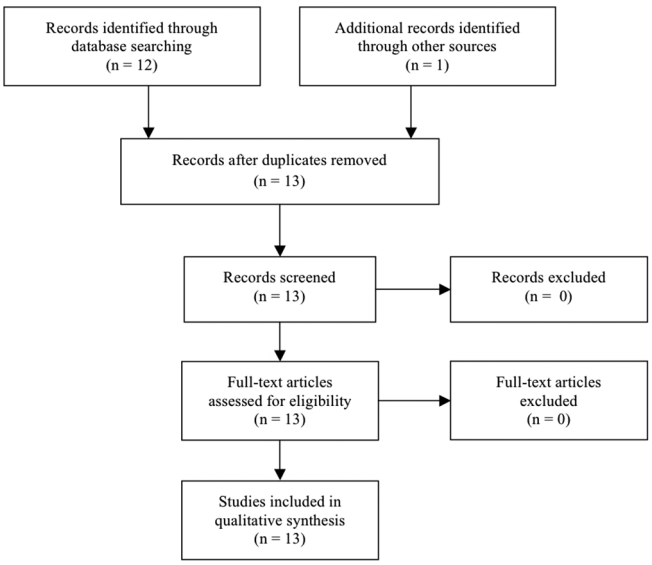

Figure 3: Flow diagram representing study selection

Table 1: Summary of literature published on ureteral injury as a result of transvaginal oocyte retrieval

Author	Patient age	Infertility etiolog	Anatomic/prior pelvic surgery	Difficult TVOR	Presenting symptoms	Time to presentation	Work-up	Diagnosis	Treatment	Pregnancy
Jones *et al*. (1985)	34	Endometriosis	• Endometriosis with adhesions • Prior LOR (4) • Prior TVOR (2)	No	Groin pain, urinary frequency, emesis	4 months	RUS	• Chronic ureteral obstruction • Pyelonephritis	• Nephrostomy tube • Laparoscopy • Nephrectomy	Unknown
Cahill *et al*. (1994)	30	Unknown	• Uterine pexy • Laparoscopy • Pelvic adhesions	Unknown	Abdominal pain, fever	Unknown	PUS, IV pyelogram	• Ureteral obstruction • Large pelvic hematoma	• IV Antibiotics • Ureteral stenting	Unknown
Coroleu *et al*. (1997)	33	1° male factor infertility	• None	No	Abdominal pain, dysuria, vomiting, peritoneal signs	5 days	PUS, RUS, cystoscopy, cystogram, IV methylene blue	• Ureterovaginal fistula with vaginal wall urinoma	• I&D of vaginal urinoma • Laparotomy with ureteral reimplantation	Yes
Fugita *et al*. (2001)	41	Unknown	• Laparoscopic myomectomy • Prior TVOR (5)	Unknown	Dysuria, frequency, fevers, flank pain	2 weeks	RUS, antegrade nephrostogram, CT A/P	• Ureteral obstruction	• Nephrostomy tube • Laparoscopic ureteral reimplant	Unknown
Miller *et al*. (2002)	34	Unknown	• Obesity (60 kg) • Laparoscopy	No	Lower abdominal pain, flank pain, emesis	7 hours	PUS, RUS, CT A/P, cystoscopy, ureteroscopy	• Acute ureteral obstruction	• Ureteral stenting • IV Antibiotics	No
Ludwig *et al*. (2006)	_	Unknown	Unknown	Unknown	Abdominal pain	Unknown	Unknown	• Ureteral lesion	• Unknown	Unknown
Corleta *et al*. (2008)	31	Male factor infertility	• Normal pelvic anatomy on prior laparoscopy	No	Lower abdominal pain, flank pain, vaginal leakage	12 hours	PUS, vaginal fluid creatinine, RGP	• Ureterovaginal fistula	• Ureteral stenting	No
Fiori *et al*. (2006)	33	Voluntary oocyte donation	• C-section (2)	No	Abdominal pain, dysuria, tachycardia	2 hours	PUS, RUS, MRI A/P, CT Urogram	• Urinoma of the retroperitoneum	• Ureteral stenting • IV Antibiotics	Not applicable
Mongiu *et al*. (2009)	33	Unknown	2 prior TVOR	Unknown	Fever, cramping lower abdominal pain	2 days	US, vaginal fluid creatinine, tampon test, cystoscopy, methylene blue	Ureterovaginal fistula	Nephrostomy tube	Yes
Grynberg *et al*. (2011)	26	1° ovulatory & male factor infertility	• PCOS	No	Pelvic pain, uneasiness, lower back pain	24 hours	PUS, RUS, CT Urogram	• Ureteral perforation with extravasation of contrast	• Ureteral stenting	Yes
Catanzarite *et al*. (2015)	34	Male factor infertility	• None • Normal BMI (20.8)	No	Gross hematuria, clot retention	4 hours	PUS, cystoscopy, laparoscopy, RGP, ureteroscopy	• Ureteral injury • Hematuria with clot retention	• Ureteral stenting • Clot evacuation • Hematuria catheter	Yes
Burnik Papler *et al*. (2015)	28	Endometriosis Uterine Factor	• Endometriosis s/p lap ablation • Uterine septum s/p resection	No	Lower abdominal pain, adnexal tenderness	1 day	PUS, RUS, cystoscopy, ureteroscopy	• Ureteral injury • Hematuria • Acute blood loss anemia	• Clot evacuation • Ureteroscopic fulguration • Ureteral stenting	No
Vilos *et al*. (2015)	37	Unknown	• Obesity (BMI 42) • Prior IUI (3) • Prior TVOR (3) • Prior miscarriage	Yes	Clear vaginal leakage	12 hours	CT Urogram, cystoscopy	• Ureteral injury	• Ureteral stenting	No
Present study	33	Anovulatory infertility	• Obesity (BMI 36) • Sleep apnea • EIN	Yes	Lower abdominal pain, flank pain, vaginal leakage, vomiting	2 hours	PUS, vaginal fluid Cr, CT Urogram, cystoscopy, cystogram, RGP	Ureterovaginal fistula	Ureteral stenting	Yes

C-section: Cesarean section, Cr: Creatinine CT A/P: Computed tomography of abdomen/pelvis, Cysto: Cystourethroscopy, EIN: Endometrial intraepithelial neoplasia, I&D: Incision and drainage, LOR: Laparoscopic oocyte retrieval, MRI A/P: Magnetic resonance imaging of abdomen/pelvis, PCOS: Polycystic ovarian syndrome PUS: Pelvic ultrasound RGP: Retrograde Pyelogram RUS: Renal ultrasound, TVOR: Transvaginal oocyte retrieval

UVF.[3,9,12] We present the fourth reported case of UVF following TVOR.

Coroleu *et al*. reported the initial case of UVF after TVOR in 1997.[12] This case involved a 33-year-old female with a history of primary infertility for 7 years with a severe male factor etiology. She developed symptoms 5 days after the procedure including severe abdominal pain, dysuria and bladder spasms. She presented 7 days postoperatively and underwent renal ultrasound and cystoscopy, which demonstrated a mass posterior to the right hemitrigone causing external compression of the bladder. She underwent transvaginal drainage of a serosanguinous fluid collection within the vaginal wall. Only following incision and drainage of the fluid collection did she develop passing of urine per vagina, unlike the other cases in which leakage was spontaneous. She was later diagnosed with an UVF and was ultimately managed with an open ureteral reimplantation.

von Eye Corleta *et al*. subsequently reported a case in 2008 involving a 31-year-old female again with a 7 year history of primary infertility due to male factor, who presented 12 h after surgery with clear, odorless, vaginal drainage, and recurrent episodes of abdominal pain. She underwent ureteral stent placement.[3]

Finally, in 2009, Mongiu *et al*. reported a case of a 33-year-old female with history of unexplained infertility who presented after TVOR with a fever, leukocytosis and abdominal pain without urinary symptoms. She was empirically treated with antibiotics for presumed oophritis, her symptoms resolved, and she underwent embryo transfer 5 days later. Seven days after TVOR, she began developing increasing leakage of fluid per vagina. She was diagnosed with a delayed UVF after she presented with continuous vaginal leakage 21 days after oocyte retrieval. She was ultimately managed with nephrostomy tube placement after unsuccessful ureteral stent placement.[9]

Our patient is similar to those previously reported cases of UVF formation following TVOR in that her presenting symptoms included flank pain, lower abdominal pain and vaginal leakage. However, the delayed interval between presentation and diagnosis is much shorter in this case. This patient's presentation was unique given the acute onset of symptoms, including vaginal leakage immediately postoperatively and presentation for evaluation within 2 h of the oocyte retrieval. In all three prior cases of UVF formation, time to re-presentation was at least 12 h, and there had been a delayed onset of vaginal drainage of urine.[3] Of note, our patient had no signs of peritoneal irritation on presentation – likely due to early drainage of urine per vagina resulting in absence of true ureteral obstruction or urinoma formation.

Risk for ureteral injury may be increased with distortion of pelvic anatomy due to prior surgery or endometriosis. The case report presented by von Eye Corleta *et al*. was of a patient with a history of diagnostic laparoscopy, which could theoretically alter pelvic or abdominal anatomy by formation of adhesions.[3] The case of ureteral injury resulting in UVF reported by Mongiu *et al*. had undergone two prior TVORs, which could potentially have resulted in alterations in her pelvic anatomy due to adhesions as well.[9] While our patient had a history of EIN and dilation and curettage, it is unlikely that this would contribute to adhesions within the pelvis. The patient's retrieval was, however, complicated by her sleep apnea and elevated BMI.

This is the third case of a pregnancy following successful treatment of an UVF after TVOR.[9,12] In addition, this is the second case of UVF that was successfully managed conservatively with ureteral stenting, demonstrating that this treatment option should be considered before more invasive interventions such as nephrostomy tube placement or open surgical repair.[3]

CONCLUSIONS

TVOR remains a safe procedure; however, it is important to recognize the potential for significant, albeit rare, complications. The relatively rare nature of genitourinary complications following TVOR makes case reporting and systematic literature review necessary to empower urologists and reproductive specialists to identify ureteral injury early to allow for prompt intervention and prevention of long-term morbidity.

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Conflicts of interest
There are no conflicts of interest.

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