Why are recurrent cervical cancers of the pelvic stump misdiagnosed as interstitial cystitis?: The urologist's point of view based on a case report

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Abstract

A 50-year-old female who had undergone laparoscopic total hysterectomy at a local clinic owing to leiomyoma of the uterus was referred to our hospital after having dysuria, urgency, frequency, lower abdominal pain and right flank pain over several months. After routine examinations, cystoscopy, computed tomography and magnetic resonance imaging were performed, and non-ulcerative interstitial cystitis accompanied by postoperative fibrosis secondary to a previous surgery was suggested. Pentosan sulfuric polyester (Elmiron, Alza Pharmaceuticals, Mountain View, CA) reduced her severely debilitating symptoms and improved her quality of life. Both the hydronephrosis and the symptoms were relieved by ureteral stent insertion and percutaneous nephrostomy. However, a few days later, she presented with vaginal bleeding along with her previous symptoms, and punch biopsy of the vaginal stump resulted in a diagnosis of adenocarcinoma. Both ureterocutaneostomy with radical cystectomy and lower anterior resection for rectum invasion were conducted. After the slide review of the original specimen from the local clinic, she was diagnosed with recurrent cervical cancer of the vaginal stump.

Introduction

Interstitial cystitis (IC) is a chronic syndrome characterized by the symptoms of urinary urgency, frequency, pelvic pain and nocturia, in the absence of bacterial infection or any other identifiable pathology. In 1987, the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) formulated criteria for a diagnosis of IC.[1] Strict application of the NIDDK criteria requires cystoscopy with hydrodistention to document either a Hunner's ulcer or glomerulations.[1] However, the NIDDK criteria are too restrictive for clinical use and exclude 60% of patients from the diagnosis. The pathogenesis of IC is not completely understood, but is thought to be multifactorial; therefore, early identification of IC can be challenging, because the clinical presentation is similar to other common conditions, including recurrent urinary tract infection, endometriosis, chronic pelvic pain, vulvodynia and overactive bladder. We present a case of recurrent cervical cancer after laparoscopic total hysterectomy that was initially misdiagnosed as IC. In this case, a discrepancy was found between the original and the referral histopathological diagnosis.

Case report

On October 15, 2009, a 50-year-old female was referred to the obstetrics and gynecology department of our hospital after having dysuria, urgency, frequency, lower abdominal pain and right flank pain for several months. She had undergone a laparoscopic total hysterectomy because of leiomyoma of the uterus on March 13, 2007, at a local clinic. No abnormal results were found on the physical examination or in the laboratory data, including urine cytology, urinalysis, urine culture and tumour markers CA125 and CA19-9. Computed tomography (CT) revealed both lateral ends of the vaginal stump to be prominent with irregular enhancement, especially on the right side (Fig. 1). The conclusion was that the vaginal lesion was a result of postoperative tissue complications, such as infection or fibrosis. She was referred to the urologist for evaluation and management of her symptoms. Under the impression of IC, she was treated with antispasmodics, digestive medicines, alpha1-blocker and pentosan sulfuric polyester (Elmiron, Alza Pharmaceuticals, Mountain View, CA), and her symptoms improved. Four months later, on February 19, 2010, she visited our hospital presenting with voiding difficulty, dizziness, anorexia, nausea, vomiting, fatigue and flank pain on both sides. Non-contrast CT showed severe hydronephrosis. To resolve the azotemia and hydronephrosis, we conducted a ureteral stent insertion and

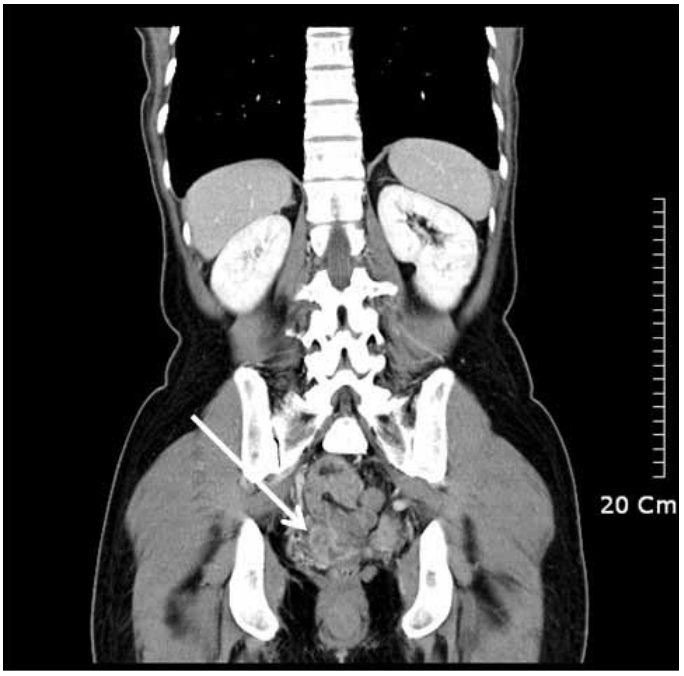

Fig. 1. Initial computed tomography showed prominent both lateral ends of vaginal stump with irregular enhancement, especially right side (arrow). There was no hydronephrosis in both kidneys.

percutaneous nephrostomy. Magnetic resonance imaging (MRI) revealed an approximately 4-cm irregular thickening of the vaginal stump and focal traction of bladder posterior wall at the midline toward the vaginal stump. On the MRI, the vaginal lesion extended laterally to entrap the ureter and showed a low signal intensity on both T2-weighted images and T1-weighted images with an inhomogeneous pattern (Fig. 2a, Fig. 2b). The irregular thickening of the vaginal stump was reported as postoperative tissue complications, such as infection or fibrosis because of the belief that the previous total hysterectomy had been performed because of a benign cause. A biopsy was planned to confirm the pelvic mass and bladder mucosa histopathologically.

Before the planned biopsy for the pelvic mass, the patient presented with vaginal bloody discharge. In consultation with obstetrics and gynecology, on speculum examination, the vaginal stump appeared to be a bloody and cancerous lesion; a punch tissue biopsy of the vaginal stump was conducted. The pathologic report for the punch vaginal stump biopsy was adenocarcinoma, and the results of urine cytology, including cytospin, showed atypical cells consistent with adenocarcinoma. There was no evidence of bone metastasis in a bone scan.

On May 18, 2010, she underwent surgical procedures including both ureterocutaneostomy with radical cystectomy and lower anterior resection for rectal invasion. Intraoperatively, there were multifocal ulcerative lesions in the proximal part of the vagina and a pelvic mass adhered to the vagina, rectum and the posterior wall of the bladder. Both ureters were encased by the pelvic mass around the distal parts. The pelvic mass was diagnosed histopathologically as adenocarcinoma, well-differentiated and 5.5 × 4.5 cm with extension to the muscle layer of the urinary bladder and submucosa of the rectum. To decide on a further treatment plan, we first reviewed the slides of her primary surgery (from the laparoscopic total hysterectomy at the local clinic in 2007). At the local clinic, the original histopathologic diagnosis was of leiomyoma, adenomyosis uteri, chronic cervicitis and atypical glandular hyperplasia of endocervical glands. However, the review in our hospital was leiomyoma, adenomyosis, atrophic endometrium and atypical glandular proliferation highly suggestive of adenocarcinoma of the cervix. Chemotherapy with paclitaxel and carboplatin was started 1 month later for stage IV cervical cancer. She died of progressive disease 7 months after surgery.

Discussion

There is no single test to confirm the diagnosis of IC and its pathophysiology remains unknown. The gold standard for diagnosis has been to identify symptoms, exclude underlying causes and perform cystoscopy with hydrodistention demonstrating bladder glomerulations or Hunner's ulcers. The actual prevalence rate is unknown, and estimates range widely from 67 per 100 000 to 575 per 100 000 based on the diagnostic criteria and methods used to estimate the rate.

There has been a recent trend to diagnose IC by use of noninvasive methods, such as the potassium sensitivity test (PST);[2,3] a pelvic pain, urgency and frequency (PUF) questionnaire;[4] and the O'Leary-Sant IC symptom and problem indexes.[5] However, the minimally invasive tools for diagnosing IC in the office are not specific for IC, and false-positive results may occur with bacterial cystitis, bladder cancer, follicular cystitis, radiation cystitis and other inflammatory diseases of the bladder. Further studies are needed to reach a consensus on the diagnostic criteria for IC.

According to one widely held theory, the symptoms of IC originate from a defect in the glycosaminoglycan component of the mucin layer that covers and protects the bladder urothelium. A deficiency of this layer is thought to cause IC. Another working theory its etiology includes mast cell abnormalities. Increased numbers of submucosal mast cells are found in IC patients and antigenic exposure of mast cells causes the release of pharmacologically active mediators (e.g., histamine, prostaglandins, leukotrienes and tryptases) that have significant effect on smooth muscle, vascular epithelium and inflammation. As another additional approach, Wesselmann took into account the observation that IC shares many features with other chronic nonmalignant visceral pain syndromes by the neurophysiologic mechanisms.[6]

The clinical presentation of IC is similar to other common conditions, including recurrent urinary tract infection,

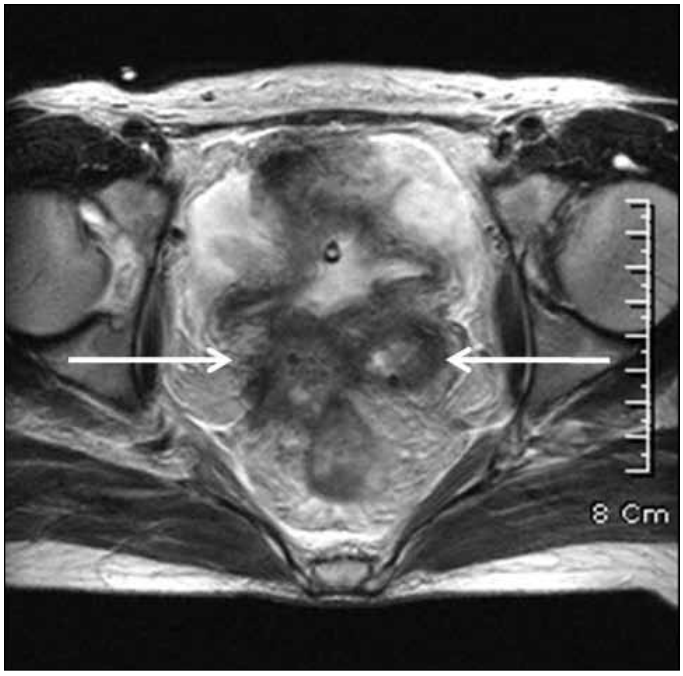

Fig. 2a. T2-weighted magnetic resonance imaging showing irregular thickening of vaginal stump (arrows) and focal traction of bladder posterior wall at midline toward vaginal stump.

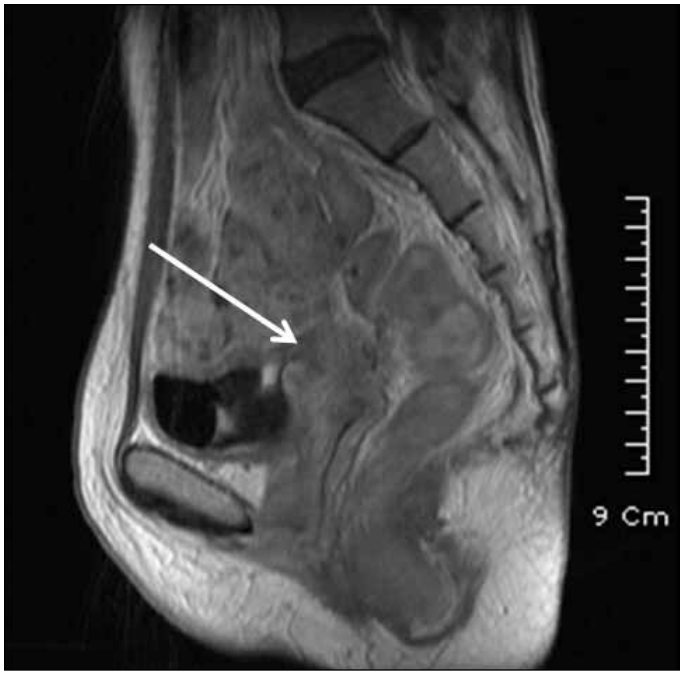

Fig. 2b. T1-weighted magnetic resonance imaging showing sagittal section of lesions (arrow) around vaginal stump with suspicious bladder invasion.

endometriosis, chronic pelvic pain, vulvodynia and overactive bladder. The diagnosis of endometriosis is based on history, physical examination, laparoscopic examination and confirmation through histology, although IC and endometriosis frequently coexist. Diagnosing the cause of chronic pelvic pain can be complex and challenging, as many conditions can cause chronic pelvic pain and can occur concurrently in many women with IC. Vulvodynia is defined as chronic vulvar burning, stinging or pain in the absence of clear pathology. In a case-control study, 47 women with IC were compared with 47 IC-negative women and the prevalence of vulvodynia in the 2 groups was 85.1% versus 6.4%, respectively ($p < 0.0001$).[7] IC should be considered in all patients who present with vulvodynia. Moreover, the patients with IC actually had transitional cell carcinoma as the cause of symptoms. Tissot and colleagues reviewed 600 patient records retrospectively.[8] Of the 600 patients previously diagnosed with IC, 6 (1%) had transitional cell carcinoma as the cause of irritative voiding symptoms. In 1974, Utz and Zincke reported on the long-term follow-up of 486 patients treated for IC and found that 1.3% of 224 women and 23% of 53 men subsequently were shown to have carcinoma in situ.[9]

In this case, after surgical procedure, the initial pathological reports were suggestive of vaginal adenocarcinoma with bladder and rectal invasion. The final diagnosis, recurrent cervical cancer of vaginal stump, was not made until the histopathological slide review for the original specimen at local clinic was analyzed. By reviewing 351 cases, Khalifa and colleagues suggested that the mandatory slide review in gynecologic oncology is essential in managing gynecologic cancer patients because it completes reporting on missing parameters required for planning subsequent therapy in 10.1% of cases and recognizes discrepancies altering management in 8.3% of patients.[10] They emphasized that the inter-institutional pathology review is important, although it poses a significant burden on the system through increasing workload and cost.

Conclusion

Suspicion should be maintained in patients who persistently had irritative lower urinary tract symptoms and re-evaluation should be performed when appropriate. IC continues to remain a diagnosis of exclusion. In addition, before treating and managing patients referred to tertiary care, a pathologic review of the original specimen from previous clinics is suggested.

Competing interests: None declared.

This paper has been peer-reviewed.

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