Squamous Cell Carcinoma of an Ileal Neobladder

- A Case Report -

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CASE REPORT

A 46-year-old woman was seen at the urological unit with a one-week history of urinary frequency and gross hematuria. The patient had undergone a left nephrouretectomy, partial cystectomy, hysterectomy and enterocystoplasty for tuberculosis 25 years previously. Abdomen and pelvic computerized tomography images revealed the presence of a 6.3 cm homogeneous mass at the anterior wall of the ileal neobladder (Fig. 1). A transurethral resection was performed. The biopsy obtained from the neoplasm showed a moderately differentiated squamous cell carcinoma. The patient underwent a radical cystectomy of the neobladder and orthotopic neobladder formation. Grossly, the resected neobladder had two components including the small bowel and bladder that measured 20 × 7 cm. In the neobladder, an 11 × 8 cm-sized, polypoid mass with a verrucous configuration was observed in the glistening surface background, which was seen with a friable configuration in the cut surface (Fig. 2). Microscopically, the mass was a squamous cell carcinoma accompanied by a spectrum of squamous cell lesions including squamous...
dysplasia, squamous papilloma and squamous metaplasia (Fig. 3). The tumor cells expressed COX-2 (Fig. 4B). The adjacent non-tumor epithelium consisted of columnar epithelium of the small bowel. One month after the surgery, an abnormal odor
and protruding vaginal mass developed. A pelvic CT showed a recurrent mass in the neobladder. A biopsy of the vaginal mass showed poorly differentiated carcinoma with extensive necrosis in up to 90% of the specimen. In addition, the tumor cells had an extremely unusual appearance (Fig. 4C) and expressed vimentin (Fig. 4D) and cytokeratin, which was consistent with a sarcomatoid carcinoma. Thereafter, multiple metastatic nodules were identified in the liver, lung and peritoneum. The bladder mass was enlarged and a rectovaginal fistula developed, resulting in a very large conglomerated mass in the lower abdomen. The patient died four months after the radical cystectomy.

**DISCUSSION**

Keratinizing squamous cell metaplasia of the bladder or neobladder is not common and the pathogenesis remains unclear. Moreover, the presence of a squamous cell carcinoma with squamous metaplasia is rare in the urinary tract and is extremely rare in a neobladder with ileum. The present case had a broad spectrum of squamous cell lesions, including a squamous cell carcinoma, squamous dysplasia, squamous papilloma and non-tumor squamous metaplasia in the ileal mucosa of the neobladder. In contrast to non-keratinizing squamous metaplasia, a keratinizing squamous metaplasia is usually associated with chronic irritation and risk for an invasive carcinoma. Urinary tract infections or irritations have most frequently been incriminated as causes of squamous metaplasia. Several conditions including urinary calculi, urinary tract obstruction, a fistula, tumor, bladder extrophy, neurogenic bladder, previous bladder surgery, and vitamin A deficiency are also potential causes. Among these conditions, tuberculosis has been traditionally associated with squamous metaplasia of the urinary tract, particularly prior to the availability of tuberculosis medications.
The patient in the present report underwent a cystectomy for tuberculosis 25 years previously and received tuberculosis medication for many years. These findings support tuberculosis as an etiology of squamous metaplasia of the urinary bladder. For squamous metaplasia, chronic inflammation has been implicated in the development of bladder cancer, especially squamous cell carcinoma. However, the mechanism associated with an increased risk of squamous cell carcinoma due to chronic inflammation has not been elucidated. Shirahama et al. suggested that inflammation stimulates production of COX-2 by bacterial lipopolysaccharides or inflammatory cytokines, and the increased level of COX-2 metabolically activates nitrosamines, which are produced in patients with chronic urinary tract infections, resulting in squamous cell carcinoma. In the present case, the patient had a marked increase in the expression of COX-2. The production of COX-2 may have contributed to the development of squamous cell carcinoma. However, we did not study the nitrosamine activation status in this case. Squamous cell carcinomas of the urinary bladder account for approximately 5% of all malignant bladder tumors, including some tumors that develop on the background of chronic cystitis with marked squamous metaplasia. According to a study by Newman et al., death within the first year occurred in 59% of patients with a vesical squamous cell carcinoma. However, a series of squamous cell carcinomas developing from squamous metaplasia have indicated a more ominous prognosis, where six out of eight patients died within 15 months after treatment. The development of a neoplasia after ureterosigmoidostomy is a well known complication, due to the mixing of urinary and fecal material. The number of patients that have undergone procedures using intestinal segments, in the urinary tract, such as an ileal neobladder diversion, has increased steadily, and the number of malignancies, including most commonly adenocarcinomas and less commonly various other tumors, have been reported.

REFERENCES