



## LITERATURE REVIEW

# A CHALLENGING DIAGNOSIS AND TREATMENT OF PRIMARY BLADDER ADENOCARCINOMA

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### Abstract

Bladder adenocarcinoma is a histological variant that only represents 0.5-2% of cases. The bladder cancer is expected to affect one in 27 men and one in 89 women over the course of their lifetime, with a lifetime risk of approximately 2.2% in the general population in the united states. The bladder can develop primary or secondary adenocarcinomas, with secondary adenocarcinomas being more frequent than primary adenocarcinomas. The primary bladder adenocarcinoma falls into two broad categories: urachal and non-urachal. Patients with non-urachal primary bladder adenocarcinoma appear to have a worse prognosis than those with urachal adenocarcinoma. It is essential to know better about the diagnosis, current treatment, and prognosis of the primary bladder adenocarcinoma. Here we describe the article review regarding the primary bladder adenocarcinoma.

**Keyword: bladder adenocarcinoma, diagnosis, treatment**

## INTRODUCTION

The sixth most common cancer in the United States, bladder cancer is expected to affect one in 27 men and one in 89 women over the course of their lifetime, with a lifetime risk of approximately 2.2% in the general population. While the majority of bladder tumors have urothelial histology, adenocarcinoma only accounts for 0.5–2 percent of cases and typically behaves invasively. <sup>1</sup> Males in their sixth decade are more likely to experience it, and common symptoms include hematuria and irritation of the bladder. <sup>2</sup>

Adenocarcinomas of the bladder can be primary or secondary, and secondary adenocarcinomas of the bladder are more prevalent than primary adenocarcinomas. The

phenotype of primary bladder adenocarcinoma, which is histologically pure glandular, is derived from the bladder urothelium. The growth patterns of primary bladder adenocarcinoma include enteric, mucinous, signet-ring cell, not otherwise specified, and mixed patterns. Secondary adenocarcinomas involve the bladder either directly or through metastasis from a distant site. Primary bladder adenocarcinoma (PBA) is a relatively uncommon type that can be broadly divided into urachal and non-urachal adenocarcinomas. Secondary bladder adenocarcinomas typically originate from the colon, prostate, endometrium, cervix, breast, or lung. The colon, the prostate, the rectum, and the cervix were found to be the most common primary sites in a retrospective study conducted by the Royal Hospitals Trust, accounting for 21



percent of secondary neoplasms. The majority of tumors from these locations spread directly to the bladder.<sup>3</sup> Because of their significant morphologic overlap, it can be challenging to distinguish between primary and secondary bladder adenocarcinomas.

## DIAGNOSIS, TREATMENT AND PROGNOSIS

Primary adenocarcinoma of the bladder is a malignant neoplasm derived from urothelium with histologically only glandular type cell. The base of the urinary bladder is the source of many PBA. The male to female proportion is 3:1 in non-urachal cancers when contrasted with 1:1 in the urachal remnants. Unlike urothelial carcinoma, which typically presents as multiple lesions, it typically presents as a single lesion. The tumor may look like a papillary, sessile, solid, or ulcerating lesion on the outside. Due to the abundant production of mucin, the cut surface frequently appears gelatinous.<sup>3,5,6</sup> The carcinoma should only be diagnosed as a primary adenocarcinoma of the bladder when it displays only glandular differentiation. The most crucial and challenging aspect of diagnosing adenocarcinoma of the bladder is distinguishing it from metastatic adenocarcinoma in other organs like the uterus, lung, breast, and colon in many cases.

The uncommon tumor known as urachal adenocarcinoma arises in urachal remnants that are found in the bladder's dome and frequently affects the bladder subsequently. The tissues from the embryonic allantoic stalk linking the bladder and umbilicus make up the urachal leftovers. The finding of urachal adenocarcinoma is an excluding diagnosis. The likelihood of primary or secondary nonurachal adenocarcinoma must be ruled out. The widespread adoption of practical strategy to diagnose a urachal adenocarcinoma described by Johnson et al. consist of tumors located in the bladder dome, a sharp demarcation between the

tumor and the surface epithelium, and the exclusion of adenocarcinoma of other organs that has spread secondarily to the bladder.<sup>3,8</sup> It is important to recognize the diagnosis upfront due to the differences in surgery and chemotherapy as compared to traditional urothelial cancer.<sup>9</sup>

The immunohistochemical staining pattern of urachal adenocarcinoma shows significant overlap with primary bladder adenocarcinoma and metastatic colorectal adenocarcinoma. CK20 and CDX2 are expressed in almost all urachal adenocarcinomas, and CK7, B-catenin, and high molecular cytokeratin expression varies between tumors.<sup>10</sup>

In addition to relying on assumptions regarding sensitivity to multimodal therapy (i.e., chemotherapy, radiation, and intravesical agents), variant histology management is challenging.<sup>2</sup>

Patients with primary bladder adenocarcinoma typically undergo radical cystectomy and pelvic lymph node dissection because the majority of them have a disease that invades muscle. When compared to cystectomy alone, rates of local control (96 vs. 53%) and 5-year DFS (61 vs. 37%) have been reported to be higher in retrospective case series.<sup>11</sup> There is currently no evidence that patients with primary bladder adenocarcinoma benefit from effective neoadjuvant or adjuvant chemotherapy.<sup>2</sup> Adenocarcinoma appears to be unaffected by the conventional MVAC-based cisplatin-based chemotherapy regimens that are effective for urothelial carcinoma.<sup>12</sup>

Patients with non-muscle-invasive bladder adenocarcinomas are frequently treated with cystoscopy and transurethral resection of the tumor.<sup>12,13</sup> BCG or mitomycin-C intravenous therapies may also be effective in some patients<sup>14</sup>



The most common treatment for urachal adenocarcinoma is partial cystectomy with pelvic lymph node dissection and en-bloc resection of the urachal ligament and umbilicus. Urachal adenocarcinoma can be successfully managed with partial cystectomy due to its low malignant potential (15 %), favorable location, and absence of a field defect.<sup>2</sup>

However, radical cystectomy may be required in some cases due to the importance of negative margins and adequate local control, as well as the poor outcomes of salvage surgery. Gemcitabine, 5-fluorouracil, leucovorin, and cisplatin were used in a clinical trial at our institution to treat metastatic disease. The results showed an objective response rate of 30-40% and a median survival of 24 months, up from 12 months.<sup>2,9</sup>

adjuvant chemotherapy might be sufficient enough to be considered in patient with positive margins, lymph node positive, involvement of the peritoneal surface, or where the umbilicus was not resected en-bloc because of the higher risk of relapse following a medical procedure. Combinations of 5-fluorouracil and cisplatin are active in patients with metastases, despite the fact that there is currently no established role for neoadjuvant or adjuvant chemotherapy. Perioperative chemotherapy might be beneficial because the combination's activity has also resulted in surgical consolidation of node-positive disease.<sup>15</sup>

Patients with primary bladder adenocarcinoma appear to have a worse prognosis than those with urachal adenocarcinoma.<sup>9,15</sup> The urachal adenocarcinoma is frequently discovered in younger people than those with bladder adenocarcinoma, therefore it is linked with less comorbidities, which contributes to the positive prognosis. Even after controlling for grade, histologic subtype, stage, age, gender, and surgical therapy, a recent retrospective analysis discovered that patients

with urachal adenocarcinoma (48%) had a better 5-year overall survival than those with non-urachal adenocarcinoma (35%). The distinct clinical outcome of urachal adenocarcinoma and bladder cancer may possibly be caused by inherent anatomical and genetic variations.<sup>16</sup>

## Conclusion

Adenocarcinomas of the bladder can be primary or secondary, with secondary adenocarcinomas being more common than primary adenocarcinomas. Urachal and non-urachal adenocarcinomas are two general categories for the relatively infrequent primary bladder adenocarcinoma (PBA). In comparison to individuals who have urachal adenocarcinoma, patients with primary bladder adenocarcinoma appear to have a worse prognosis. Given the variations in surgery and chemotherapy compared to typical urothelial carcinoma, it is critical to make the diagnosis promptly.

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