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Primary Bladder Adenocarcinoma: A Case Report and Review of the Literature

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ABSTRACT

Urinary bladder cancer is the second most frequent tumour of the genitourinary tract with bladder adenocarcinoma comprising for about 0.2-2% of all malignant bladder tumours. Other primary sites for such tumours include rectum, stomach, endometrium, breast, prostate, seminal vesicles and ovaries. Such non-urothelial bladder tumours with intramural bladder tumour growth may delay the onset of symptoms which may lead to a delay in diagnosis and thereby adversely affecting the prognosis as compared to urothelial bladder tumours. Traditionally bladder adenocarcinomas were believed to be resistant to both chemotherapy and radiotherapy, but recent advancements have shown encouraging responses with adjuvant chemotherapy and radiotherapy.We present here-in a case of primary adenocarcinoma of the urinary bladder highlighting its relative rarity of occurrence and the difficulties encountered in diagnosing primary bladder adenocarcinoma, its management and a review of the literature.

Résumé

Cancer de la vessie est la deuxième tumeur la plus fréquente de l'appareil génito-urinaire avec adénocarcinome de la vessie comprenant de 0,2 à 2% environ de toutes les tumeurs malignes de la vessie. D'autres sites primaires de telles tumeurs comprennent le rectum, l'estomac, l'endomètre, le sein, la prostate, des vésicules séminales et les ovaires. De telles tumeurs de la vessie non-urothéliales avec la croissance intra-murale de la tumeur vésicale peuvent retarder l'apparition des symptômes qui peuvent conduire à un retard dans le diagnostic et, par conséquent susceptible de nuire le pronostic par rapport aux tumeurs de vessie urothéliales.

Traditionnellement les adénocarcinomes de la vessie ont été soupçonnés d'être résistants à la fois la chimiothérapie et la radiothérapie, mais les progrès récents ont montré les réponses encourageant avec la chimiothérapie et la radiothérapie adjuvante.

Nous présentons un cas d'adénocarcinome primaire de la vessie en soulignant sa relative rareté de survenue et les difficultés rencontrées dans le diagnostic de l'adénocarcinome primaire de la vessie, sa prise en charge et revue de la littérature.

Introduction

Bladder cancer is the second most common malignant tumor of the urogenital tract.Primary adenocarcinoma of the bladder is an uncommon malignant neoplasm and accounts for fewer than 2% of all malignant urinary bladder tumors [1] and represents less than 3% of invasive bladder tumors [2]. This neoplasm may be of urothelial or urachal origin with intravesical extension [2].

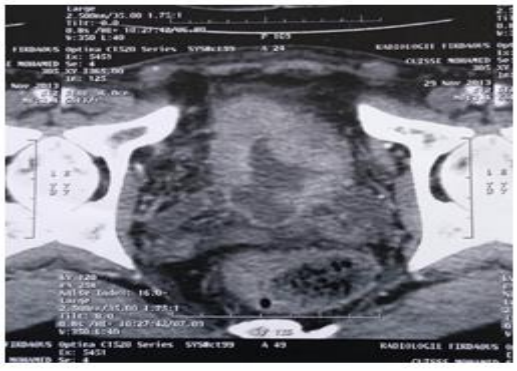
This neoplasm is a source of diagnostic confusion with adenocarcinomas arising in adjacent organs especially colon. These tumors show varied histological picture and degree of differentiation.

Clinical, imaging, histologic, and immunohistochemical correlation should be done while rendering this diagnosis, as prognosis and therapeutic options for primary versus metastatic adenocarcinoma vary widely.

The authors present and discuss a case report of primary adenocarcinoma of the bladder, the difficulties encountered in diagnosing and management of this rare tumour.

Case Report

A 63-year old patient with a smoking history was admitted with complaints of gross hematuria, with small blood clots for the preceding two months without any other associated symptoms. General physical, urological and digital rectal examination was unremarkable. Abdominal ultrasonography suggested a distended urinary bladder with irregular mass lesion of 4.40x3.20x3.98 cm in size projecting from the bladder dome partially along with the right and left lateral walls abutting on the bladder dome without any peritoneal free fluid or signs of distant metastasis. A contrast enhanced abdominal computed tomography revealed an extravesical lesion of 4.5 cm in size [Figure-1a, b, c] with vesical fascia present on either side. The mass was located along the mid anterior surface of the bladder with partially infiltrated perivesical fat but no regional infiltration or metastasis. Extensive clinical and radiologic workup did not reveal digestive tumor.PSA level was normal



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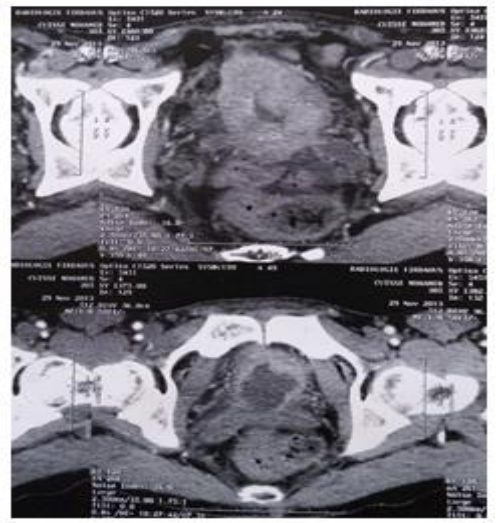

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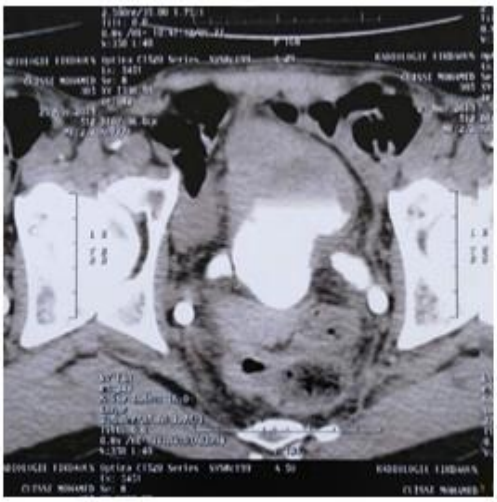

(c)

Fig 1. CT scan image(s) showing urinary bladder tumor on the anterior wall.

The patient underwent an uneventful transurethral resection of the bladder tumor and histopathology report revealed transitional epithelial lining with squamous metaplasia, lamina infiltration with well formed glands lined by mucus secretory columnar epithelium with moderate pleomorphism along with areas of papillary formation and large pools of extracellular mucin in the background with intracellular mucin and signet ring cells, suggestive of an invasive bladder adenocarcinoma.

After informed counselling the patient underwent cystoprostatectomy with ileal conduit urinary diversion (BRICKER) with en-bloc excision of the surgery specimen, and bilateral iliac lymphadenectomy.

The histopathology was reported as primary adenocarcinoma of the urinary bladder invading the bladder muscularis propria, submucosa with partially infiltrated perivesical fat, lymph nodes free of tumor.

The patient was subsequently referred to a medical oncologist, underwent three sessions of adjuvant chemotherapy consisting gemcitabine and cisplatinum and is currently doing well on a six months interval follow-up.

Discussion

Primary malignant epithelial bladder cancers derives from the urothelium in 90% of cases, less frequent are the squamous cell (3-5%) and adenocarcinomas (0.2-2%) as well as sarcomas or metastases from other primary tumors.

Primary adenocarcinoma of the bladder is a malignant neoplasm derived from urothelium of the bladder showing histologically pure glandular differentiation.

This tumor is present usually in the sixth decade of life with a male predilection with a mean age of 63 years [3]. The most common clinical presentation is hematuria [4]. Bladder irritation symptoms are also frequently reported [5]. About 90% of the tumors arising in exstrophied bladder are adenocarcinomas [6]. They are also more prevalent in settings of vesical schistostomiasis [7, 8]

Adenocarcinomas can arise anywhere in the urinary bladder. However, they commonly appear at the trigonum, dome and lateral bladder walls.[9-13].

About two-thirds of adenocarcinomas present as solitary, polypoid or nodular [14], unlike the “usual” urothelial carcinomas which tend to be multifocal [15].

Adenocarcinomas comprise less than 2% of all bladder tumors. The most common adenocarcinomas that spread to the bladder, usually by direct extension are colon, prostate, and tumors of the female reproductive tract. [14]

In many cases of adenocarcinoma of the bladder, the most important and the most difficult task is to differentiate these tumors from metastatic adenocarcinoma from other organs.

The most frequent secondary tumor to involve the urinary bladder is adenocarcinoma of the colon, which morphologically resembles adenocarcinoma of the urinary bladder [16, 17].

There is considerable overlap between colonic and vesical adenocarcinoma, extensive clinical and radiologic workup is required for diagnostic accuracy. Histologically, positive labeling for CK20 and negative labeling for CK7 is usually indicative of colorectal adenocarcinoma [18]. Other immunohistochemical stains have demonstrated a utility for solving this differential diagnostic dilemma. Thrombomodulin (TM) is a specific marker for primary bladder tumors and very rarely shows positivity in colorectal tumors. Unfortunately, the sensitivity of TM is low, with only 59% positivity in primary bladder adenocarcinoma [3].

On the other hand, nuclear staining of b-catenin is relatively specific for colorectal tumors.

As a general rule, the final interpretation should be a combination of histomorphology, immunohistochemical profile and clinical correlation.

Urachal carcinoma is a less common tumor that can present as a bladder mass and should be considered in the list of differential diagnosis. This tumor tends to occur in the dome and anterior bladder wall and usually has a male predominance [19, 20].

Immunostains do not unequivocally discriminate urachal from colorectal adenocarcinoma. Diffuse positivity for 34bE12 may support a diagnosis of urachal carcinoma, while diffuse nuclear staining for b-catenin would favor a colorectal origin [21]. Homogeneous positivity for carcinoembryonic antigen in 100% of urachal adenocarcinomas and in only 29% of bladder adenocarcinomas such as linitis plasticlike signet ring cell carcinoma, has also been reported [22].

Prostatic adenocarcinomas often directly extend into the bladder and may coexist with a bladder adenocarcinoma. The most reliable immunohistochemical marker is prostate-specific antigen (PSA), which stains approximately 90% of poorly differentiated prostatic adenocarcinomas and is negative in bladder adenocarcinomas [19,23].

CA 125, which stains the tumor cells of endometrial and ovarian malignancies, has been reported to be of use to

differentiate endometrial and ovarian carcinoma from primary bladder adenocarcinomas [23]. Vimentin highlights endometrial carcinoma cells as opposed to bladder adenocarcinoma cells [19].

One should also keep in mind of other possible primary tumors that can be responsible for bladder metastasis such as; stomach, breast, vesicle seminal cancers.

Pathological types of adenocarcinoma of urinary bladder include the glandular carcinomas, papillary adenocarcinomas of the colloidal, the signet ring cell cancer and ultimately the mesonephroid or clear cell carcinoma [24, 25].

Prognosis of all histological types of adenocarcinoma of the bladder, including mesonephroid carcinoma is poor and depends primarily on the tumor stage (depth of invasion). One possible explanation is late diagnosis in many cases with advanced tumor stages as a consequence. Consequently, the reported 5-year survival rate is low (18-55%). [14].

Primary adenocarcinoma of the bladder is treatable and potentially curable with radical cystectomy or pelvic exenteration. If complete resection is achievable, cure is possible.

Chemotherapy and radiotherapy were of uncertain value for adenocarcinomas of the bladder, but therapeutic successes have been published as case reports [14].

Chemotherapy has been used only sporadically and in general has not been useful. However, there have been various reports on the use of 5-FU with or without other modalities in the treatment of adenocarcinoma of the urinary bladder. Logothetis *et al*. reported eight patients with unresectable adenocarcinoma of the urinary bladder who were treated primarily with systemic chemotherapy [26].

Kotaro kasahara et al. report a case of a 53-year-old woman with a history of asymptomatic macrohematuria. She was treated with the combination known as PMUE, consisting of cisplatinum (CDDP), mitomycin-C (MMC), etoposide (VP-16) and tegafur-uracil (UFT) chemotherapy. Subsequently, she underwent radical cystectomy and cutaneous ureterostomy. Three years after the operation, she has no evidence of disease recurrence. Treatment of advanced adenocarcinoma of the urinary bladder by this combination chemotherapy is of benefit [27].

Conclusion

Primary adenocarcinoma of the bladder is an uncommon neoplasm with a spectrum of histomorphologic appearances.

Clinical implications of diagnosis of adenocarcinoma of the bladder are important, since the diagnosis of bladder adenocarcinoma will prompt a clinical workup to rule out the possibility of secondary involvement of the bladder by an adenocarcinoma from a different site.

More common metastatic adenocarcinomas, especially colonic, need to be ruled out before making a diagnosis of primary vesical adenocarcinoma.

More comprehensive studies involving great numbers of patients with adenocarcinoma of the urinary bladder treated by PMUE combination chemotherapy will be necessary to determine whether this chemotherapy contributes to better prognosis.

Further basic and clinical studies are needed to establish evidence-based treatment recommendations for this specific tumor type.

Financial or Other Competing Interests

The authors declare no financial or competing interest.

Authors Contribution

All mentioned authors have contributed to the elaboration and development of this manuscript.

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