Print ISSN: 2321-6379
Online ISSN: 2321-595X

Case Report

A Rare Case of Urothelial Carcinoma with Divergent Differentiation Showing Multiple Varied Histomorphology with Review of Literature

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Abstract

Urothelial carcinoma with divergent differentiation is a variant of urothelial carcinoma and it is being increasingly recognized with the increase in awareness and advancement of immunohistochemistry. It is important to quantify the degrees of each differentiation for the prognosis and treatment of the patient. Here, we present a unique case of urothelial carcinoma of urinary bladder with divergent differentiation showing urothelial, squamous, papillary, and glandular differentiation.

Key words: Divergent differentiation, Mixed histology, Urothelial carcinoma

INTRODUCTION

Bladder cancer is the most common malignancy arising in the urinary tract. It is a heterogeneous group of cancers and it arises from the epithelial lining of the bladder called the urothelium. It is the seventh most common cancer in the world. A variant of urothelial carcinoma called urothelial carcinomas with variant histology also known as urothelial carcinoma with divergent differentiation has been noted. These patients were seen to be associated with an increased chance of locally advanced disease and metastasis. Therefore, early diagnosis and treatment of these patients are essential.

CASE REPORT

A 42-year-old male came to the urology outpatient department with complaints of macrohematuria for the past 2 months. The patient did not have history of pain, difficulty in micturition, loss of weight, loss of appetite and was not on any antiplatelet drugs. History revealed that the patient is a known case of chronic kidney disease on hemodialysis. The patient belonged to a socioeconomic class 2 and did not have any adverse social habits. On examination, the patient was pale and vitals were stable. Systemic examination was normal and examination of external genitalia showed penoscrotal edema. The patient was advised a transabdominal ultrasonogram, which revealed increase in renal cortical echoes, mild hydroureteronephrosis, and ill-defined heteroechoic lesion in the urinary bladder measuring 6.0 cm × 3.2 cm, with minimal ascites [Figure 1]. He underwent a computed tomography whole abdomen showing an ill-defined endophytic lesion with papillary projections arising in the dome of the bladder. The patient then underwent a transurethral resection of bladder tumor (TURBT) and the specimen was subjected for histopathological examination. The specimen was processed and it revealed an urothelial carcinoma with divergent differentiation showing a high grade papillary urothelial carcinoma with divergent differentiation showing papillary areas (30%), urothelial areas (30%), squamous areas (30%), and glandular areas (10%) [Figure 2]. Extensive areas of necrosis and brisk mitosis were noted. Immunohistochemistry for p63 and

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www.ijss-sn.com

Month of Submission : 03-2020
Month of Peer Review : 04-2020
Month of Acceptance : 05-2020
Month of Publishing : 05-2020

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GATA3 was done. p63 was positive in the squamous areas and urothelial areas. GATA3 was positive in the papillary and urothelial areas [Figure 3].

DISCUSSION

Urothelial carcinoma is one of the most common cancers worldwide. It is more common in older age males. It can arise anywhere within the urinary tract, but most commonly from the urinary bladder and the other sites include ureter, renal pelvis, and proximal urethra. Many risk factors have been identified for urothelial carcinomas, some of them are tobacco smoking, occupational exposures, chemicals, urinary tract infection, genetic factors, chronic inflammation, and irradiation.

Almost 90% of the urothelial carcinomas are conventional urothelial carcinomas, the rest of the urothelial carcinomas are urothelial carcinoma with divergent differentiation or non-urothelial carcinomas. Based on the recent WHO 2016 classification of bladder tumors, about 11 histologic variants of urothelial carcinoma are recognized such as the urothelial carcinoma with divergent differentiation, nested variant, microcystic, micropapillary, lymphoepithelioma like carcinoma, plasmacytoid, sarcomatoid, giant cell variant, lipid rich variant, clear cell, and poorly differentiated variant.[1]

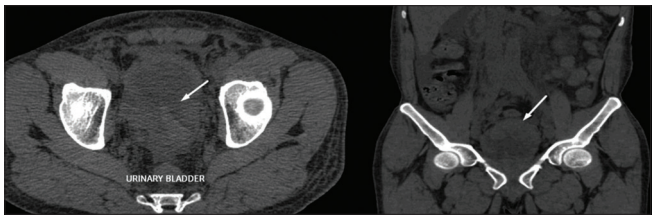

Figure 1: Ultrasonogram of pelvis showing a heteroechoic lesion in the urinary bladder

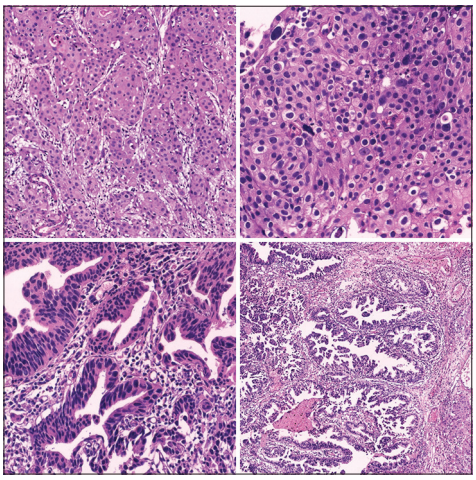

Figure 2: (a) H&E, ×40, urothelial differentiation; (b) H&E, ×40, squamous differentiation; (c) H&E, ×40, glandular differentiation; (d) H&E, ×40, papillary areas

Urothelial carcinoma with divergent differentiation is associated with squamous cell differentiation, glandular differentiation, with trophoblastic differentiation, and small cell differentiation. The squamous differentiation was found to be the most common type accounting for about 20–40%, the glandular differentiation was seen in 6–18% and syncytiotrophoblastic giant cells are seen in 28–35% of urothelial carcinomas with divergent differentiation.[1] Makise *et al.* report a case of urothelial carcinoma with squamous, glandular, and plasmacytoid differentiation confirmed by immunohistochemistry.[2]

Charlise *et al.* studied the impact of urothelial carcinomas with divergent differentiation on tumor stage and report that squamous differentiation was most common. These tumors are associated with higher stage, lymphovascular and perineural invasion and associated with a worse outcome even in T1 high grade urothelial carcinomas.[3] These tumors were seen to be associated with a higher chance of lymph node metastasis.

Our case of urothelial carcinoma was diagnosed by TURBT. Billis *et al.* report a series of 165 cases of urothelial carcinomas with divergent differentiation diagnosed on TURBT. They suggest that these tumors are associated with a higher stage at clinical presentation.[4] Wasco *et al.* also report a series of 448 cases of urothelial carcinoma with divergent differentiation diagnosed on TURBT and these patients were found to have a locally aggressive disease.[5] Genetic studies have indicated that the variants of urothelial carcinomas arise from a common clonal precursor. Thus, extensive search for divergent differentiation in urothelial carcinomas must be done by the pathologist.

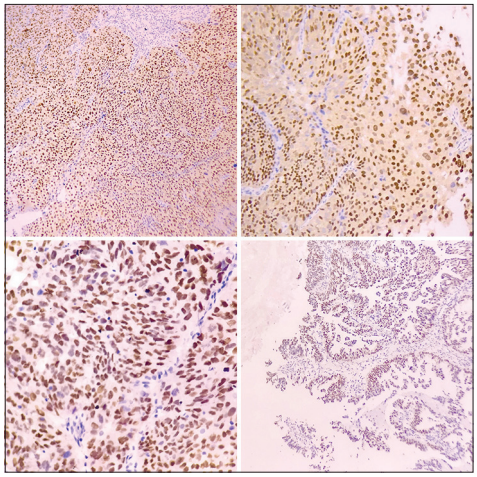

Figure 3: (a) Immunohistochemistry, ×40, p63 positive in urothelial areas, (b) immunohistochemistry, ×40, p63 positive in squamoid areas, (C) immunohistochemistry, ×40, GATA3 positive in urothelial areas, (d) immunohistochemistry, ×40, GATA3 positive in papillary areas

CONCLUSION

Urothelial carcinomas with divergent differentiation have an impact on the local aggressiveness, tumor stage, and lymph node metastasis. An early cystectomy and strict follow-up of these patients will help to improve the oncological outcome.

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How to cite this article: Correya MA, Sundaram S, Cruze LD, Natarajan K. A Rare Case of Urothelial Carcinoma with Divergent Differentiation Showing Multiple Varied Histomorphology with Review of Literature. Int J Sci Stud 2020;8(2):1-3.

Source of Support: Nil, **Conflicts of Interest:** It is the policy of "International Journal of Scientific Study" that individuals who submit or review manuscripts for publication disclose any proprietary, financial, professional, or other personal interest that may influence positions presented in, or the review of, the manuscript.