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Unusual manifestations of secondary urothelial carcinoma

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Abstract High-grade papillary urothelial carcinoma regularly invades the bladder wall, adjacent prostate, seminal vesicles, ureters, vagina, rectum, retroperitoneum, and regional lymph nodes. In advanced stages, it may disseminate to the liver, lungs, and bone marrow. On rare occasions, unusual metastatic foci like skin have been reported. The incidence of urothelial carcinoma has increased with associated rise in variants of urothelial carcinoma and unusual metastatic foci. It is imperative that urologists and pathologists are aware of the unusual variants and unusual metastatic locations to expedite the diagnostic process. Hereby we report an unusual case of secondary involvement of spinal nerve by conventional urothelial carcinoma. Also a second case of rhabdoid variant of urothelial carcinoma showing synchronous involvement of bladder and subcutaneous tissue of upper extremity is presented.

1. Introduction

Urothelial carcinoma (UC) is the fifth most common malignancy in the USA with rising incidence [1]. Aggressive urothelial carcinomas invade the bladder wall and usually extend into the adjacent organs like prostate, seminal vesicles, ureters, vagina, rectum, and retroperitoneum. Distant metastasis by hematogenous dissemination usually occurs in bone, lung, liver and peritoneum. The behavior of UC cannot be clinically predicted; however findings like extension beyond the bladder wall on bimanual examination, infiltration of the ureteral orifices, lymph node metastases, and systemic dissemination are associated with poor prognosis. Life expectancy for metastatic UC is usually three years or less and there is rarely any cure; therefore early diagnosis is of utmost importance.

Several variants of UC have been illustrated in the current WHO classification [2]. More common variations like UC with squamous or glandular differentiation appear not to affect the outcome, but less common variants like nested, micropapillary, lymphoepithelioma-like, plasmacytoid, small cell, and sarcomatoid UC show more aggressive behavior and poor outcome.

Unusual metastasis of UC rarely occurs where determination of urothelial origin may be challenging. It is very important that urologists and pathologists are aware of unusual metastatic foci of the UC to expedite the diagnosis and proper management. To our knowledge, secondary involvement of a spinal nerve trunk in the absence of

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disseminated UC has not been reported in the English literature. In addition, we report a unique case of rhabdoid variant of UC with synchronous presentation in bladder wall and subcutaneous soft tissue of upper arm.

2. Case report

2.1. Case # 1

A 71-year-old male, a known case of UC, underwent therapeutic radical cystoprostatectomy. The specimen revealed an ulcerated tumor on right posterolateral bladder wall measuring 3.5 × 2.5 × 0.8 cm. Histopathology revealed an invasive UC with squamous differentiation extending into perivesical fat (pT3b). Tumor was noted to invade nerve bundles with perineural spread approaching the surgical margin on the right side. No tumor cell was identified at the margin; therefore all margins were reported free from tumor. The accompanying right pelvic lymph node dissection revealed 4 benign lymph nodes (pN0). The prostate contained an incidental focus of low grade prostate adenocarcinoma (Gleason score 3 + 3 = 6, pT2b N0). The patient tolerated the operation well and left the hospital without any complication.

Nine months later, the patient returned with progressive unilateral right lower extremity pain radiating down the leg with associated weakness, numbness, right-sided foot drop and unsteady gait. The pain partially improved but was not eradicated by oxycodone. He also complained about fecal incontinence. No clinical evidence of recurrent UC was noted. MRI of the spinal cord showed asymmetric thickening with increased signal in the right lumbosacral trunk involving the S1 and S2 roots (Fig. 1A & B). The sciatic nerve revealed non-enhancing thickening just beyond sciatic notch extending distally in the right thigh to the level of the hamstring complex. Right gluteus muscles and thigh extensors showed significant edema and fatty atrophy. Biopsy of right sciatic nerve at the level of the sciatic notch revealed metastatic UC with focal squamous and glandular differentiations – similar to prior UC – involving the nerve trunk (Fig. 1C). Tumor cells stained positive for CK7, P63 and high molecular weight cytokeratin (HMWCK), supporting the diagnosis (Fig. 1D, Table 1). CK20 was negative in the tumor cells.

Palliative radiation therapy to the sacrum and sciatic nerve (total doze 59.4 Gy) with neuroleptic medications was administered. Initially, significant pain alleviation and improved strength in the right lower extremity were reported; however fecal incontinence did not improve. A few weeks

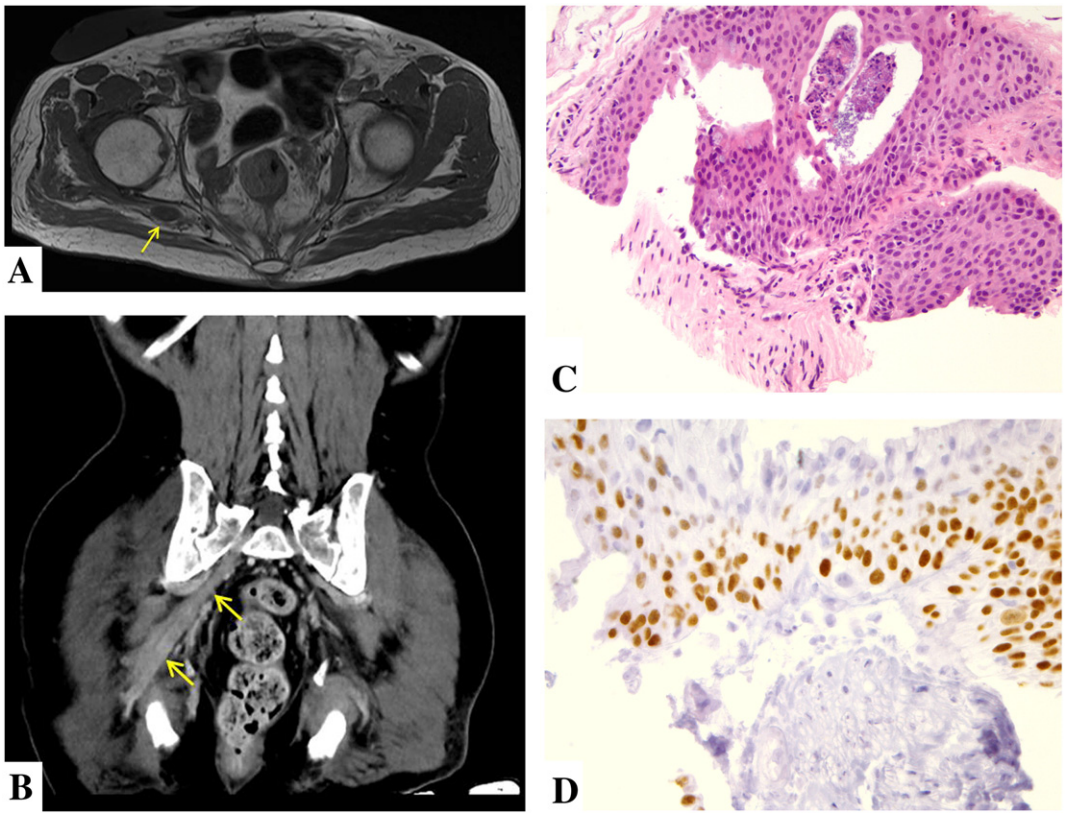

Fig. 1 Case 1. (A) Axial T1-Weighted Non-Contrast MRI of the Pelvis. Fusiform enlargement of the right sciatic nerve just distal to the greater sciatic foramen (arrow). Note also made of lipoatrophy of the right gluteal musculature. (B) Coronal Contrast-Enhanced CT of the Abdomen and Pelvis. Enhancing fusiform enlargement of the right sciatic nerve as it exits the greater sciatic foramen (arrows). (C) Metastatic UC involving the sciatic nerve (H&E staining 100×). (D) Expression of P63 in the metastatic focus confirmed urothelial origin (200×).