Urology Case Reports 2 (2014) 93–96

Contents lists available at ScienceDirect

Urology Case Reports

journal homepage: www.elsevier.com/locate/eucr

Oncology

High-grade Neuroendocrine Carcinoma With Focal Squamous Metaplasia of Renal Pelvis Associated With Renal Calculus: Study of a Case

Yan-Ping Huang [a], Bin Chen [a,*], Xiang-Zhou Sun [b], Yan Guo [b], Shi-Cong Yang [b], Chun-Hua Deng [b], Yi-Ran Huang [a]

[a] Department of Urology, Renji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai Institute of Andrology, Shanghai, People's Republic of China
[b] Department of Urology, The First Affiliated Hospital of Sun Yat-sen University, Guangzhou, People's Republic of China

ARTICLE INFO

Article history:
Received 4 December 2013
Accepted 5 December 2013

Keywords:
Neuroendocrine carcinoma
Renal pelvis
Squamous metaplasia
Kidney calculi

ABSTRACT

Mixed neuroendocrine and non-neuroendocrine type of tumor in renal pelvis is rare and presents a high-grade malignancy. We present a case report that a 57-year-old man had no history of small cell cancer but presented a high-grade neuroendocrine carcinoma with focal squamous metaplasia and multiple stones simultaneously in the right renal pelvis. The patient underwent nephroureterocystectomy 9 months before this presentation, with evidence of multiple metastatic tumors in various parts of the body. The case of mixed neuroendocrine tumor with stones in the renal pelvis carries a poor prognosis and poses a therapeutic challenge to urologists.

Introduction

High-grade neuroendocrine carcinomas, which are also known as poorly differentiated neuroendocrine carcinomas, arise more frequently in the lung, and approximately 2.5% occur in extrapulmonary sites, including the genitourinary tract.[1] Neuroendocrine tumors of the urogenital system accounts only for a small proportion, and urinary bladder and prostate are the common occurrence sites. Renal neuroendocrine tumor is a very rare and poorly differentiated cancer and comprised a group of highly malignant tumor cell types associated with poor outcome and short survival. Compared with parenchyma-arising neuroendocrine tumors, the pelvis-arising neuroendocrine tumors are more rare and more likely to present mixed neuroendocrine and non-neuroendocrine type.[2] In this study, we report a case of high-grade neuroendocrine carcinoma with focal squamous metaplasia of renal pelvis associated with renal calculus, which is extremely rare. Only 2 cases of renal pelvis carcinomas reported in the previous English-language literature were consistent with such histopathologic features.[3,4]

Case presentation

A 57-year-old man presented with right flank pain and microscopic hematuria for 15 days. Ultrasonography revealed multiple stones in the right pelviureteral site, accompanied hydroureteronephrosis and a space-occupying mass. Intravenous pyelogram showed right pelviureteral nonvisualization. Computed tomography revealed stones along with upper-ureteric thickening and dilating and a 28 × 27 mm uneven enhancing mass in ureteropelvic junction. No enlarged mesenteric lymph nodes and retroperitoneal lymph nodes were observed, and no thrombus in the renal vein and inferior vena cava (Fig. 1). Percutaneous nephrolithotripsy was performed to remove the stones and establish diagnosis. Initial impression of biopsy specimens reviewed by the pathologist was that of urothelial carcinoma with necrosis. In view of the malignancy, the patient underwent radical nephroureterocystectomy, and a nodular and sessile tumor measuring 3.0 × 2.5 × 1.7 cm with gray-whitish cut surface was found in the dilated pelvis of the resected specimen (Fig. 2). A final diagnosis of high-grade neuroendocrine carcinoma with focal squamous metaplasia was rendered (Fig. 3). Preoperative and postoperative systemic examinations detected no tumors in other sites.

The patient did not receive chemotherapy after surgery. Six months later, postoperative review showed some enlarged

* Corresponding author. Tel.: +86-21-63261981; fax: +86-21-63111100.
E-mail address: dr_binchen@126.com (B. Chen).

2214-4420/
http://dx.doi.org/10.1016/j.eucr.2013.12.004

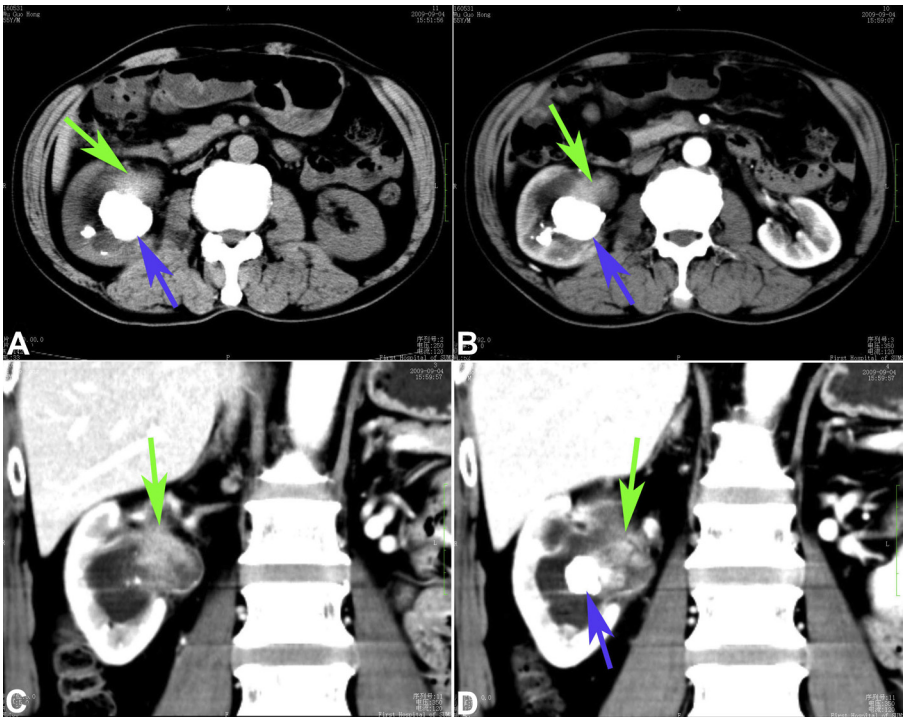

Figure 1. Computed tomographic plain scan shows multiple stones within the right renal pelvis and calyceal, an irregular soft tissue mass in the ureteropelvic junction **(A)**. Uneven enhancing visualization appears in the mass along with an upper-ureteric thickening in the enhancement scanning **(B)**. Right hydronephrosis reconstruction was obtained in images **(C, D)**.

retroperitoneal lymph nodes and no metastatic tumors found in other anatomic sites using the computed tomography detection, and the patient had no subjective symptoms except discomfort of the operative site. However, 9 months after the surgery, multiple metastatic tumors were found in the lung and liver, and the patient presented cachexia.

Discussion

The histogenesis of high-grade neuroendocrine carcinomas, independently of the site of origin, remains controversial and needs further studies. Some people consider they originate from urothelial cells with the neuroendocrine differentiation or neuroendocrine cells presenting in renal pelvis, some authors hold that these tumors originate from the entrapped neural crest in the kidney during embryogenesis.[5] A more persuasive view based on the theory of clinic-pathologic similarities among tumors originating in different sites is that these tumors arise from undifferentiated stem cells with multipotential differentiation toward a neuroendocrine and sometimes an exocrine differentiation such as squamous, glandular, or urothelial cell lineage when these incentive factors are present, and they tend to be of high grade.[1,6] The view of stem cells of origin can explain why the neuroendocrine and non-neuroendocrine components can be simultaneously observed in neuroendocrine carcinomas. For example, the neuroendocrine component of lung and gastrointestinal tract commonly appear in combination with squamous cell carcinoma or adenocarcinoma, the neuroendocrine component of renal pelvis is frequently accompanied with transitional cell carcinoma (TCC). However, the present case we reported showed squamous metaplasia component, which is extremely rare. Generally, TCC is the most common type in renal pelvis neoplasmas, whereas the type of squamous cell carcinoma or TCC with squamous metaplasia in renal pelvis is often accompanied with incentive factors such as pyelonephritis, kidney stones, and

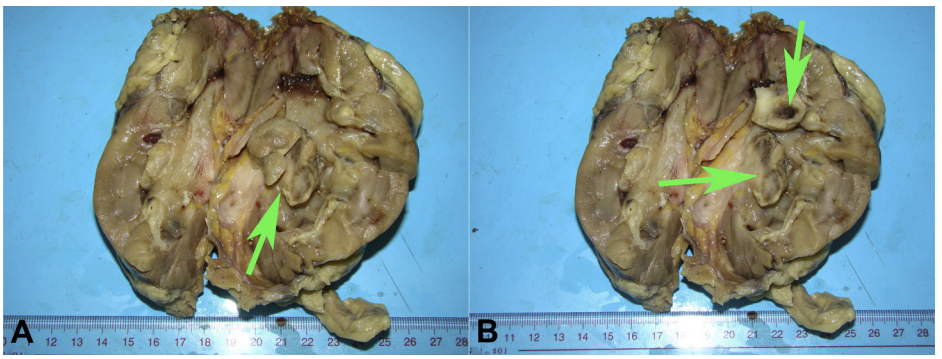

Figure 2. Macroscopically, the tumor predominantly located in the dilated renal pelvis, well-circumscribed, solid and nodular **(A)**. White-gray appearance with necrosis and hemorrhage presents on cut sections **(B)**.

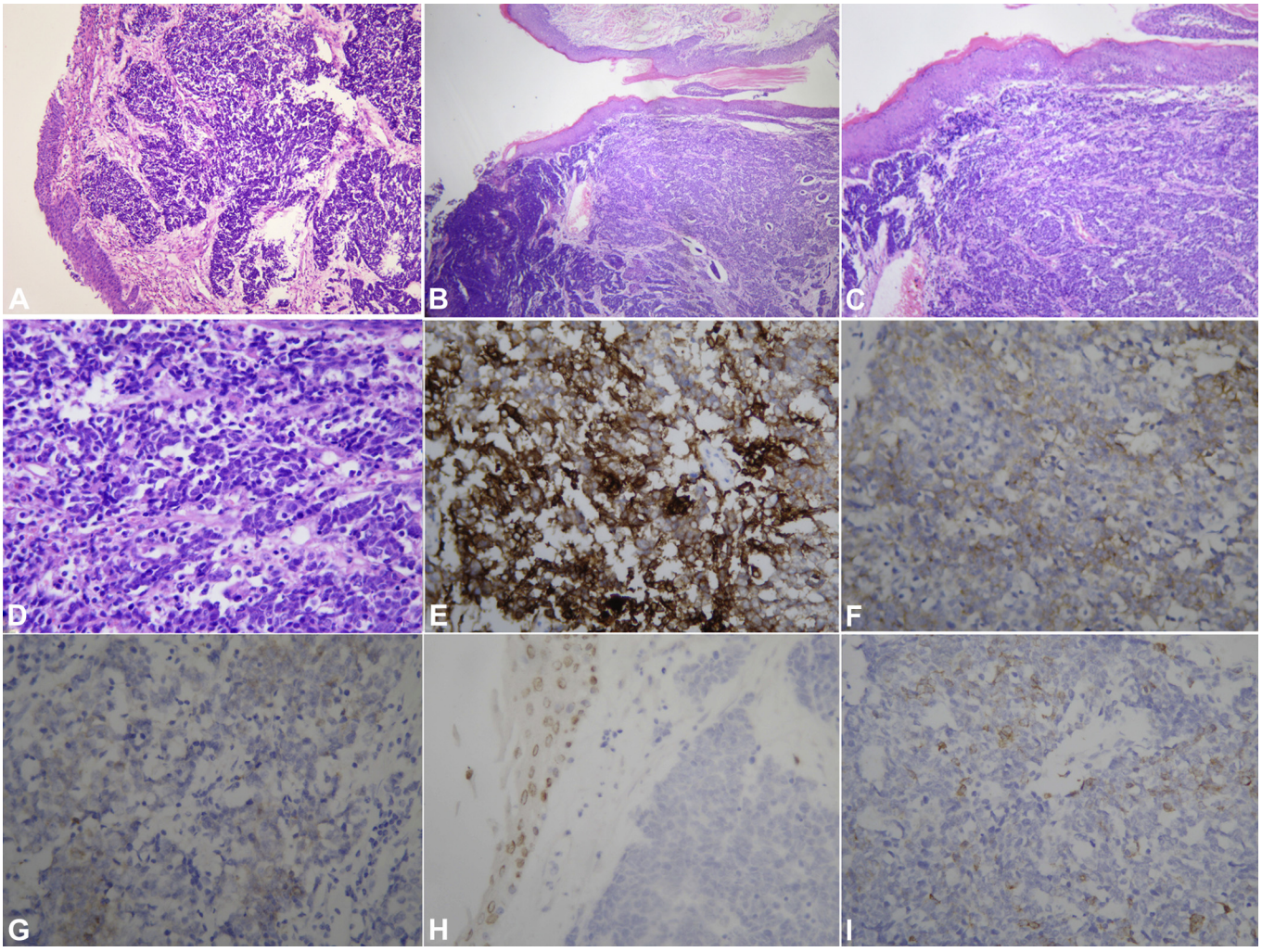

Figure 3. Microscopic findings: the tumor cells present ribbon-like, trabecular, and nest arrangement **(A)** (HE ×100), small to intermediate in size nucleoli, scanty cytoplasm, and poorly defined cytoplasmic borders **(D)** (HE ×400). Focal squamous metaplasia appears in pathologic sections **(B)** (HE ×40); **(C)** (HE ×100). Immunohistochemistry: tumor cells present strongly positive for CD56 **(E)**, partly positive for synaptophysin **(F)**, neuron-specific enolase **(G)**, and focally positive for P63 **(H)** and CK **(I)**.

renal pelvis leukoplakia. In this case, we consider that the kidney stones induce the squamous metaplasia component located within the tumor.

Although neuroendocrine carcinoma has typical morphologic features including highly cellular atypia, high mitotic/proliferative indices, and extensive necrosis, sometimes it is difficult to make a rapid and definite diagnosis by conventional histologic preparations. The differential diagnoses include malignant lymphoma, lymphoepithelioma such as carcinoma, plasmacytoid carcinoma, poorly differentiated urothelial carcinoma, and primitive neuroectodermal tumor. For this case, the primary diagnosis of nephroscopy biopsy was urothelial carcinoma with necrosis. However, the resected tumor was confirmed to be a high-grade neuroendocrine carcinoma with focal squamous metaplasia by immunohistochemical markers, including synaptophysin, neuron-specific enolase, CD56, and P63 (Fig. 3). As neuroendocrine carcinoma frequently occurs in lung and gastrointestinal and rarely arises from urogenital system, the confirmation of the primary site is important. However, no neuroendocrine carcinomas were found in other anatomic sites before surgery, indicating this rare neuroendocrine carcinoma might originate from urothelial epithelium of the renal pelvis.

Hematuria and flank discomfort or pain were the most frequent clinical symptoms in the cases of renal pelvis high-grade neuroendocrine carcinomas. Surprisingly, no endocrine syndromes were described in these cases. This type of tumor is characterized by an aggressive clinical course with early metastasis, and the usual sites of metastasis are lymph nodes and bone. It has been reported that patients with urologic poorly differentiated neuroendocrine carcinomas treated with chemotherapy independently showed a better survival than patients treated with surgery or combination therapy of surgery and chemotherapy.[7] However, the overall survival rate for patients with small cell carcinoma of the bladder with local disease has been reported as low as 8%,[8] and many patients diagnosed renal high-grade neuroendocrine carcinomas died after a few months regardless of the chosen therapeutic regimen. The patient in our report appeared multiple metastatic tumors in the lung and liver and progress of cachexia after radical nephroureterectomy for 9 months, indicating the poor prognosis of this type of tumor.

Conclusion

We report such a particular case: a patient with a tumor and multiple stones simultaneously in the renal pelvis. Histologic and immunohistochemical analyses showed that the tumor presented a feature of high-grade neuroendocrine carcinoma with focal squamous metaplasia probably induced by stones in the pelvis. Further

studies should be required to elucidate the pathogenesis and improve the therapy.

Conflict of interest

None of the authors have any potential conflicts of interest to declare.

References

1. Remick SC, Ruckdeschel JC. Extrapulmonary and pulmonary small-cell carcinoma: tumor biology, therapy, and outcome. *Med Pediatr Oncol*. 1992;20:89–99.
2. La Rosa S, Bernasconi B, Micello D, et al. Primary small cell neuroendocrine carcinoma of the kidney: morphological, immunohistochemical, ultrastructural, and cytogenetic study of a case and review of the literature. *Endocr Pathol*. 2009;20:24–34.
3. Shimasaki N, Inoue K, Nishigawa H, et al. Combined small cell carcinoma and sarcomatoid squamous cell carcinoma in the renal pelvis. *Int J Urol*. 2005;12:686–689.
4. Kitamura M, Miyanaga T, Hamada M, et al. Small cell carcinoma of the kidney: case report. *Int J Urol*. 1997;4:422–424.
5. Guy L, Begin LR, Oligny LL, et al. Searching for an intrinsic neuroendocrine cell in the kidney. An immunohistochemical study of the fetal, infantile and adult kidney. *Pathol Res Pract*. 1999;195:25–30.
6. Kim TS, Seong DH, Ro JY. Small cell carcinoma of the ureter with squamous cell and transitional cell carcinomatous components associated with ureteral stone. *J Korean Med Sci*. 2001;16:796–800.
7. Majhail NS, Elson P, Bukowski RM. Therapy and outcome of small cell carcinoma of the kidney: report of two cases and a systematic review of the literature. *Cancer*. 2003;97:1436–1441.
8. Blomjous CE, Vos W, De Voogt HJ, et al. Small cell carcinoma of the urinary bladder. A clinicopathologic, morphometric, immunohistochemical, and ultrastructural study of 18 cases. *Cancer*. 1989;64:1347–1357.