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Case report

Urinary bladder carcinoma with divergent differentiation featuring small cell carcinoma, sarcomatoid carcinoma, and liposarcomatous component

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ABSTRACT

Both small cell carcinoma and sarcomatoid carcinoma of the urinary bladder are highly aggressive tumors, and a concurrence of these tumors is extremely rare. We report a case of urinary bladder cancer with small cell carcinoma as a predominant component, accompanied by sarcomatoid carcinoma and conventional urothelial carcinoma (UC). Although the small cell carcinoma component had resolved on receiving chemoradiotherapy, rapid growth of the residual tumor led to a fatal outcome. A 47-year-old man presented with occasional bladder irritation and had a 2-year history of asymptomatic hematuria. Cystoscopy revealed a huge mass in the urinary bladder, and transurethral resection was performed. Microscopically, small cell carcinoma was detected as the major tumor component. Spindle-shaped sarcomatoid cells were also observed that were intermingled with small cell carcinoma and conventional UC. In addition, a sheet-like growth of the lipoblast-like neoplastic cells was observed focally. Initially, by providing chemoradiotherapy, we achieved a marked tumor regression; however, the tumor rapidly regrew after the completion of chemoradiotherapy, and the patient underwent radical cystectomy. Only conventional UC and sarcomatoid carcinoma were identified in the cystectomy specimen. The patient died of the disease 4 months after cystectomy. Urinary bladder cancer may include a combination of multiple aggressive histologies as in the present case. Because the variation in the tumor components may affect the efficacy of therapy, a correct diagnosis of every tumor component is necessary.

1. Introduction

Although the majority of urinary bladder cancer cases are urothelial carcinoma (UC) cases, urinary bladder cancer may show diverse histological variations [1]. Both small cell carcinoma and sarcomatoid carcinoma of the urinary bladder are rare and clinically highly aggressive [2,3]. Concurrence of small cell carcinoma and sarcomatoid carcinoma is extremely rare [4–7]. Herein, we report a case of urinary bladder cancer featuring small cell carcinoma, sarcomatoid carcinoma, and lipoblast-like morphology. We report the clinical, histopathological, and immunohistochemical characteristics of this tumor; additionally, we discuss the implications of the histological variations on the patient's treatment.

2. Clinical summary

A 47-year-old man was presented with occasional bladder irritation. He was an office worker without known exposure to chemical substances. He had a 2-year history of asymptomatic hematuria; however, his medical history was unremarkable. Atypical cells were identified based on urinary cytology examination. Computed tomography (CT) revealed a large mass arising from the left bladder wall accompanied by extravesical tumor extension. Further, cystoscopy revealed a solid tumor occupying a wide area from the left to the posterior bladder wall, and transurethral resection of bladder tumor (TURBT) was performed. Serum pro-gastrin-releasing peptide and neuron-specific enolase levels were elevated to 99.5 pg/mL

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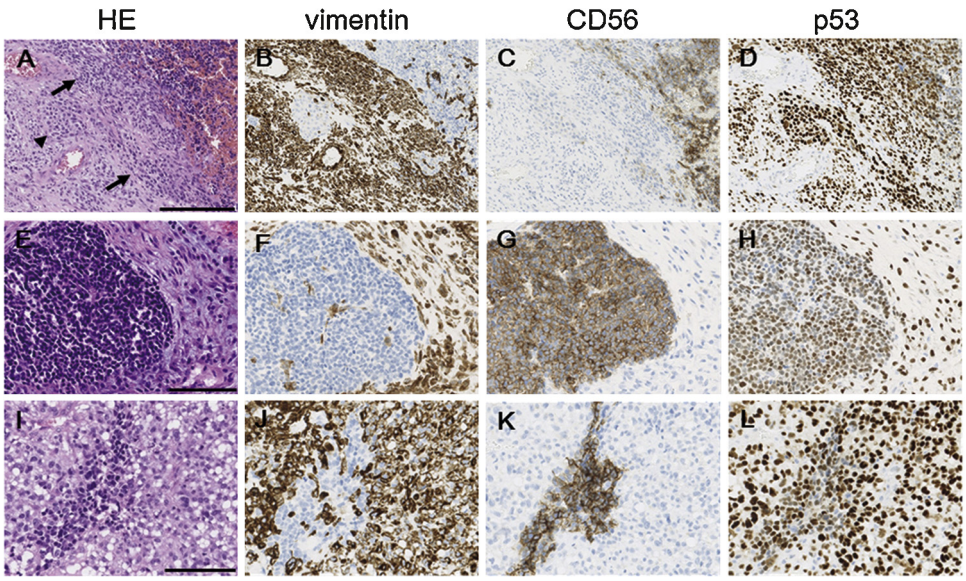

Fig. 1. Histological and immunohistochemical findings of the transurethral resection specimen. (A) The boundary of the small cell carcinoma (upper right), sarcomatoid carcinoma (arrows), and conventional urothelial carcinoma (arrowhead). Hematoxylin and eosin (H&E) staining. Bar, 200 μm. (B-D) Immunostaining for (B) vimentin, (C) CD56, and (D) p53 performed at the same location as shown in A. (E) A photomicrograph of small cell carcinoma (left) and sarcomatoid carcinoma (right). H&E staining. Bar, 100 μm. (F-H) Immunostaining for (F) vimentin, (G) CD56, and (H) p53 performed at the same location as E. (I) Lipoblast-like neoplastic cells are present in a focal area, intermingled with small cell carcinoma (center). H&E staining. Bar, 100 μm. (J-L) Immunostaining for (J) vimentin, (K) CD56, and (L) p53 performed at the same location as I.

(normal ≤80.0 pg/mL) and 33 ng/mL (normal ≤10.0 ng/mL), respectively.

After TURBT, the patient received chemotherapy (six cycles of a combination of cisplatin and etoposide) and radiation therapy (total 45 Gy). Initially, the tumor size reduced remarkably; however, 12 months after TURBT, CT revealed that the tumor had increased in size up to 7.5 cm. The patient underwent radical cystectomy and bilateral ureterocuteneostomy 15 months after TURBT. Intraoperatively, the tumor was found to invade to the left pelvic wall, resulting in incomplete surgical resection. Three months after the surgery, local recurrence in the pelvic cavity and multiple lung metastases were revealed on CT. The patient died of the disease 4 months after cystectomy.

3. Pathological findings

3.1. TURBT specimen

Microscopically, a highly invasive tumor was observed that formed irregular solid nests and sheets with extensive necrosis. While conventional high-grade UC was observed in some areas, various histological components were observed in the other areas (Fig. 1). The major tumor component was small cell carcinoma that was composed of small round cells with scant cytoplasm. The spindle-shaped sarcomatoid cells were observed in the other areas. Conventional UC, small cell carcinoma, and sarcomatoid carcinoma were mixed with each other. In addition, a sheet-like growth of lipoblast-like neoplastic cells that contained large clear vacuoles with indented nuclei was observed in a focal area, and these cells were intermingled with small cell carcinoma. The cytoplasmic vacuoles were negative for periodic acid Schiff and Alcian blue stains. The small cell carcinoma component had invaded the muscularis propria. Additionally, vascular invasion was observed.

Immunohistochemical analysis was performed as previously described [8], and the results are summarized in Table 1. All the components were diffusely positive for p53, and at least focally positive for epithelial membrane antigen (EMA) or cytokeratin AE1/AE3. Whereas the small cell carcinoma component was negative for vimentin, sarcomatoid carcinoma and lipoblast-like cells were diffusely stained. In contrast, the small cell carcinoma component was diffusely positive for synaptophysin and CD56; however, the other components were negative. S-100 protein was focally positive only in lipoblast-like cells (Fig. 2).

Table 1
Summary of the immunohistochemical results in the transurethral resection specimen.

	UC	Small cell	Sarcomatoid	Lipoblast-like
AE1/AE3	+++	–	+	+
EMA	+	+	+	+
Vimentin	–	–	+++	+++
Synaptophysin	–	+++	–	–
Chromogranin A	–	–	–	–
CD56	–	+++	–	–
p53	+++	+++	+++	+++
S-100	–	–	–	+

EMA, epithelial membrane antigen; UC, conventional urothelial carcinoma. The ratio of the positive cells was classified into four groups as follows: –, 0–4%; +, 5–30%; ++, 31–60%; and +++, 61–100%.

3.2. Cystectomy specimen

Macroscopically, a tan-white protruded lesion that measured 11 × 9 × 6 cm was observed at the left bladder wall (Fig. 3). Microscopically, the lesion was composed of conventional high-grade UC and sarcomatoid carcinoma; however, small cell carcinoma and lipoblast-like cells were not identified (Fig. 4). Immunohistochemical analysis showed that the tumor cells were diffusely positive for vimentin and p53, very focally positive for EMA and cytokeratin AE1/AE3; however, they were negative for synaptophysin, chromogranin A, and CD56 (Fig. 4). The tumor had invaded extravesically and was exposed on the surgical margin. There was no lymph node metastasis.

4. Discussion

In this case, we identified three aggressive variants of bladder cancer featuring small cell carcinoma, sarcomatoid carcinoma, and lipoblast-like morphology together with conventional UC. To the