

Urothelial Carcinoma of the Bladder, Lipid Cell Variant: Case Report and Literature Review

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The lipid cell variant of urethral carcinoma (UC) is rare and poorly understood clinicopathologically. A nodular tumor detected in the bladder of an 87-year-old man with asymptomatic gross hematuria was transurethraly resected, and high-grade UC, lipid cell variant, was diagnosed pathologically. The tumor cells resembled lipoblasts and contained numerous cytoplasmic vacuoles. Immunohistochemically, the tumor cells stained positive for the epithelial markers CK7, CK20, EMA, CAM5.2, and 34betaE12 and negative for vimentin and S100. Focal positivity for adipophilin was detected in cytoplasm but not in the vacuoles. These findings suggest that the patient had lipid-producing UC.

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Key words: lipid cell variant, urothelial carcinoma, immunohistochemistry, urinary bladder

Introduction

The lipid cell variant of urothelial carcinoma (UC) is a rare form of bladder cancer, first reported by Mostofi et al.¹. A literature search showed that only 44 cases have been reported previously^{2–7}. Thus, the clinicopathological features of this variant are poorly understood. Herein, we describe the clinical and immunohistochemical characteristics of a patient with the lipid cell variant of UC and review the relevant literature.

Case Report

An 87-year-old man was admitted to the Nippon Medical School Hospital with asymptomatic gross hematuria, which was first observed 1 month before admission. Cystoscopy revealed a nodular tumor (diameter, 40 mm) at the lateral urinary bladder wall (**Fig. 1a**). Abdominal computed tomography and magnetic resonance imaging showed that the tumor (clinical stage, cT2N0M0) had invaded the muscle layer; however, there were no definitive findings of metastasis (**Fig. 1b**). The results of hematological and biochemical tests were unremarkable. Urine cytodiagnosis was class III. On the basis of these find-

ings, transurethral resection of the tumor was performed.

Analysis of the resected tissue sample indicated a pathological diagnosis of high-grade UC of the bladder (lipid cell variant). The tumor had invaded the muscularis propria, and the surgical margins were positive. The pathological stage was \geq pT2. Hematoxylin and eosin staining revealed that the tumor comprised solid nests of cells that resembled lipoblasts and contained cytoplasmic vacuoles of varying sizes, as well as cells that had eosinophilic cytoplasm without vacuoles (**Fig. 2a**). About 40% of the tumor was lipid cells. In addition, numerous mitotic figures were present in these cells. The cytoplasmic vacuoles were negative on periodic acid-Schiff and Alcian blue staining, indicating the absence of mucous protein.

Immunohistochemically, the tumor cells were positive for CK7, CK20, CAM5.2, CK34betaE12, and EMA, which is characteristic of UC (**Fig. 2b, c**). Cytoplasmic vacuoles in cells resembling lipoblasts were negative for the aforementioned cytokeratins; however, cytoplasm outside vacuoles was positive (**Fig. 2c**). All tumor cells, including the cells resembling lipoblasts, were negative for

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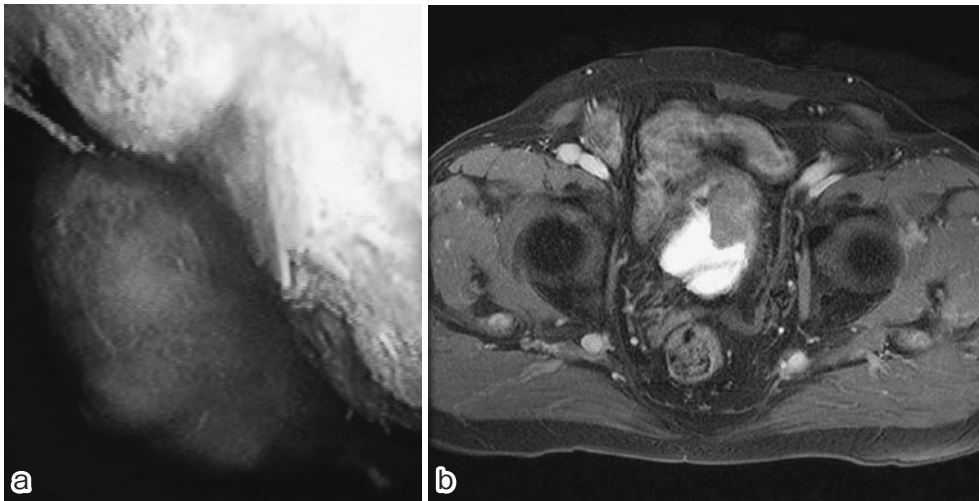


Fig. 1 (a) White-light cystoscopic image showing a nodular tumor (approximately 40 mm in diameter) at the lateral wall of the urinary bladder; (b) Magnetic resonance image (T2 enhanced) showing the tumor invading the muscle layer.

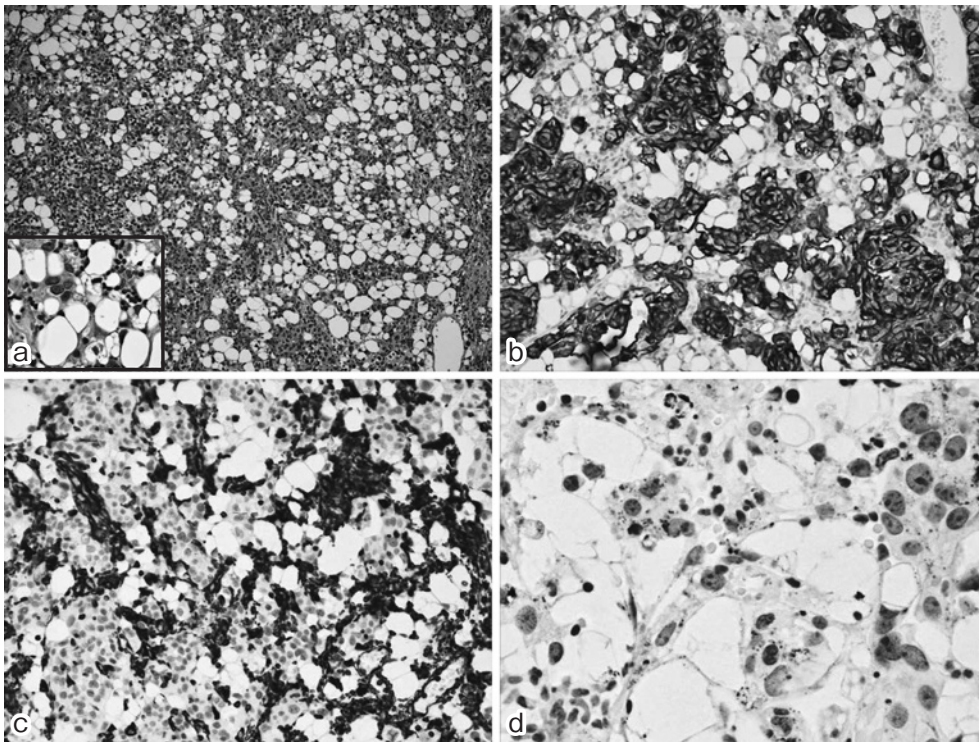


Fig. 2 Microscopic tumor findings

(a) The presence of numerous vacuoles in tumor cells is a characteristic feature of urothelial carcinoma. Hematoxylin and eosin (HE) ($\times 10$). Inset: The tumor comprised cells that contained cytoplasmic vacuoles of varying sizes and resembled lipoblasts (HE $\times 40$); (b) Almost all tumor cells were positive for cytokeratin 7, regardless of the presence of vacuoles ($\times 20$); (c) Tumor cells, including lipoblast-resembling cells, were negative for vimentin. Positive cells in the tumor were small, round, and inflammatory ($\times 20$); (d) Some tumor cells were positive for adipophilin; however, vacuoles of lipoblast-resembling cells were negative ($\times 40$).

vimentin (Fig. 2c) and S-100. Adipophilin was focally positive in the cytoplasm of tumor cells but not in the vacuoles of cells resembling lipoblasts (Fig. 2d). A few tumor cells were present in the lymphatic vessel. After pathological diagnosis, we performed radical cystectomy

and dissection of the obturator, external iliac, and internal lymph nodes. The urethrocutaneous fistula was selected for urinary diversion. Gross and microscopic examination showed no evidence of tumor recurrence in the resected bladder and no metastatic lesions in the dis-

Table 1 Reports of urothelial carcinoma of the bladder, lipid cell variant, in Japan

Authors	Year	Age	Gender	TNM Stage/Pathology	Treatment	Follow up
1 Shimada et al. ⁶	2009	80	Female	T3N0M0/HG	TURBT	DOD, 5 months
2 Kojima et al. ⁴	2013	78	Male	T2NxMx/HG	TURBT	Not described
3 Miyama et al. ⁷	2015	64	Male	T3N2M0/HG with micropapillary	TURBT	DOD, 75 months
4 Present case	2019	87	Male	T2N0M0/HG	TURBT/Cystectomy	Alive, 30 months

HG, high grade; DOD, died of disease; TURBT, transurethral resection of bladder tumor

sected lymph nodes. The patient did not receive adjuvant or neoadjuvant chemotherapy and is free of recurrence 30 months after surgery.

Discussion

In the current World Health Organization classification, the lipid cell variant of UC is categorized independently of other UC types. Histologically, this variant comprises tumor cells that have cytoplasmic vacuoles of varying size and resemble lipoblasts or signet ring cells¹, and the present patient exhibited this characteristic feature of the lipid cell variant of UC. Immunohistochemically, this variant has the characteristic features of UC (i.e., positivity for epithelial markers CK7, CK20, EMA, CAM5.2, and 34betaE12)². Because the liposarcoma and lipid cell variants of UC are morphologically similar, findings indicating vimentin and S100 negativity in tumor cells may be useful in distinguishing these tumor types.

No previous study of humans reported that vacuoles contained lipid. The presence of lipids was reported in a study using Oil Red O and Sudan Black B staining of a lipid cell variant of UC in cows³. Recently, Kojima et al. showed that, in patients with the lipid cell variant of UC, lipoblast-resembling cells were positive for adipophilin, a protein associated with synthesis of neutral lipids⁴. Therefore, immunopositive staining for adipophilin may indirectly indicate the presence of lipids, even in paraffin sections. In the present case, we detected focal positivity for adipophilin in the cytoplasm of tumor cells but not in the vacuoles of lipoblast-resembling cells. These findings suggest a diagnosis of lipid-producing UC.

The lipid cell variant of UC often occurs concurrently with high-grade UC or the micropapillary variant of UC⁵. In addition, this UC variant was reported to be resistant to chemotherapy and radiotherapy, thus resulting in poor outcomes. Lopez et al. investigated 27 cases of lipid cell variant UC, which was characterized by advanced stage (>pT2), high mortality (59%), and a median duration of survival of 33 months⁵. These findings suggest that prognosis is worse for this UC variant than for other types of UC of the urinary bladder⁵. In addition to the

present case, only three cases of the lipid cell variant of UC were reported in Japan (Table 1): all were diagnosed as high-grade UC, and one case was derived from the ureter^{4,6,7}. The present patient underwent surgery to remove the bladder tumor early in the disease and is currently free of recurrence 30 months after cystectomy. However, because of the poor prognosis for the lipid cell variant of UC, careful follow-up is warranted.

Conflict of Interest: The authors declare no conflict of interest.

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