Renal cell neoplasm of oncocytosis: a type of unclassified renal cell carcinoma

Masatake Shinohara · Shoji Samma · Yoshihiro Matsumoto ·
Yoriaki Kagebayashi · Yasushi Nakai · Kazumasa Torimoto ·
Keiji Shimada

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Abstract A 69-year-old woman was referred to us because a cyst in the lower pole of the left kidney had been pointed out on screening ultrasound. Computed tomography (CT) demonstrated a mural nodule of the wall of the cyst with an enhancement effect, suggesting cystic renal cell carcinoma (cT1aN0M0). The patient underwent retroperitoneoscopic non-ischemic partial nephrectomy using a microwave tissue coagulator. A hematoxylin–eosin-stained specimen showed that the wall of the cystic tumor consisted of the proliferation of large cells with rich eosinophilic granules in the cytoplasm and round-shaped nuclei, which were the characteristics of oncocytoma. This was followed by immunohistochemical studies, because of findings of local cell invasion, mitosis, and necrosis, suggesting malignancy. The results were: CK7, strongly positive; PAX2, negative; colloidal iron stain, negative; c-kit, weakly positive; vimentin, positive; and RCC marker, negative. Thus, although the tumor showed characteristics of oncocytoma and/or chromophobe renal cell carcinoma (pT1a), it could not be classified according to the known categories: it should be designated as renal cell carcinoma (neoplasm) of oncocytosis, a novel category of unclassified renal cell carcinomas. The present case

indicated the fact that renal cell carcinomas resembling oncocytoma certainly exist.

Keywords Renal cell neoplasm of oncocytosis · Renal cell carcinoma · Oncocytoma · Chromophobe renal cell carcinoma · Immunohistochemistry

Introduction

Renal tumors are classified mainly into the following 6 types: 4 types of adenocarcinomas are clear cell carcinoma, papillary renal cell carcinoma, chromophobe renal cell carcinoma, and collecting duct carcinoma, and 2 types of benign tumors are oncocytoma and angiomyolipoma [1]. Renal carcinomas which can not be classified into these 6 categories are designated as unclassified carcinomas.

We encountered a case of unclassified renal carcinoma which showed the characteristics of both oncocytoma and chromophobe cell carcinoma. This case was finally classified as renal cell neoplasm (carcinoma) of oncocytosis, a novel category of unclassified renal cell carcinoma advocated by Gobbo et al. [2], after detailed analyses of immunohistochemical studies.

Case report

A 69-year-old woman was referred to us because a cystic mass, 4 cm in diameter, in the lower pole of the left kidney had been detected by ultrasound in a screening test.

Hematology and blood chemistry showed no abnormal findings. Serum creatinine was 0.58 mg/dL and C-reactive protein was 0.1 mg/dL. On ultrasound, the border of the mass was clear, and its contents appeared to be liquid but

M. Shinohara · S. Samma (✉) · Y. Matsumoto ·
Y. Kagebayashi · Y. Nakai
Department of Urology, Nara Prefectural Nara Hospital, 1-30-1
Hiramatsu, Nara, Nara 631-0846, Japan
e-mail: urodept@m3.kcn.ne.jp

K. Torimoto
Department of Urology, Nara Medical University, Nara, Japan

K. Shimada
Department of Pathology, Nara Medical University, Nara, Japan

nonuniform. The wall showed poor vascularity. Enhanced computed tomography (CT) demonstrated a mural nodule with an enhancement effect (Fig. 1). These findings led to the diagnosis of probable cystic renal cell carcinoma (cT1aNOM0).

The patient underwent retroperitoneoscopic partial nephrectomy without ischemia using a microwave tissue coagulator. We placed the coagulator needle about 5 mm away from the wall to keep the surgical margin. For this process, we would avoid heating the fluid too much and prevent explosion of the cystic mass. The resected specimen was of dimensions $4.0 \times 3.5 \times 3.5$ cm. The tumor was cystic, with a nodular change on the wall surface (Fig. 2).

Histopathologically, a hematoxylin–eosin-stained specimen of the protruding portion showed the proliferation of

large cells with rich eosinophilic granules in the cytoplasm and round-shaped nuclei. These findings indicated the tumor to be cystic renal oncocytoma. However, local cell invasion, mitosis, and necrosis, suggestive of malignancy, were observed, although these were faint. Thus, immunohistochemical studies were subsequently performed (Fig. 3a–e). The results were: CK7, strongly positive; colloidal iron stain, negative; c-kit, weakly positive; vimentin, positive; RCC marker, negative; and PAX2, negative. The final diagnosis was cystic renal cell neoplasm of oncocytosis with a low malignant potential (pT1a).

The present case has been followed up as carcinoma with a low malignant potential. At present, recurrence and metastasis have not been observed 30 months after surgery.

Discussion

Oncocytoma and chromophobe renal cell carcinoma have several common characteristics: both are thought to be originated from the intercalated cells of the renal collecting duct, and show a similar gross appearance in the cut-surface. However, the microscopic findings of these 2 types of tumors are clearly distinct. Oncocytoma was distinguished from renal cell carcinoma as a renal epithelial benign tumor by Klein and Valensi [3]. The typical oncocytoma cells are eosinophilic, and the cytoplasm is filled with mitochondria. Chromophobe renal cell carcinoma was first reported as a type of renal cell carcinoma by Thoenes et al. [4]. This type of tumor does not show the chromosomal aberrations of 3p that is characteristic of renal clear cell carcinoma. Histologically, there are 2 variants: one is the typical variant and the other is eosinophilic [5]. Chromophobe cells show a positive reaction for the colloidal iron staining [6].

In the present case, the histological findings in hematoxylin–eosin-stained specimens suggested an oncocytoma, showing the clear eosinophilic cytoplasm. With further observation, findings such as local cell invasion, mitotic figures, and necrosis were suggestive of malignancy. With subsequent immunohistochemical studies, this case was finally diagnosed as being unclassified renal cell carcinoma. The following descriptions are analyses of the results of the immunohistochemical studies, which led to the final diagnosis: granular cell carcinoma, already withdrawn from the classification of renal cell carcinomas, was clearly ruled out because of a positive reaction for CK7, together with negative reactions for PAX2 and RCC marker. Type 2, or oncocytic variant, of papillary renal cell carcinoma was withdrawn from the candidates because of lack of the papillary architecture. The results of the strong reaction for CK7, partially positive vimentin, and negative PAX2 did not support oncocytoma. The strong, diffuse

Fig. 1 Enhanced computed tomography (CT). In the lower pole of the left kidney, a cystic tumor was demonstrated, on the wall of which a mural nodule with an enhancement effect (arrow) was shown

Fig. 2 Inner cut-surface of the tumor. The tumor was cystic. On the surface of the wall, a nodular change (arrow) was observed

Fig. 3 Microphotograph of the resected specimen (H&E stain). **a, b** The protruding portion showed the proliferation of large cells with rich eosinophilic granules in the cytoplasm and round-shaped nuclei (**a** $\times 40$, **b** $\times 400$). **c** Mitosis ($\times 40$). **d** Necrosis ($\times 40$). **e** Cell invasion ($\times 400$)

Table 1 Characteristics of immunohistochemistry

	H&E	CK7	Colloidal iron	PAX2	c-kit	RCCMA
Oncocytoma	Eosinophilic	(–)	(–)	(+)	(+) > (–)	(–)
Chromophobe	Eosinophilic (part), koilocytosis-like appearance	(+)	(+)	(+) > (–)	(+)	(+) > (–)
Current case	Eosinophilic, no papillary architecture	(+)	(–)	(–)	(+) (weak)	
Papillary, type 2	Papillary architecture	(–) > (+)	(–)	(+)	(–)	(+)

reaction for CK7 is the characteristic of chromophobe renal cell carcinoma [7, 8]. The weak reaction for c-kit and the coexistence of cells with a positive reaction for vimentin in addition to a negative reaction in the colloidal iron staining were observed: these results were thought to be in opposition to chromophobe renal cell carcinoma [6, 8]. The tumor consisted of eosinophilic cells without pale cells. The negative reactions for PAX2 and in the colloidal iron staining, and the weakly positive reaction for c-kit are supportive of an eosinophilic variant of chromophobe cell renal cell carcinoma. However, a positive reaction for vimentin as well as a lack of findings such as koilocytosis-like appearance, without perinuclear halo, is the negative reason for this type of chromophobe renal cell carcinoma. In summary, the tumor of this case had morphological similarity to oncocytoma, whereas the characteristic sign of chromophobe renal cell carcinoma, such as perinuclear halo, was absent. In contrast, the findings of immunohistochemistry indicated several positive factors for

chromophobe renal cell carcinoma, whereas there were no results suggestive of oncocytoma. Consequently, hybrid oncocytoma/chromophobe renal cell carcinoma [9], so called hybrid tumor, was ruled out. According to these biological characteristics, this tumor could be considered to stay midway between oncocytoma and chromophobe renal cell carcinoma (Table 1). Because it was not compatible with the current classification, we finally judged this tumor as cystic renal cell neoplasm of oncocytosis, a type of unclassified renal cell carcinoma.

In 2010, Gobbo et al. [2] analyzed 3 cases of renal cell carcinoma which had characteristics of both oncocytoma and chromophobe cell carcinoma, and could not be classified into the known categories of renal carcinomas. In their report, they designated this type of tumor as renal cell neoplasm (carcinoma) of oncocytosis. The present tumor showed similar biological characteristics to renal cell neoplasm (carcinoma) of oncocytosis, and was accompanied by a cystic change. Thus, we diagnosed this case as

being cystic renal cell carcinoma of oncocytosis. To make this diagnosis more definite, additional tests such as parvalbumin stain, S100A stain, and chromosome analysis might be necessary [2].

As a different diagnosis of the present case, there remains a possibility of chromophobe renal cell carcinoma with oncocytoma-like variant, recently advocated by Kuroda et al. [10]. Although the immunohistochemical characteristics were compatible with chromophobe renal cell carcinoma except for a focally positive reaction for vimentin, the tumor morphologically resembled oncocytoma. In addition, its infiltration pattern was expansive with the clear border. Chromophobe renal cell carcinoma with oncocytoma-like variant showed a strongly positive reaction for CK7 [10]; this finding is consistent with that of the present case. However, chromosomal analyses have not been performed in this case like that carried out by Kuroda et al.

The important thing is the fact that renal cell carcinomas resembling oncocytoma certainly exist. A simple and reliable method to make a differential diagnosis would be a CK7 staining. Although there have been reported cases of oncocytoma with recurrence, metastasis, or vascular involvement, these cases might include renal cell carcinomas with morphological similarity to oncocytoma. It is necessary to accumulate cases of renal cell carcinoma showing oncocytosis which is different from a hybrid tumor, and it is also necessary to analyze its clinicopathological characteristics.

Conclusions

We encountered a case of cystic renal cell carcinoma of oncocytosis. First, this case was histologically diagnosed as being oncocytoma after a common hematoxylin–eosin stain, and was then led to the final diagnosis after several series of immunohistochemical studies. It seems to be very important to recognize the fact that renal cell carcinomas resembling oncocytoma certainly exist.

Conflict of interest The authors have declared that no conflict of interest exists.

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