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A case of metastatic renal cell carcinoma to the ovary

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CASE REPORT *Manuscript No. 60507*

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ABSTRACT

A 52-year-old woman had a pathological fracture of the right femur. On histopathological examination bone metastasis from renal cell carcinoma was suspected. Abdominal computed tomography showed a heterogeneous mass (9.1 x 7.8 x 6.5 cm) in the left kidney and a cystic multilocular mass (12 x 10 cm) in the pelvis. Bone scintigraphy revealed an abnormal uptake in the left coracoid process, right third rib, and right distal femur and proximal tibia. Clinical diagnosis was left renal cancer with multiple bone metastases (cT2N0M1, stage IV) and a right ovarian tumor. We performed left radical nephrectomy and resection of right ovarian tumor with bilateral adnexectomy. On histopathological examination, the left kidney tumor was diagnosed as renal cell carcinoma (clear cell carcinoma with chromophobe component, G2>G1). The ovarian tumor consisted of carcinoma of clear cell type (G2) that resembled components of left renal cell carcinoma, confirming the diagnosis of metastatic renal clear cell carcinoma to the ovary. Although she underwent immunotherapy by interferon, she died in 10 months after nephrectomy.

Metastasis to the ovary from renal clear cell carcinoma is very rare and only 18 cases have been reported in the literature. This rarity may be related to the difficulty of differential diagnosis between metastatic renal cell carcinoma to the ovary and primary ovarian clear cell carcinoma. Elaborate analysis of microscopic features and immunohistochemical profiles may help the distinction of this metastatic lesion.

INTRODUCTION

Ovarian metastasis of renal cell carcinoma (RCC) is very rare and only 18 cases have been reported in the literature. Herein we reported a case of ovarian metastasis of renal clear cell carcinoma and discussed several aspects of its histopathological diagnosis.

CASE REPORT

A 52-year-old woman had a pathological fracture of the right femur in 2001. On histopathological examination of fractured bone specimens, bone metastasis of RCC was suspected. On physical examination, no tender mass was palpable in left abdominal region and laboratory examination showed no abnormality except a high level of CA 125 (102 U/ml, normal value less than 35). Abdominal computed tomography (CT) showed a heterogeneous mass (9.1 x 7.8 x 6.5 cm) in the left kidney (Fig. 1A). A multilocular cystic mass (12 x 10 cm) in the pelvis was also revealed on CT and magnetic resonance imaging (Fig. 1B and 1C). Bone metastases in the left coracoid process, right third rib, and right distal femur and proximal tibia were suspected by bone scintigraphy. Lung metastasis was not identified.

Clinical diagnosis was left renal cancer with multiple bone metastases (cT2N0M1, stage IV), and a right ovarian tumor. The ovarian tumor was highly suspected of malignancy,

however differential diagnosis of primary or metastatic ovarian tumor was not concluded. We performed transabdominal left radical nephrectomy and resection of right ovarian tumor with bilateral adnexectomy. On histopathological examination, renal tumor was diagnosed as renal cell carcinoma (clear cell carcinoma with chromophobe component, G2>G1, INFα: Fig. 2A). Ovarian tumor consisted of carcinoma of clear cell type (G2) that resembled components of left renal cell carcinoma (Fig. 2B) and fractured right femur (Fig. 2C). Thus the ovarian tumor was diagnosed as metastasis of RCC. Immunohistochemical stain could not be performed. Recovery was uneventful and she underwent immunotherapy by natural IFNα. However, bone metastases rapidly progressed and multiple lung metastases subsequently developed. Although further treatment with recombinant IFNα 2a or IFNγ was attempted, she died in 10 months after nephrectomy. Consent for autopsy was not obtained.

DISCUSSION

Metastatic ovarian tumors were mainly derived from gastric or colon cancer, breast cancer and lymphoma. Ovarian metastasis of RCC is very rare. In one review of 324 autopsies of women with RCC, no ovarian metastasis was found [1]. Bruegge et al. reviewed 13 publications that presented sites of metastasis from a total of 1595 renal tumors and they revealed only 4 cases (0.5%) with ovarian metastasis [2]. Including our case, we summarized a

total of 19 cases of metastatic RCC to the ovary in the literature (Table). Age ranged from 17 to 68 years (mean age 50.4 years). Of 19 cases 13 were first diagnosed as renal cancer and 2 were first detected as ovarian tumor. In remaining 4 cases, both renal and ovarian tumors were diagnosed simultaneously. Laterality of renal cancer was right in 8 cases and left in 11. Laterality of ovarian metastasis was right in 4 cases, left in 9, bilateral in 5 and unknown in 1. Renal cancer and ovarian metastasis had the same laterality in 6 cases; left in 5 and right in 1. It has been plausibly mentioned that ovarian metastasis of RCC is likely to occur predominantly in the left side because the left ovarian vein directly drains into the left renal vein facilitating retrograde tumor spread through the left ovarian vein. However, this hypothesis may not be true and other mechanisms such as Krukenberg tumor in gastric cancer may be involved in occurrence of ovarian metastasis of RCC. Prognosis of ovarian metastasis of RCC is poor and only 5 patients were alive above 2 years after operation.

Exact reason for rarity of ovarian metastasis of RCC remains obscure. Ovaries have increasingly fibrotic and atrophic change at the peak age of RCC incidence (sixth and seventh decades). After menopause the ovary reduced the weight and its blood flow was decreased. Therefore fewer emboli would be carried to the ovary after menopause than to larger and more vascular organs. Furthermore, vascular sclerosis of the ovary would reduce the clumps of tumor cells getting through the arterioles into the more suitable environment of capillary beds or into thin-walled veins [2].

Other reason for rarity may be related to the difficulty associated with differential diagnosis

of metastatic ovarian tumor from renal clear cell carcinoma and primary ovarian clear cell carcinoma. Although metastatic tumors of the ovary generally present a significant diagnostic problem in the interpretation of ovarian tumors, particularly between metastatic ovarian tumor from RCC and primary ovarian clear cell carcinoma, certain histopathological features may help to establish the correct diagnosis. Primary ovarian clear cell carcinoma shows a tubular or glandular pattern lined by hobnail cells, at least focally, in 87% of cases. The tubules often contain intraluminal mucin. Hyaline, membrane-like material occurs in 91% of cases. The mixture of histological patterns (solid, papillary and tubulocystic or glandular) is found in 83% of cases [3,4]. Renal clear cell carcinoma is lacking in these histological findings and vascularity is more prominent in renal clear cell carcinoma. Because our case had no characteristic histopathological features related to primary ovarian clear cell carcinoma, we diagnosed ovarian metastasis of RCC.

Recently, immunohistochemical staining for renal and ovarian clear cell carcinoma has been reported [5-8]. Ohta et al. [5] performed immunohistochemical staining for 24 cases of renal clear cell carcinoma and 29 cases of primary ovarian clear cell carcinoma. All ovarian clear cell carcinomas were positively stained for 34βE12 (recognizing high-molecular weight cytokeratin) and all RCCs were negative. On the contrary, all renal cell carcinomas were positive for CD10 (monoclonal antibody recognizing a cell surface zinc-dependent metalloproteinase) and 23 of 29 cases of ovarian clear cell carcinoma were negative. Moreover, all ovarian clear cell carcinomas were positive for cytokeratin 7 (CK7) and 9 of 24 cases of renal

cell carcinoma were positive for CK7. Number of CK7-positive cells in renal cell carcinoma was clearly lower than ovarian clear cell carcinoma [5]. Cameron et al. [6] showed that CD10 and RCC marker (monoclonal antibody binding to a 200 kD glycoprotein expressed in renal proximal tubules) were positive in all renal clear cell carcinomas and that CD10 was negative in all and RCC marker was negative in most ovarian tumors. CK7 was positive in all ovarian clear cell carcinomas and negative in most renal cell carcinomas. CK7 is often positive in papillary and chromophobe renal cell carcinoma [6]. Nolan and Heatley [7] demonstrated that 8 of 10 ovarian clear cell carcinomas were positive with CA125, whereas all 10 renal cell carcinomas were negative. From the results of these studies, immunohistochemical staining in combination with 34βE12, CD10, CK7, RCC marker and CA125 seems to be able to distinguish accurately between clear cell carcinoma in the kidney and ovary.

In conclusion, the possibility of ovarian metastasis of RCC, although very rare, should be considered in the differential diagnosis of ovarian clear cell tumors, especially in those patients who underwent prior nephrectomy due to RCC. Elaborate analysis of microscopic features and immunohistochemical profiles may help the distinction of this metastatic lesion.

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FIGURE LEGENDS

Fig. 1. 1A: Abdominal CT scan revealed a heterogeneous mass in the left kidney (9.1 x 7.8 x 6.5cm). 1B, 1C: CT and MRI showed a multilocular cystic ovarian tumor (12 x 10cm) in the pelvis.

Fig. 2. Histopathological findings (H-E staining).

2A: renal tumor, 2B: ovarian tumor, 2C: metastatic tumor of right femur.

Renal tumor consisted of clear cell carcinoma with chromophobe component, G2>G1 and right ovarian tumor and femur tumor consisted of carcinoma of clear cell type (G2) resembling components of left renal cancer.

Table: Summary of 19 cases with metastatic renal cell carcinoma to the ovary

Figure 1

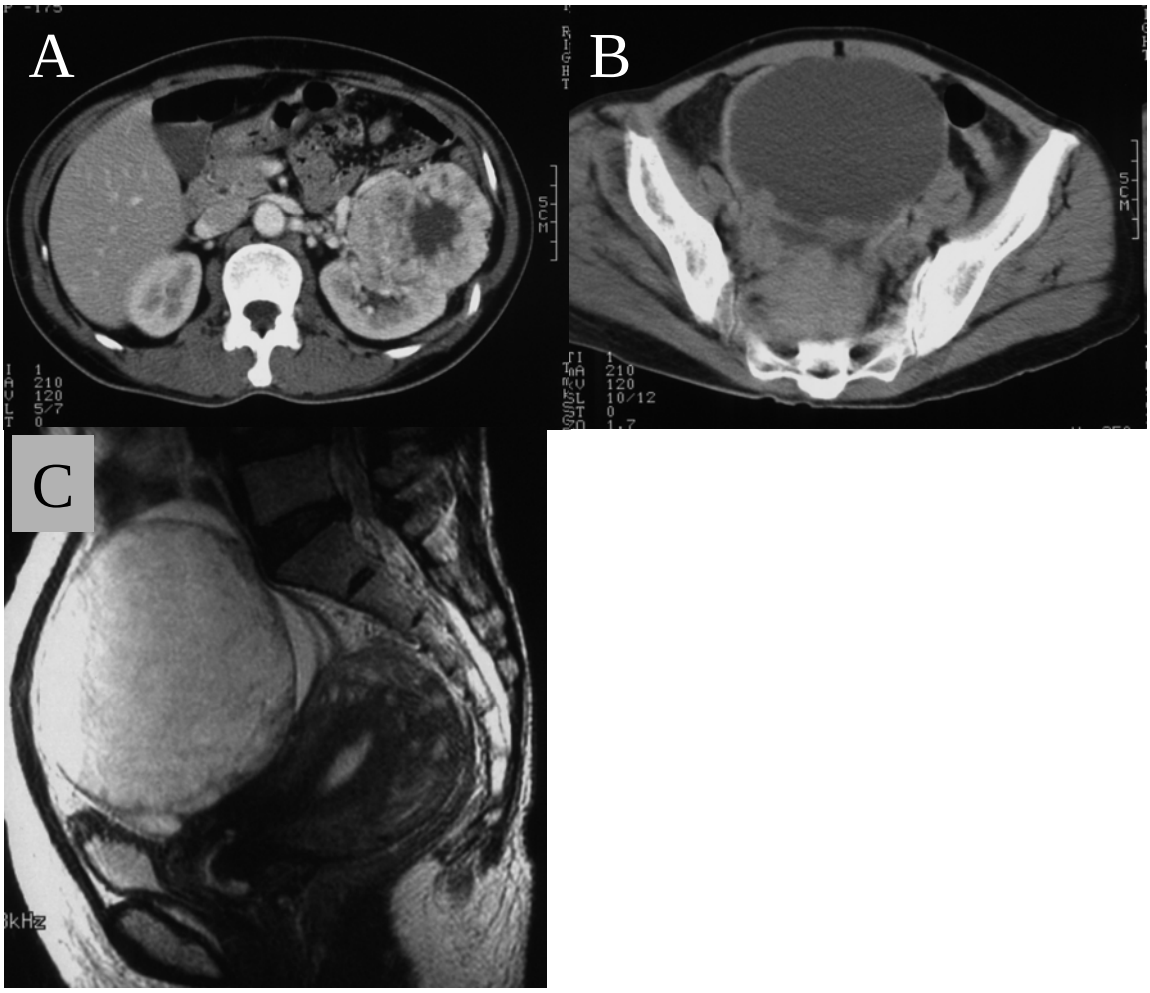

Figure 2

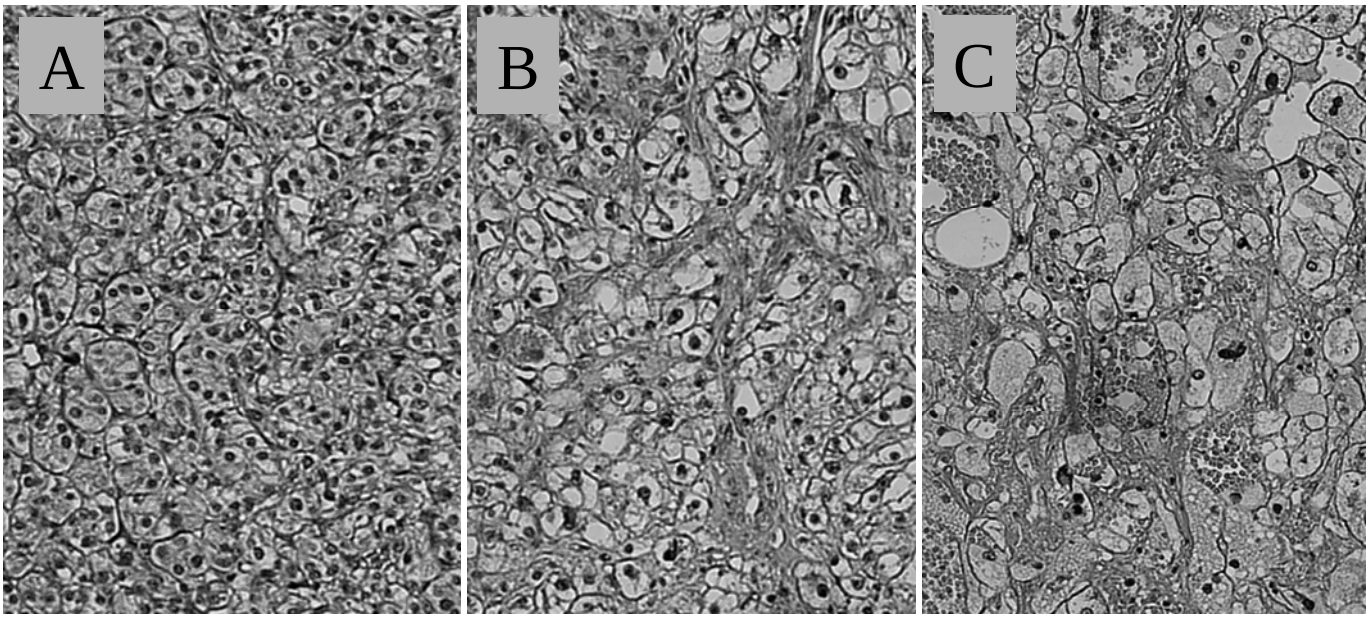

Table: Summary of 19 cases with metastatic renal cell carcinoma to the ovary

No.	age (y)	Laterality		First detected site	Duration until detection of second site (y)	RCC size (cm)	OV tumor size (cm)	Other metastasis site at first presentation	Authors	Year
		Kidney	Ovary							
1	57	L	L	kideny	8M	15×8.5×7	6.3	vagina	Martzloff et al	1949
2	64	R	B	kideny	11	NA	rt:11×8×6 lt:17×10×8	lung	Vorder Bruegge et al	1957
3	68	R	L	kideny	3M	NA	NA	no	Stefani et al	1981
4	52	L	L	simultaneous		3.5	7	no	Buller et al	1983
5	48	R	L	ovary	8	10, 5.5	18	no	Young et al	1992
6	62	L	R	kideny	1	NA	8×6×5.5	thyroid, lung, neck L/N		
7	48	L	L	simultaneous		6.5	12	no		
8	28	R	L	kideny	7M	8×5.5×5	12×10×8	bone	Liu et al	1992
9	40	L	B	ovary	7M	NA	NA	skin, parotid, brain	Spencer et al	1993
10	46	L	B	kideny	3	7×7×6	NA	no	Adachi et al	1994
11	54	R	L	kideny	3	NA	10	no	Fields et al	1996
12	66	R	B	kideny	11	NA	rt: 14×11×8 lt: normal	skin	Vara et al	1996
13	47	L	L	kideny	4	NA	11×9×7	no	Shinojima et al	2001
14	50	R	R	kideny	1	NA	7×5	no	Insabato et al	2003
15	49	R	NA	kideny	14M	8.5	10×6.5	bone, visceral		
16	17	L	L	kideny	2	5.5	NA	no		
17	48	L	R	simultaneous		6	6	bone	Hammock et al	2003
18	61	L	B	kideny	7	10×10×8	rt: 11.8×11.6×9.7 lt: 7.4×7.3×6.7	skin, paraorta, omentum	Valappil et al	2004
19	52	L	R	simultaneous		9.1×7.8×6.5	12×10	bone	Our case	

Abbreviation: RCC:renal cell carcinoma; OV:ovarian tumor; M:months; L/N:lympho node; NA:not available