Signet-ring Cell Carcinoma of the Stomach Metastasizing to Renal Cell Carcinoma: a Case Report and Review of the Literature

Sakai, Yasuhiro ; Kanomata, Naoki ; Itami, Hiroe ; Kajimoto, Kazuyoshi ; Sakuma, Toshiko ; Ohbayashi, Chiho

(Citation)
The Kobe journal of the medical sciences,55(6):122-131

(Issue Date)
2009

(Resource Type)
departmental bulletin paper

(Version)
Version of Record

(JaLCDOI)
https://doi.org/10.24546/81002360

(URL)
https://hdl.handle.net/20.500.14094/81002360

Kobe J. Med. Sci., Vol. 55 No. 6, pp. E122-E131, 2009

Signet-ring Cell Carcinoma of the Stomach Metastasizing to Renal Cell Carcinoma: a Case Report and Review of the Literature

YASUHIRO SAKAI[1]*, NAOKI KANOMATA[2], HIROE ITAMI[1], KAZUYOSHI KAJIMOTO[1], TOSHIKO SAKUMA[1], and CHIHO OHBAYASHI[1]

[1]*Department of Pathology, Hyogo Cancer Center, Hyogo, Japan*

[2]*Department of Pathology, Kawasaki Medical School, Okayama, Japan*

Received 30 October 2009/ Accepted 8 December 2009

Key Words: gastric cancer, signet-ring cell carcinoma, renal cell carcinoma, clear cell carcinoma, cancer-to-cancer metastasis, tumor-to-tumor metastasis

ABSTRACT

Metastasis of one neoplasm to another is also known as metastasis of "tumor to tumor", "cancer to cancer", "tumor in tumor", and "one to another". We describe the case of a 75-year-old woman with the metastasis of signet-ring cell carcinoma of the stomach to clear cell renal cell carcinoma. Six years earlier, the patient had undergone gastrectomy for early gastric cancer. She complained of lumbago, and a mass was found in her left kidney. Examination of a partial nephrectomy revealed clear cell renal cell carcinoma containing signet-ring cells. Morphological and immunohistochemical findings of the signet-ring cells found in kidney cancer and gastric cancer were identical. Subsequent examinations revealed the patient had multiple bone metastases. The diagnosis of carcinoma metastasizing to renal cell carcinoma can be challenging; therefore, additional clinical information and immunohistochemical panel studies are requisite.

INTRODUCTION

Metastasis of one neoplasm to another is a notable and uncommon phenomenon, and is also known as metastasis of "tumor to tumor", "cancer to cancer", "tumor in tumor", and "one to another". We describe the case of a 75-year-old woman with the metastasis of signet-ring cell carcinoma of the stomach to clear cell renal cell carcinoma.

CASE REPORT

Clinical course

A 75-year-old woman visited a local physician for recently developed lumbago. She had six years earlier undergone distal gastrectomy for gastric cancer at a community hospital. The cancer had occurred at the lesser curvature of the body, was type IIc, and measured 58 × 25 mm. The histopathologic type was signet-ring cell carcinoma admixed with a poorly-differentiated adenocarcinoma component (Fig. 1), assessed as pT1N0M0, stage IA at that time. After the surgery, the patient had been well, with no symptoms of recurrence or metastasis. The medical check-up because of lumbago at another hospital revealed, by computed tomography, an expansive solid tumor, 2.5 cm in diameter, in the upper pole of the

Phone: +81-78-929-1151 Fax: +81-78-929-2387 E-mail: sakaiyasuhiro@gaia.eonet.ne.jp

right kidney (Fig. 2). A hematological examination was not significant. Nephron-sparing surgery was carried out for the renal tumor at Hyogo Cancer Center. Thereafter, multiple bone metastases were detected by Gallium-67 scintigraphy and magnetic resonance imaging. The patient has been undergoing chemotherapy for three months since the nephron-sparing surgery.

Pathological findings

Gross

The partially resected right kidney contained a yellow solid tumor measuring 2.1 × 1.6 × 1.5 cm, with hemorrhage and cysts (Fig. 3), showing an expansive, pushing growth pattern, and a well demarcated fibrous pseudocapsule. There was no conspicuous infiltration of tumor cells into perirenal fat tissue.

Microscopic

The tumor cells were clear or slightly eosinophilic, with distinct cell membranes, arranged in compact nests, of an alveolar, microcystic, or macrocystic pattern, and separated by thin-walled blood vessels (Fig. 4). The cysts contained red blood cells and/or eosinophilic fluid. There was no infiltration of tumor cells into the renal sinus, perirenal fat tissue, lymphatics, or blood vessels. Fibrosis and hemosiderin-laden macrophages were present. The nuclei of most of the tumor cells were mildly irregular and about twice as large as red blood cells, but some nuclei measured 20 μm or larger, with large prominent nucleoli. The tumor was diagnosed as clear cell renal cell carcinoma, Fuhrman's grade three and of stage pT1aN0M0. Signet-ring cells detected in the clear cell renal cell carcinoma had eosinophilic cytoplasm or intracytoplasmic mucin (Fig. 5), and most were irregularly scattered. The transition from the clear cell renal cell carcinoma to the signet-ring cells was not recognizable.

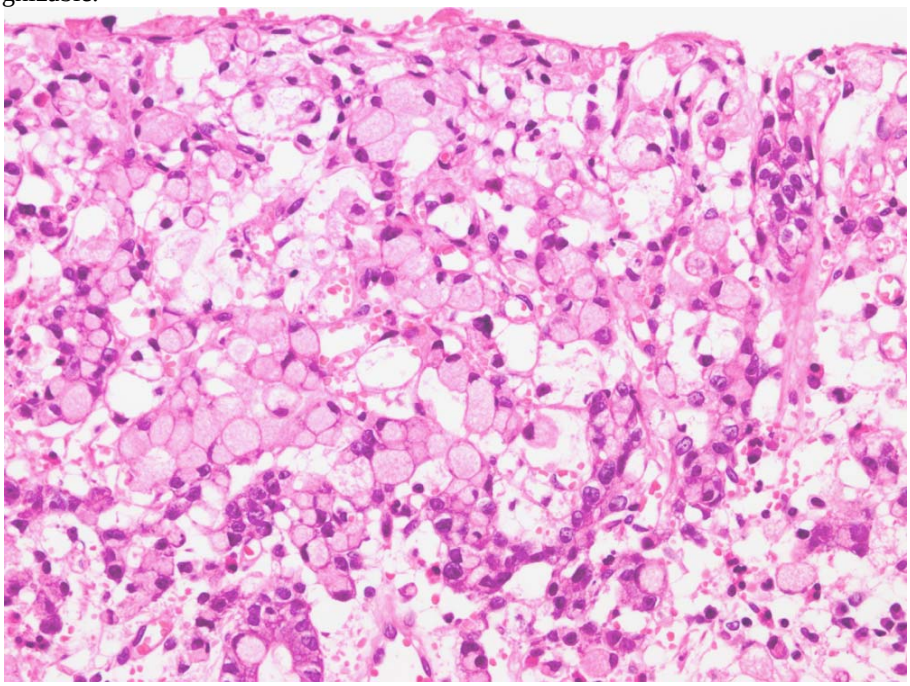

Figure1. Gastric signet-ring cell carcinoma, admixed with a poorly-differentiated adenocarcinoma component. (H&E, ×200)

Figure2. Dynamic enhanced abdominal computed tomography. A mass of the right kidney protrudes from the cortical surface.

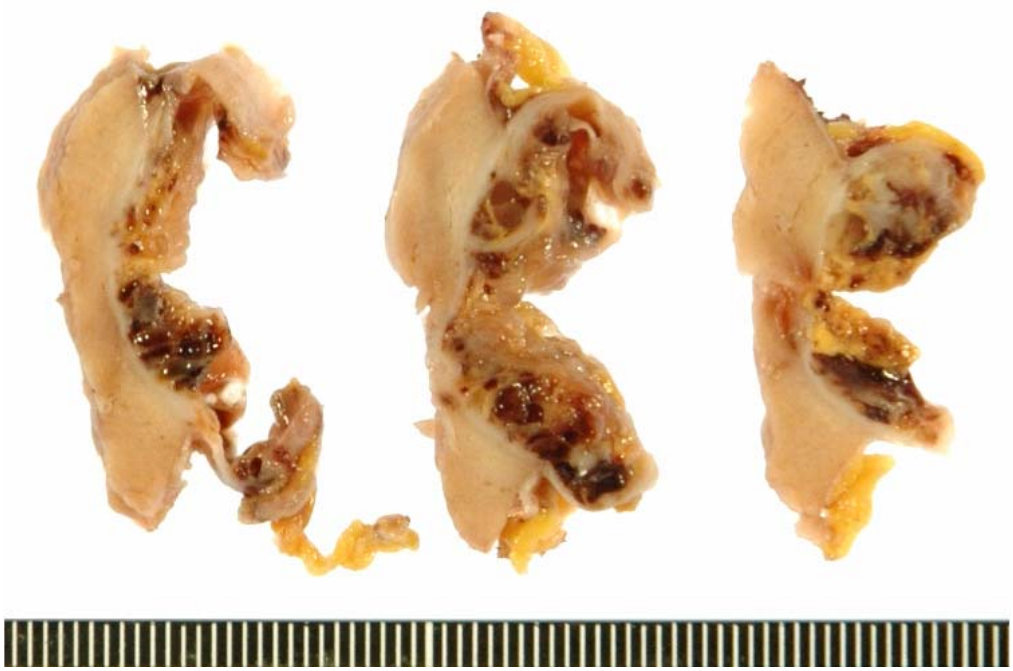

Figure3. Partially resected kidney containing a well-demarcated yellow solid mass with hemorrhage and cysts.

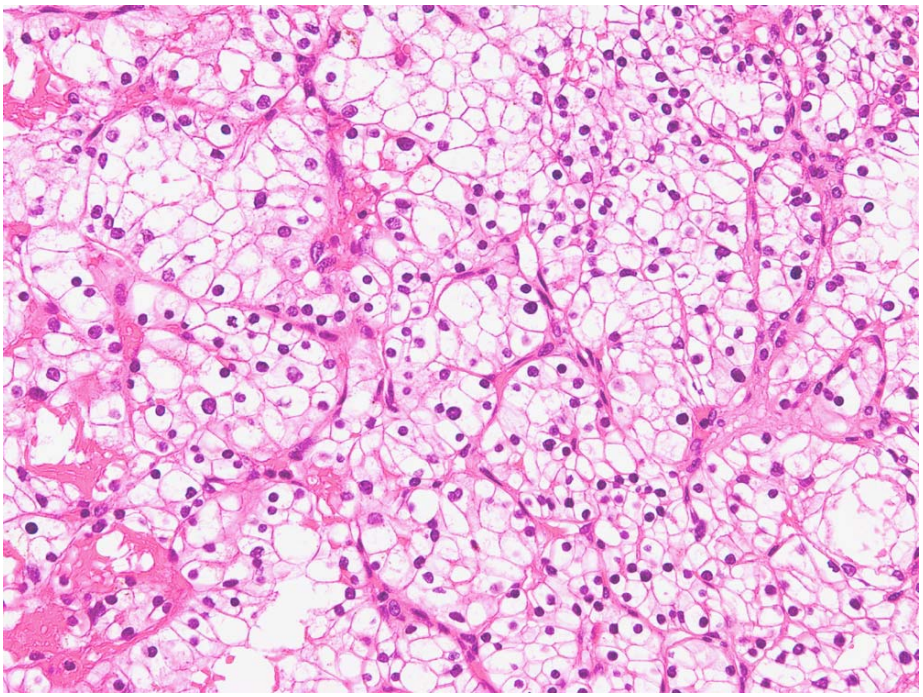

Figure4. Clear cell renal cell carcinoma, showing a typical alveolar, solid or microcystic pattern. pattern. (H&E, ×200)

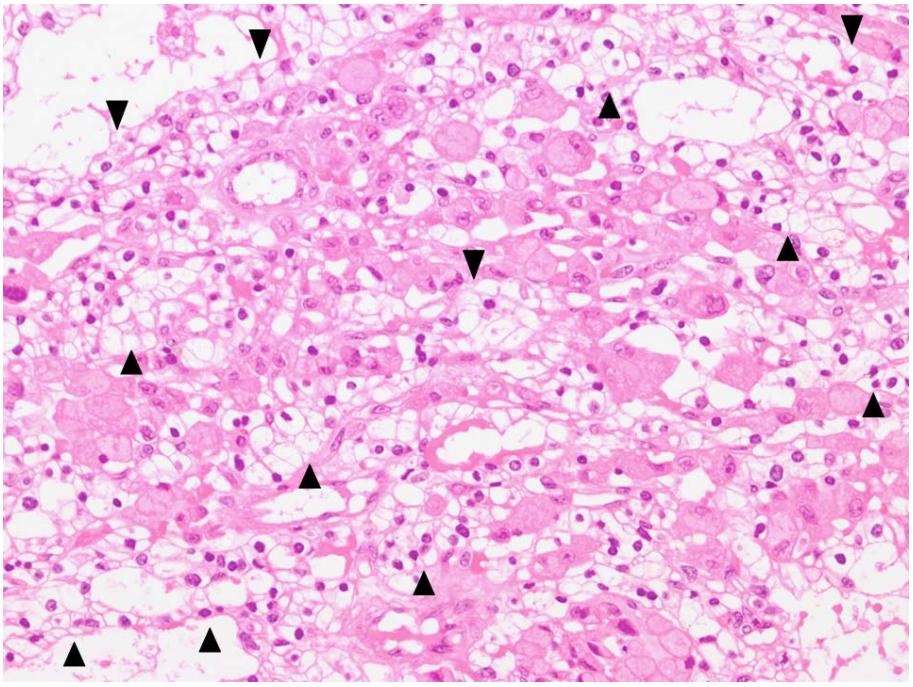

Figure5. Signet-ring cells with intracytoplasmic mucin or eosinophilic cytoplasm, admixed with clear cell renal cell carcinoma (arrow heads). (H&E, ×200)

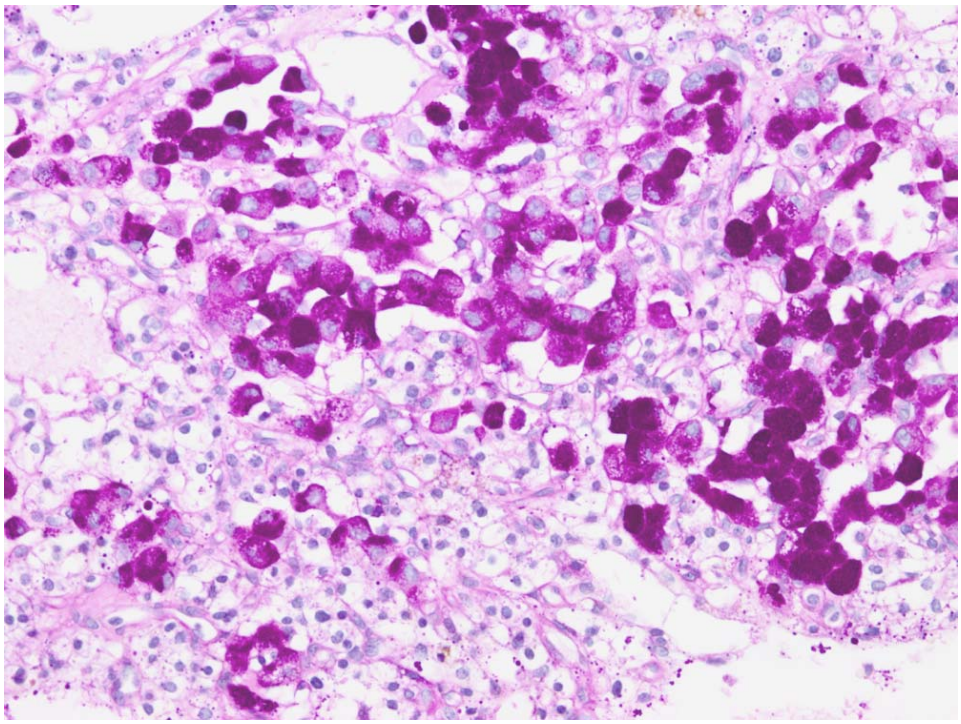

Figure6. Signet-ring cells positive for PAS after diastase digestion.

The signet-ring cells were positive for PAS before and after diastase digestion (Fig. 6) and slightly positive for Alcian blue pH 2.5, but negative for Alcian blue pH 0.9 or mucicarmine.

Immunohistochemical studies were carried out on the signet-ring cells, the clear cell carcinoma and the gastric cancer (Table I). A retrospective review of preparations of the gastric cancer revealed signet-ring cell metastases to three lymph nodes along the left gastric artery (pN1), regardless of indistinct gastric wall invasion. From the similarity of the morphology and the results of immunohistochemistry, the signet-ring cell component in the renal cell carcinoma was diagnosed as gastric cancer metastasis, confirming the cancer-to-cancer metastasis.

Table I. Immunohistochemical analysis of renal cell carcinoma, signet-ring cells, and gastric cancer.

	Renal cell carcinoma	Signet-ring cell component	Gastric cancer
AE1/AE3	+	+	+
CAM5.2	+	+	+
Vimentin	+	−	−
CK7	+	+	+
CK20	−	+	+
CD10	+	+	+
CDX2	−	+	+
MUC5AC	−	+	±
HIK1083	−	+	+
CEA	−	+	+
E-cadherin	−	+	±

DISCUSSION

The earliest description of cancer-to-cancer metastasis[1] is a case of conjunctiva melanoma metastasizing to kidney cancer.[2]

The frequently cited criteria of the metastasis of one neoplasm to another are four: (1) more than one primary tumor exists; (2) the recipient tumor is a true neoplasm; (3) the metastatic neoplasm is a true metastasis with established growth in the host tumor, not the result of contiguous growth or embolization of tumor cells; (4) tumors that have metastasized to the lymphatic system, where lymphoreticular malignant tumors already exist, are excluded.[3] Also, the two tumors should be distinctly separated.[4] The criteria based on cases of metastases to primary intracranial meningioma and neurilemoma are as follows: (1) the metastatic focus must at least be partially enclosed by a rim of benign, histologically distinct host tissue, and (2) the existence of the metastasizing primary carcinoma must be proven and compatible with the metastasis.[5]

In a study of 11,328 autopsies of cancer patients, 816 cases (7.2 %) have demonstrated renal metastases. The most common primary tumors in decreasing order of frequency have been lung, breast, skin (melanoma), and tumors of the genitourinary, gastrointestinal, and gynecologic tracts.[6] Another study of 4,455 carcinomas has demonstrated 261 cases (5.8%) of renal metastases.[7] The metastases of neoplasms to kidney cancer are summarized from the previous reports in Table II and Table III.[2,3,7-34] The tables shows a male to female ratio of 2:1, and an age range of 40 to 91 years (average, 61.7); kidney tumors measure 1 to 10.5 cm (average, 4.3 cm); lung cancer and prostate cancer are major donor tumors; adenocarcinoma is the most frequent histology. The metastasis of gastric adenocarcinoma to clear cell renal cell carcinoma, as in our case, seems to be a very rare phenomenon. Metastasis of a neoplasm to kidney cancer is usually recognized as a part of widespreading disease.

Table II. Summary of clinicopathological characteristics of renal cell carcinoma as a recipient.

Histopathologic subtype	n	Gender	n	Age [years old]	Large diameter [cm] (Average ± 2SD (n ≥ 3))
Total	44			61.1 ± 21.7	
clear cell	42	M	21	61.7 ± 20.1	4.3 ± 5.4
		W	12		
		NA	8		
NA	2	M	2	—	4.0

SD: standard deviation, n: number, NA: not available, M: men, W: women

Table III. Summary of donors' characteristics in cases with metastasis of neoplasms to renal cell carcinoma.

Donor organ	n	Histopathologic type	n	Metastasis	n
lung	18	adenocarcinoma	7	widespread	15
		small cell carcinoma	2	recipient only	1
		squamous cell carcinoma	1	NA	2
		carcinoma	7		
		rhabdomyosarcoma	1		
prostate	7	adenocarcinoma	7	widespread	5
				recipient only	2
breast	3	squamous cell carcinoma	1	widespread	3
		carcinoma	2		
stomach	3	adenocarcinoma	2	widespread	3
		undifferentiated carcinoma	1		
thyroid	2	anaplastic carcinoma	2	widespread	2
uterus	2	adenocarcinoma	1	recipient only	2
		adenosquamous carcinoma	1		
colorectum	2	adenocarcinoma	2	widespread	2
others	6				

NA: not available

The hypervascularity of kidney cancer might be an important factor in its being the favored target of the donor tumor — most kidney cancers have rich blood flow.[3,11] The plentiful glycogen and lipid content of clear cell renal cell carcinoma could serve as fertile soil for metastatic cancer cells to grow in.[35] Moreover, clear cell renal cell carcinoma may have an inadequate immunologic response of rejecting donor cancer cells, and may thus indirectly support their growth within its substance.[4,25]

Differential diagnosis between primary renal cell carcinoma with mucin and metastasis of tumors to kidney cancer can be challenging, but is very important from the aspect of post-operative therapy and prognosis.

In general, renal cell carcinoma seldom produces intracytoplasmic mucin or mucin lake, although mucinous tubular and spindle cell carcinoma (one of the special histopathologic types of renal neoplasms) is well known for its secretion of mucin. Very rarely do papillary renal cell carcinoma, collecting duct carcinoma and unclassified renal cell carcinoma contain mucin.[36-39] Therefore, it may be more prudent to conduct diagnosis (keeping in mind the possibility of signet-ring cell carcinoma of the stomach metastasizing into clear cell renal cell carcinoma) regardless of clinical information of early-stage gastric cancer.

Immunohistochemically, the vast majority of cases of gastric signet-ring cell carcinoma expresses CDX2 and Hep Par1; approximately one half to two thirds express MUC2, MUC5AC, CK20, E-cadherin, and CK7; and one sixth MUC1.[40,41] On the other hand, the most prevalent clear cell renal cell carcinoma immunoprofile is CK7-, CK20-, EMA+, Vimentin+, RCC Ma+, CD10+, AMACR-, CD117-, parvalbumin-, E-cadherin-, and MUC1+.[42] The retrospective review and the immunhistochemical study of the preparations of gastric cancer were helpful in the differential diagnosis of our case (Table I).

Well-considered immunohistochemical panel and clinical information would be useful for correct diagnoses.

ACKNOWLEDGEMENTS

The authors are grateful to Dr. Yutaka Kondo (Department of Urology, Hyogo Cancer Center), Dr. Kazuki Yamanaka (Department of Urology, Miki City Hospital), Dr. Shinichi Matsumoto (Department of Diagnostic Radiology, Hyogo Cancer Center), and Dr. Yongsik Kim (Department of Surgery, Mitsubishi Kobe Hospital) for their corporation. The authors have no conflict of interest to declare.

REFERENCES

1. **Onuigbo W.** 2005. An early description of cancer-to-cancer metastasis in 1848. N Z Med J **118:** U1315.
2. **Smith H.** 1848. Malignant disease of the kidney, heart, and brain. Tr Path Soc Lond **1:** 281-282.
3. **Ortega P. Jr., Li I.Y., Shimkin M.** 1951. Metastasis of neoplasms to other neoplasms. Ann West Med Surg **5:** 601-609.
4. **Campbell L.V. Jr., Gilbert E., Chamberlain C.R. Jr., Watne A.L.** 1968. Metastases of cancer to cancer. Cancer **22:** 635-643.
5. **Chambers P.W., Davis R.L., Blanding J.D., Buck F.S.** 1980. Metastases to primary intracranial meningiomas and neurilemomas. Arch Pathol Lab Med **104:** 350-354.
6. **Bracken R.B., Chica G., Johnson D.E., Luna M.** 1979. Secondary renal neoplasms: an autopsy study. South Med J **72:** 806-807.
7. **Ottosson L., Berge T.** 1968. Metastasis from carcinoma to carcinoma. Acta Pathol

Microbiol Scand **73:** 481-488.
8. **Walther H.E.** 1948. Krebsmetastasen. Basel: Benno, Schwabe & Co., **1948:** p.172.
9. **Berent W.** 1902. Seltene Metastasenbildung. Centralbl f allg Path u path Anat **13:** 406-410 (in German).
10. **Boyd W.** 1955. Pathology for the surgeon. Philadelphia: Saunders, **1955:** p.52.
11. **Dobbing J.** 1958. Cancer to cancer. Guy Hosp Rep **107:** 60-65.
12. **Dote T., Hokano M., Takashima Y.** 1956. A thyroid cancer, which metastasized into Grauwitz's tumor. Gann **47:** 736-738 (in Japanese).
13. **Furuse K., Fukuoka M., Kobayashi Y., Sugimoto K.** 1972. Autopsy case of primary metastatic rhabdomyosarcoma associated with renal cancer. Gan No Rinsho **18:** 279-284 (in Japanese).
14. **Gore I., Barr R., Roxbury W.** 1958. Metastasis of cancer to cancer. Arch Pathol **66:** 293-298.
15. **Granville L.A., Ostrowski M.L., Truong L.D., Shen S.** 2005. Pathologic quiz case. Unusual morphology in an otherwise classic renal cell carcinoma. Arch Pathol Lab Med **129:** e49-50.
16. **Hammann E.** 1927. Ungewoehnliche Metastasierung eines Sarkoms bei Bestehen zweier Tumoren. Frankfurt Ztschr f Pathol **35:** 256-264.
17. **Horie A., Nomura Y.** 1977. Synchronous triple cancers with cancer-to-cancer metastasis. Gan No Rinsho **23:** 557-560 (in Japanese).
18. **Ichijima K., Yamabe H., Kobashi Y., Iwata T.** 1980. Metastasis of cancer to cancer. Acta Pathol Jpn **30:** 293-300.
19. **Inatomi H., Yamada Y., Okamura T.** 1996. A case of prostate carcinoma metastasizing to renal cell carcinoma. Int J Urol **3:** 155-157.
20. **Khurana K.K., Powers C.N.** 1997. Basaloid squamous carcinoma metastatic to renal-cell carcinoma: fine-needle aspiration cytology of tumor-to-tumor metastasis. Diagn Cytopathol **17:** 379-382.
21. **Kikuchi K., Tsuji Y., Itakura K., Katagiri H.** 1964. A case of metastases of gastric cancer to hypernephroma and its metastatic foci. Acta Pathol Jpn **14:** 103-110.
22. **Majmudar B.** 1976. Metastasis of cancer to cancer: report of a case. Hum Pathol **7:** 117-119.
23. **Maloney J.D., Immergut M.** 1968. The kidney as host in cancer-to-cancer metastasis. J Urol **98:** 657-660.
24. **Petraki C., Vaslamatzis M., Argyrakos T., Petraki K., Strataki M., Alexopoulos C., Sotsiou F.** 2003. Tumor to tumor metastasis. Report of two cases and review of the literature. Int J Surg Pathol **11:** 127-135.
25. **Rabson S.M., Stier P.L., Baumgartner J.C., Rosenbaum D.** 1954. Metastasis of cancer to cancer. Am J Clin Pathol **24:** 572-579.
26. **Schmorl G.** 1928. Pathological study of Schneeberg lung cancer. In: report of international conference of cancer. London: Wright, p.272-274.
27. **Schneider L.A.** 1955. Metastasis of cancer to cancer. Report of a case. Am J Clin Pathol **25:** 1288-1289.
28. **Sella A., Ro J.Y.** 1987. Renal cell cancer: best recipient of tumor-to-tumor metastasis. Urology **30:** 35-38.
29. **Sharma H.M., Old J.W.** 1969. Metastasis of carcinoma to carcinoma. Report of a case. Arch Pathol **88:** 191-193.
30. **Shuangshoti S.** 1983. Metastasis of bronchogenic adenocarcinoma to renal adenocarcinoma. South Med J **76:** 791-794.

31. **Singh E.O., Benson R.C. Jr., Wold L.E.** 1984. Cancer-to-cancer metastasis. J Urol **132:** 340-342.
32. **Sperb R.A., Arnold W., Gebbers J.O.** 1996. Carcinoma-in-carcinoma metastasis. In situ DNA quantification and immunohistochemical diagnosis. Pathologe **17:** 385-390 (in German).
33. **Tiszlavicz L., Krenács T., Rózsa Z.** 1991. Prostatic cancer metastasized into the kidney and kidney cancer metastasized into the lung. Orv Hetil **132:** 1539-1542 (in Hungarian).
34. **Walter A.** 1928. Ein Fall von Metastasen des Uteruscarcinoms in ein Nierenhypernephrom. Ztschr f Krebsforsch **27:** 451-456.
35. **Willis R.A.** 1934. Spread of tumors in the human body. London: J & A Churchill, Ltd., p.540.
36. **Grignon D.J., Ro J.Y., Ayala A.G.** 1988. Primary mucin-secreting adenocarcinoma of the kidney. Arch Pathol Lab Med **112:** 847-849.
37. **Val-Bernal J.F., Mayorga M., García-Arranz P., Gómez-Román J.J.** 1998. Mucin secretion in papillary (chromophil) renal cell carcinoma. Am J Surg Pathol **22:** 1037-1040.
38. **Val-Bernal J.F., Gómez-Román J.J., Vallina T., Villoria F., Mayorga M., García-Arranz P.** 1999. Papillary (chromophil) renal cell carcinoma with mucinous secretion. Pathol Res Pract **195:** 11-17.
39. **Pinto J.A., Menolascino F., Daboin I., Romero K., Hernández S.** 2001. Ductal cell carcinoma of the kidney with extensive signet ring cell mucosecreting areas. A case report with immunohistochemical analysis. Pathol Res Pract **197:** 827-832.
40. **Chu P.G., Weiss L.M.** 2004. Immunohistochemical characterization of signet-ring cell carcinomas of the stomach, breast, and colon. Am J Clin Pathol **121:** 884-892.
41. **Geller S.A., Dhall D., Alsabeh R.** 2008. Application of immunohistochemistry to liver and gastrointestinal neoplasms. Liver, stomach, colon, and pancreas. Arch Pathol Lab Med **132:** 490-499.
42. **MacLennan G.T., Cheng L.** 2008. Neoplasms of the kidney, p.97. In Bostwick D.G., Cheng L (eds.), Urologic surgical pathology, 2nd ed, Mosby-Elsevier, St. Louis, USA.