An Unusual Case of Metastatic Renal Cell Carcinoma Presenting as Melena and Duodenal Ulcer, 16 Years After Nephrectomy; a Case Report and Review of the Literature

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Abstract
Renal cell carcinoma comprises about 2% of adult tumors. The overall 10-year survival rate of patients with RCC after nephrectomy is about 18-27%. The incidence of metastasis of initial RCC is about 24-28%, but this rate after nephrectomy is as high as 51%. The most common site of recurrence is the lung, however liver and bone metastases are common.

Herein we report our experience with a case of gastrointestinal bleeding secondary to metastatic renal cell carcinoma to duodenum, 16 years after nephrectomy.

To the best of our knowledge, about 30 of such cases have been reported in the English literature. Many of the previous cases have been part of disseminated disease and isolated duodenal metastasis is very rare. The longest reported duration between nephrectomy for renal cell carcinoma and duodenal metastasis has been 13 years, thus it seems our case to be also unique because of very late duodenal metastasis.

Keywords ● Duodenal ulcer ● Gastrointestinal hemorrhage ● Renal cell carcinoma ● Pancreatectoduodenectomy

Introduction
Renal cell carcinoma (RCC) as the most common malignant tumor of the kidney has an unpredictable and bizarre natural history, i.e. on the one hand it has an indolent growth rate and showed metastasis at the time of presentation and on the other hand it can remain stable years after nephrectomy.1

The most common sites of metastasis in RCC are the lung and bone; other less common metastatic locations are lymph nodes, adrenal, liver, opposite kidney and brain.2

Gastrointestinal metastasis of RCC is rare and reported in 4% of the cases, however, in the GI tract, the least common site of metastasis is small intestine and it is extremely rare for metastatic RCC to be presented as duodenal ulcer and melena.3

To the best of our knowledge, less than 30 cases of duodenal...
metastasis of RCC have been reported in the English literature and the longest duration after nephrectomy has been 13 years.

Herein we report our experience with a 61-year-old man presented with melena 16 years after nephrectomy that was diagnosed to be metastatic RCC. The patient underwent Whipple’s operation with excellent postoperative course.

**Case Report**

A 61-year-old man was presented with melena. He was in a good health condition. His past medical history showed right kidney nephrectomy (16 years ago) with the diagnosis of clear cell RCC without any further treatment. He had been completely normal during the last 16 years.

Laboratory findings were:
- Liver function tests were normal: ALT=19 U/L (normal<40), AST=25 U/L (normal<40), Alkaline phosphatase=193 U/L (normal 80-306)
- Complete Blood Count was normal: WBC: 6000/µl, RBC: 5×10^6/µl, and Platelet: 263000/µl

Physical examination showed normal heart and lung examination. There was no lymphadenopathy. Blood pressure, pulse rate, heart rate, and temperature were all unremarkable.

Stool occult blood test was positive in several occasions, so the patient underwent upper and lower gastrointestinal endoscopy. An ulcer was found in the second part of duodenum with fine oozing of blood (figure 1a, 1b as indicated by arrows). A biopsy was taken and sections from duodenum showed surface ulceration beneath of which there was subepithelial collection of cells with clear cytoplasm (figure 2a, 2b). Immunohistochemistry was positive for cytokeratin, CD10, vimentin, and RCC antibody (figure 3a, 3b).

With the pathologic diagnosis of metastatic RCC, abdominal CT scan was performed that showed a mass in the distal pancreas measuring 7 cm in greatest diameter with central necrosis, most probably arisen from duodenum extending to the pancreas (figure 4). Whipple’s operation was performed and the pancreatoduodenal mass was resected. The specimen showed a mass measuring 7×5.5 cm
Metastatic RCC after 16 years, as a duodenal ulcer

in the duodenum extending to the head of the pancreas (figure 5). Pathology of the specimen showed metastatic RCC involving the duodenum and distal pancreas (figure 6). The patient was discharged in good condition to be followed for further evaluation.

This case is being reported by the informed consent of the patient.

Discussion

The behavior of RCC is completely unpredictable. Metastatic masses can be the first presentation of RCC or can be diagnosed years after the initial diagnosis and nephrectomy. Most common sites of metastatic RCC are the liver and lung. Metastases to the pancreas and small intestine are rare, but can present as gastrointestinal bleeding. About 4% of RCCs metastasize to the small intestine, of these; the duodenum is the least frequent site and can be involved by direct invasion of the tumor, or through lymphatic, transcoelomic or haematogenous spread and also direct invasion of pancreatic metastasis. In our patient, at the time of surgery, the main bulk of tumor was in the duodenum with extension to the head of pancreas.

According to the previous reports, duodenal involvement of RCC can be presented with jaundice, anemia and gastrointestinal bleeding, malabsorption and obstruction. Primary presentation of metastatic RCC as gastrointestinal bleeding has been rarely reported.

The longest duration between nephrectomy and duodenal metastasis was 13 years in
previous reports. Diagnosis of duodenal metastasis in RCC most commonly has been made by endoscopy. On endoscopy, the lesion can be seen as an ulcer, submucosal mass with ulceration or multiple nodules or small polyps of varying sizes.

Some patients present with concomitant metastasis in more body locations or other segments of the intestine such as the colon and duodenum. Our case presented with melena and duodenal ulcer 16 years after right nephrectomy for RCC. In previous studies, most of the duodenal metastasis of RCC was after right kidney nephrectomy. Most of the metastatic RCCs in the duodenum were primarily in the second portion with and without pancreatic involvement.

The treatment of choice for localized metastatic RCC is surgery. In previous reports, most of the patients with duodenal metastasis of RCC were treated with Whipple’s operation; however, there were successful surgeries of duodenal saving segmental or wedge resection. Any type of metastasectomies can increase the survival of the patient.

To the best of our knowledge, less than 30 cases of RCC with duodenal metastasis have been reported in the English literature (table 1). The longest duration after nephrectomy has been 13 years. Our case presented with melena 16 years after right nephrectomy for RCC, which to the best of our knowledge is the longest duration after nephrectomy. As a conclusion, distant metastasis of RCC can be presented very late with unusual and unpredictable symptoms. In all patients with a history of RCC, GI bleeding should be considered as a possible cause of metastasis.

Conflict of Interest: None declared.

References

1 Freedman AI, Tomaszewski JE, Van Arsdalen

| Author/Year | Sex/Age | Presenting symptom | Concomitant other organ involvement | Years after initial nephrectomy | Treatment |
|-------------|---------|-------------------|----------------------------------|--------------------------------|-----------|
| Lawson et al./1966 | 69/F | Anemia, GI bleeding | - | 0 | Whipple’s operation |
| Heyman et al./1978 | 64/M | GI bleeding | Colon | 8 years | Complex resection |
| McNicholas/1981 | 52/M | Malabsorption | - | 10 years | No surgery |
| Lynch et al./1987 | 67/M | GI bleeding | Pancreas | 2 years | No surgery |
| Lynch et al./1987 | 61/M | Jaundice | - | 6 years | No surgery |
| Lynch et al./1987 | 16/M | GI bleeding | - | 1 year | No surgery |
| Robertson et al./1990 | 70/M | GI bleeding | Pancreas | 13 years | Whipple’s operation |
| Toh et al./1996 | 59/F | Anemia, Bowel obstruction | - | 10 years | Segmental resection |
| Ohmura et al./2000 | 62/M | Obstruction | - | 5 years | - |
| Hashimoto et al./2000 | 57/M | GI bleeding | Pancreas | 11 years | Pancreatectoduodenectomy |
| Nabi et al./2001 | 40/M | Obstruction | - | 4 years | Segmental resection |
| Lee et al./2002 | 76/F | Abdominal pain | Colon | 4 years | No surgery |
| Loualidi et al./2004 | 76/M | Anemia, GI bleeding | - | 5 years | No surgery |
| Chang et al./2004 | 63/F | GI bleeding | - | 9 years | Segmental resection |
| Bhatia et al./2006 | 50/M | Jaundice | Liver | 1 year | No surgery |
| Sadler et al./2007 | 67/M | GI bleeding | - | 0 | No surgery |
| Sadler et al./2007 | 75/M | Anemia | - | 9 | No surgery |
| Adomo et al./2008 | 86/F | Anemia, Obstruction | - | 9 years | Pancreatectoduodenectomy |
| Eo et al./2009 | 47/M | Intussception | Lung | 2 years | Segmental resection |
| Teo MY/2010 | 50/F | Jaundice | Lung | 1 year | No surgery |
| Rustagi et al./2011 | 66/M | GI bleeding | - | 13 years | Whipple’s operation |
| Cherian et al./2011 | 80/M | GI bleeding | Lung and Bone | 11 months | No surgery |
| Vashi et al./2011 | 53/M | GI bleeding | - | 2 weeks | Segmental resection |
| Chua et al./2011 | 56/M | GI bleeding, Anemia | Lung | 0 | Segmental resection |
| Zhao et al./2012 | 56/M | GI bleeding | - | Whipple’s operation |
| Yang et al./2012 | 72/M | GI bleeding | - | 10 years | Whipple’s operation |
| Ashraf Teli et al./2012 | 52/M | GI bleeding | Liver | 8 years | Segmental resection |
| Current Case | 61/M | GI bleeding | - | 16 years | Whipple’s operation |
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KN. Solitary late recurrence of renal cell carcinoma presenting as duodenal ulcer. Urology. 1992;39:461-3. doi: 10.1016/0090-4295(92)90248-U. PubMed PMID: 1580040.

2 Toh SK, Hale JE. Late presentation of a solitary metastasis of renal cell carcinoma as an obstructive duodenal mass. Postgrad Med J. 1996;72:178-9. doi: 10.1136/pgmj.72.845.178. PubMed PMID: 8731713; PubMed Central PMCID: PMC2398404.

3 Zhao H, Han K, Li J, Liang P, Zuo G, Zhang Y, et al. A case of wedge resection of duodenum for massive gastrointestinal bleeding due to duodenal metastasis by renal cell carcinoma. World J Surg Oncol. 2012;10:199. doi: 10.1186/1477-7819-10-199. PubMed PMID: 23009644; PubMed Central PMCID: PMC3502181.

4 Yang J, Zhang YB, Liu ZJ, Zhu YF, Shen LG. Surgical treatment of renal cell carcinoma metastasized to the duodenum. Chin Med J. 2012;125:3198-200. PubMed PMID: 22932210.

5 Sadler GJ, Anderson MR, Moss MS, Wilson PG. Metastases from renal cell carcinoma presenting as gastrointestinal bleeding: two case reports and a review of the literature. BMC Gastroenterol. 2007;7:4. doi: 10.1186/1471-230X-7-4. PubMed PMID: 17266757; PubMed Central PMCID: PMC1800859.

6 Loualidi A, Spooren PF, Grubben MJ, Blomjous CE, Goey SH. Duodenal metastasis: an uncommon cause of occult small intestinal bleeding. Neth J Med. 2004;62:201-5. PubMed PMID: 15460501.

7 Ashraf Teli M, Shah OJ, Jan AM, Khan NA. Duodenal Metastasis from Renal Cell Carcinoma presenting as Gastrointestinal Bleed. Journal of Medical Sciences. 2012;15:65-8.

8 Teo MY, Ryan B, Swan N, McDermott RS. A Case of Metastatic Renal Cell Cancer Presenting as Jaundice. World J Oncol. 2010;1:218-20. doi: 10.4021/wjon247w.

9 Bhatia A, Das A, Kumar Y, Kochhar R. Renal cell carcinoma metastasizing to duodenum: a rare occurrence. Diagn Pathol. 2006;1:29. doi: 10.1186/1476-1596-1-29. PubMed PMID: 16972996; PubMed Central PMCID: PMC1578589.

10 Lee JG, Kim JS, Kim HJ, Kim ST, Yeon JE, Byun KS, et al. Simultaneous duodenal and colon masses as late presentation of metastatic renal cell carcinoma. Korean J Intern Med. 2002;17:143-6. PubMed PMID: 12164092.

11 Antonelli A, Arrighi N, Corti S, Legramanti S, Zanotti T, Cozzoli A, et al. Surgical treatment of atypical metastasis from renal cell carcinoma (RCC). BJU Int. 2012;110:E559-563. doi: 10.1111/j.1464-410X.2012.11271.x. PubMed PMID: 22639956.

12 Lawson LJ, Holt LP, Rooke HW. Recurrent duodenal haemorrhage from renal carcinoma. Br J Urol. 1966;38:133-7. doi: 10.1111/j.1464-410X.1966.tb09690.x. PubMed PMID: 5295908.

13 Heymann AD, Vieta JO. Recurrent renal carcinoma causing intestinal hemorrhage. Am J Gastroenterol. 1978;69:582-5. PubMed PMID: 308314.

14 McNichols DW, Segura JW, DeWeerd JH. Renal cell carcinoma: long-term survival and late recurrence. J Urol. 1981;126:17-23. PubMed PMID: 7253072.

15 Lynch-Nyhan A, Fishman EK, Kadir S. Diagnosis and management of massive gastrointestinal bleeding owing to duodenal metastasis from renal cell carcinoma. J Urol. 1987;138:611-3. PubMed PMID: 3498049.

16 Robertson GS, Gertler SL. Late presentation of metastatic renal cell carcinoma as a bleeding ampullary mass. Gastrointest Endosc. 1990;36:304-6. doi: 10.1016/S0016-5107(90)71032-2. PubMed PMID: 2365217.

17 Ohmura Y, Ohta T, Doihara H, Shimizu N. Local recurrence of renal cell carcinoma causing massive gastrointestinal bleeding: a report of two patients who underwent surgical resection. Jpn J Clin Oncol. 2000;30:241-5. doi: 10.1093/jjco/hyd061. PubMed PMID: 10857504.

18 Hashimoto M, Miura Y, Matsuda M, Watanabe G. Concomitant duodenal and pancreatic metastases from renal cell carcinoma: report of a case. Surg Today. 2001;31:180-3. doi: 10.1007/s005950170208. PubMed PMID: 11291718.

19 Nabi G, Gandhi G, Dogra PN. Diagnosis and management of duodenal obstruction due to renal cell carcinoma. Trop Gastroenterol. 2001;22:47-9. PubMed PMID: 11398249.

20 Chang WT, Chai CY, Lee KT. Unusual upper gastrointestinal bleeding due to late metastasis from renal cell carcinoma: a case report. Kaohsiung J Med Sci. 2004;20:137-41. doi: 10.1016/S1607-551X(09)70098-1. PubMed PMID: 15124899.

21 Adamo R, Greaney PJ Jr, Witkiewicz A, Kennedy EP, Yeo CJ. Renal cell carcinoma metastatic to the duodenum: treatment by classic pancreaticoduodenectomy and review of the literature. J Gastrointest Surg. 2008;12:1465-8. doi: 10.1007/s11605-007-0426-2. PubMed PMID: 18066632.

22 Eo WK, Kim YG, Choi SI. A case of multiple
intussusceptions in the small intestine caused by metastatic renal cell carcinoma. Cancer Res Treat. 2008;40:97-9. doi: 10.4143/crt.2008.40.2.97. PubMed PMID: 19688056; PubMed Central PMCID: PMC2697484.

23 Rustagi T, Rangasamy P, Versland M. Duodenal bleeding from metastatic renal cell carcinoma. Case Rep Gastroenterol. 2011;5:249–57. doi: 10.1159/000327996. PubMed PMID: 21577373; PubMed Central PMCID: PMC3094685.

24 Cherian SV, Das S, Garcha AS, Gopaluni S, Wright J, Landas SK. Recurrent renal cell cancer presenting as gastrointestinal bleed. World J Gastrointest Oncol. 2011;3:99-102. doi: 10.4251/wjgo.v3.i6.99. PubMed PMID: 21731909; PubMed Central PMCID: PMC3124636.

25 Vashi PG, Abboud E, Gupta D. Renal cell carcinoma with unusual metastasis to the small intestine manifesting as extensive polyposis: successful management with intraoperative therapeutic endoscopy. Case Rep Gastroenterol. 2011;5:471–8. doi: 10.1159/000331136.: 21960951; PubMed Central PMCID: PMC3180665.

26 Chua CS, Yang KC, Wu CC, Lin YM, Chong LW, Hsu YH. Triphasic computed tomography enterography with polyethylene glycol to detect renal cell carcinoma metastases to the small bowel. Case Rep Gastroenterol. 2011;5:597-601. doi: 10.1159/000330179. PubMed PMID: 22110421; PubMed Central PMCID: PMC3219484.