Treatment of Bleeding Secondary to Gastric Metastases from Renal Cell Carcinoma Primary

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Abstract

Gastric metastases from primary renal cell carcinoma (RCC) are uncommon, but not as rare as once thought. These metastases frequently present with upper gastrointestinal (UGI) bleeding. We report two such cases, and utilising lessons learnt from them, and from a literature review, propose a model of treatment for UGI bleeding secondary to metastases from RCC primaries.

Both patients presented with clinically significant UGI bleeding secondary to RCC metastasis to the stomach. A literature search was conducted and a qualitative review of the published case reports and studies were undertaken.

The two cases were discussed in a multi-disciplinary setting to plan management. One patient underwent gastric wedge resection; the second patient received palliative radiotherapy. Cessation of bleeding was achieved in both cases. A total of 48 cases were identified from the literature search. The reports indicate that surgery for gastric metastases has favourable outcomes in patients who do not have concurrent metastases. Palliative radiotherapy in this setting has not previously been described. A model of how these patients could be managed was subsequently constructed; the key question to answer is how disseminated the disease is.

Treatment modalities are still debated and should be discussed on a case-by-case basis. However, the literature suggests that surgical intervention has good therapeutic and prognostic benefit in patients with isolated metastatic disease to the stomach. For those with widespread metastases, there are several management options available. We advise that radiotherapy should also be considered as an option in the management of patients with bleeding lesions and concurrent metastatic disease.

Keywords: Renal cell carcinoma; Metastasis; Stomach; Gastrointestinal bleeding

Introduction

Gastric metastases from primary renal cell carcinoma (RCC) are considered rare. However, there are nearly 50 cases described in the literature. We present two cases of patients presenting with clinically significant bleeding from gastric RCC metastasis; utilising lessons learnt from these cases, and from a literature review, we propose a model of treatment for gastrointestinal (GI) bleeding secondary to metastases from RCC.

Case 1

A 68-year-old Caucasian lady (Ms DA) was referred to the emergency department (ED) by her general practitioner following a collapse. She complained of fatigue, anorexia and weight loss of around 1.5 stone over 6 months. Blood tests revealed a microcytic anaemia (haemoglobin = 51 grams/litre, mean corpuscular volume (MCV) = 71 femtolitres).

Past medical history was significant for left-sided clear cell renal cell carcinoma 21 years prior to this presentation, for which she underwent a nephrectomy. Her drug history included levothyroxine, aspirin and prochlorperazine. Ms DA lived with her partner, was a non-smoker and consumed no alcohol. Physical examination at the time of presentation did not reveal anything of note.

Initial treatment involved resuscitation and transfusion of 3 units of packed red cells and an infusion of vitamin B complex. Her haemoglobin levels returned to normal parameters following this.

A computerised tomography (CT) scan showed an elevated soft tissue lesion arising from the posterior wall of the central stomach with no evidence of metastatic disease.

Ms DA subsequently underwent a gastroscopy which showed 2 ulcerated, sessile polyps, the largest measuring 20 millimetres, and a submucosal polyp on the greater curvature of the stomach. All lesions were biopsied. A colonoscopy was attempted but was limited by melaena.

A positron emission tomography CT scan and a nuclear medicine bone scan were performed, neither of which showed metastatic disease.

Histological examination of the biopsies showed clear cell RCC metastasis. Her case was discussed at a multi-disciplinary meeting (MDM), where it was decided that a laparoscopic gastric wedge resection would be most appropriate for her. This procedure was performed successfully without post-operative complications.

Histology of the resected specimen showed a well circumscribed 15 millimetre nodule in the submucosa with ulceration into the mucosa, no spread into stomach muscle and clear surgical margins.

Since this, Ms DA has annual surveillance gastroscopies which have not shown any evidence of recurrence (Figure 1).

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Case 2

A 73-year-old Asian lady (Mrs HB) presented to the ED with a one day history of per rectal bleeding, including both fresh blood and melaena. There were no associated symptoms and examination was unremarkable.

Serological investigations confirmed a microcytic anaemia, with haemoglobin = 82 grams/litre, and MCV = 77.3 femtolitres. She had already been receiving iron supplementation for this.

In 2005, she underwent left-sided nephrectomy for clear cell RCC. Surveillance CT scan that year had shown nodules in the nephrectomy bed as well as pulmonary spread. She received Sunitinib for this.

During her admission she required repeated transfusions of packed red cells for continuous per rectal bleeding and persistent anaemia.

A gastroscopy showed a distal gastric lesion in the greater curvature of the stomach with ulcerated overlying mucosa and clot. Biopsies of the lesion were taken which confirmed clear cell RCC metastasis.

Mrs HB’s case was discussed in a MDM, where it was felt surgical intervention would not be appropriate given the presence of multiple metastases. Palliative radiotherapy was thought to be the best course of treatment in view of her ongoing bleeding. Thus, she underwent a repeat gastroscopy to reassess the lesion and endoscopically place marking clips for focused palliative radiotherapy. Cessation of bleeding was successfully achieved (Figure 2).

Literature Review

Renal cell carcinomas account for nearly 2% of cancers worldwide and are associated with high rates of metastases, with these often occurring several months after curative treatment [1,2]. Metastases originating from RCCs are most commonly found in the lungs, brain, breast and bones and are of clear cell histology [3-8].

Method

A review of the current literature on metastatic renal cell carcinoma to the stomach was performed using PubMed. The search terms were: “renal cell carcinoma stomach” + “renal cell carcinoma metastasis stomach”. A total of 48 cases were identified (Table I).

Demographics and clinical characteristics

The majority of patients were male (67%) with a mean age of 67 years (range 45-83 years). The mean interval post-nephrectomy was 6.9 years. This implies a significant delay in the development of gastric metastases following curative treatment. Melaena was the most frequently reported presenting complaint (46%).

Tumour characteristics

Clear cell histology was evident in all cases which reported a histopathological diagnosis. Over two thirds of patients had single lesions with the appearance of polyps, ulcers or tumours. The majority of lesions were located in the body of the stomach (63%).

Concurrent metastatic disease was found in 28 patients, the majority of which was present in the lung (86%), followed by metastases to the brain (25%), and bone (21%).

Management and outcomes

Surgical intervention was used in 20 of the 48 cases identified, half of which had no other concurrent metastatic disease. Four patients underwent total gastrectomy. The remainder had partial gastrectomies including 5 subtotal gastrectomies, 4 wedge resections and 1 antrectomy. Six cases did not specify the type of surgery. Three of the cases reporting use of wedge resections were performed for treatment of lesions <7 centimetres located in the gastric body.

Of those patients who did not receive surgery, 10 had endoscopic therapy, either in the form of polypectomy, ablation or mucosal resection. Palliative embolization was the treatment of choice in 2 cases, both requiring multiple embolizations in order to achieve haemostasis. Lamb et al. (2005) report a case of a patient who required 6 embolizations following 10 upper GI bleeds. Eight patients received chemotherapy and 7 did not receive any treatment. There were no case reports in the literature which described the use of palliative radiotherapy.

Cessation of bleeding was achieved in all patients who underwent surgical or endoscopic treatment for bleeding lesions (Figure 3).

Survival

Survival rates are generally poor with metastatic RCC, with most patients dying a few months after diagnosis [1,2]. In those with metastases to other organs in addition to the stomach, outcomes were worse (range 4 weeks to 36 months survival) than in those with isolated gastric metastases (range 4 weeks survival to alive after 6 years). Nearly half of the cases with widespread metastatic disease did not survive beyond 6 months, although several papers did not report survival data.

Of the 10 patients who received surgical intervention for isolated gastric metastases, 5 were cancer-free after 2-18 months. As only 7 cases in this category had published survival statistics, it is evident that surgical intervention carries symptomatic benefit in these patients, as well as the potential for curative treatment.

Overall survival for patients with RCC metastases to the stomach ranged from 4 weeks to alive after 6 years.

Discussion

Gastric metastases from RCC are rare and usually present with significant upper gastrointestinal haemorrhage.
| Paper                | Year | Age (years) | Sex | Presenting Complaint | Interval Post-Nephrectomy (years) | Location | Number of lesions | Type of lesion | Treatment | Other Metastases | Survival outcomes | Ref.   |
|---------------------|------|-------------|-----|----------------------|----------------------------------|----------|------------------|---------------|-----------|-----------------|-------------------|-------|
| Sullivan et al.     | 1980 | 69          | M   | Melaena              | 7.5                               | Antrum   | Single           | Polypoid      | Antrectomy | None            | Died 3 months post-op | [17] |
| Bisesti et al.      | 1984 | 64          | M   | Chest pain           | 14                                | Antrum   | Single           | Ulcer         | Subtotal Gx | None            | Died 33 days post-op | [16] |
| Nakamura et al.     | 1984 | 65          | M   | Melaena              | 9                                 | -        | -                | Partial Gx    | ileum     | None            | Died after 4 weeks | [19] |
| Ibáñez Olcoz et al. | 1989 | 60          | F   | Melaena              | 1.8                               | Body     | Multiple         | Polypoid      | None      | Lung, brain   | Died after 4 weeks post nephrectomy | [20] |
| Márquez et al.      | 1992 | 70          | M   | Melaena              | 0.1                               | Body     | Single           | Ulcer         | None      | Lung            | Died after 4 weeks | [21] |
| Durous et al.       | 1992 | 66          | M   | Anaemia              | 12                                | Fundus   | Multiple         | Interferon    | Lung, parotid | Died after 2 months | [22] |
| Otowa et al.        | 1992 | 61          | F   | Haematemesis         | 0                                 | Body     | Multiple         | Total Gx      | None      | None            | Died 3 months post-op | [23] |
| Herrera Puerto et al.| 1993 | 63          | M   | Haematemesis         | 0.1                               | Antrum   | Single           | Ulcer         | None      | None            | Died 4 weeks post nephrectomy | [24] |
| Boruchowicz et al.  | 1995 | 48          | M   | Dysphagia            | 1.3                               | Fundus   | Single           | Polypoid      | Chemotherapy | Lung, liver, oesophagus | Died after 5 months | [25] |
| Blake et al.        | 1995 | 63          | M   | Haematemesis         | 6                                 | -        | -                | Tumour        | Palliative embolization | Lung, pleura | Alive after 5 weeks | [26] |
| Odori et al.        | 1998 | 59          | M   | Asymptomatic         | 4.4                               | Body     | Single           | Ulcer         | Total Gx    | None            | No tumour recurrence at 17 months | [27] |
| Picchio et al.      | 2000 | 50          | F   | Melaena              | 14                                | Body     | Single           | Polypoid      | Subtotal Gx | None            | No tumour recurrence at 6 months | [28] |
| Mascarenhas et al.  | 2001 | 66          | M   | Haematemesis         | 7                                 | Body     | Single           | Ulcer         | Partial Gx  | None            | Died after 36 months | [29] |
| Suárez-Ortega et al.| 2004 | 70          | F   | Melaena              | 0                                 | -        | Multiple         | Polypoid      | Palliative | Lung            | -                 | [30] |
| Kobayashi et al.    | 2004 | 78          | M   | Anaemia              | 6.2                               | Body     | Single           | Not stated Gx (NOS) | None | Died after 5 months | [31] |
| Kok et al.          | 2004 | 60          | M   | Melaena              | 20                                | Body     | Multiple         | Tumour        | -          | -              | -                 | [32] |
| Suárez Fonseca et al.| 2004 | 61          | F   | Melaena              | 4                                 | Body     | Single           | Polypoid      | Palliative | Lung            | -                 | [33] |
| Lamb et al.         | 2005 | 69          | F   | Haematemesis         | 3                                 | Body     | Single           | Tumour        | Palliative embolization (x6) | Lung | Died after 23 months | [34] |
| Portanova et al.    | 2006 | 67          | F   | Melaena              | 5                                 | Body     | Single           | Polypoid      | Total Gx    | Pancreas        | Alive after 2 weeks | [35] |
| Hoferbach et al.    | 2006 | 56          | M   | Anaemia              | -                                 | Body     | Multiple         | Polypoid      | Endoscopic mucosal resection | None | Died after 2 years | [36] |
| Riviello et al.     | 2006 | 68          | M   | Melaena              | 11                                | Fundus   | Single           | Polypoid      | Total Gx, chemotherapy | Lung, spleen, pancreas, liver, lymph nodes | Died after 2 years | [37] |
| Saidi et al.        | 2007 | -           | M   | Melaena              | 10                                | Body     | Single           | Polypoid      | Wedge Rx    | None            | Disease free after 18 months | [38] |
| Pezzoli et al.      | 2007 | 78          | M   | Anaemia              | 5                                 | Body     | Multiple         | Polypoid      | Electrosurgical snare resection | - | Died after 6 months | [3] |
| Haffner et al.      | 2007 | 80          | M   | Anaemia              | 0                                 | Fundus   | Multiple         | Ulcer         | Endoscopic ablation | Lung | Alive after 5 months | [39] |
| Ko et al.           | 2008 | 71          | M   | Abdominal mass       | -                                 | Body     | Multiple         | Tumour        | -          | Lung            | -                 | [40] |
| Roh et al.          | 2008 | 60          | F   | Dyspepsia            | 8                                 | Body     | Multiple         | Polypoid      | Subtotal Gx | None            | -                 | [41] |
| Pollheimer et al.   | 2008 | 69          | M   | Abdominal pain       | 4.2                               | Body     | Single           | Ulcer         | Tamoxifen   | Lung, bone, adrenal | Died after 19 months | [5] |
| Pollheimer et al.   | 2008 | 77          | M   | Asymptomatic         | 6.3                               | Antrum   | Single           | Ulcer         | Interferon  | Lung, bone     | Died after 4 months | [5] |
| Pollheimer et al.   | 2008 | 83          | F   | Melaena              | 1.7                               | Antrum   | Multiple         | -             | Endoscopic ablation, Interferon | Lung, liver, pancreas | Died after 5 months | [5] |
| Pollheimer et al.   | 2008 | 65          | F   | Haematemesis & Melaena | 13.1                          | -        | Multiple         | -             | Endoscopic ablation | Lung, brain | Died after 3 months | [5] |
| Pollheimer et al.   | 2008 | 69          | M   | Abdominal pain       | 9.3                               | Body     | Multiple         | -             | Endoscopic ablation, Sunitinib | Lung, bone | Alive after 2 years | [5] |
| Maeda et al.        | 2009 | 49          | M   | Anaemia              | 1.7                               | Body     | Single           | Polypoid      | Partial Gx  | -               | -                 | [42] |
| Kibria et al.       | 2009 | 53          | M   | Melaena              | 0                                 | Fundus   | Single           | Polypoid      | None        | Lung, bone     | Died after 2 months | [8] |
| Yamamoto et al.     | 2009 | 74          | M   | Melaena              | 5                                 | Body     | Single           | Polypoid      | Wedge Rx    | Brain           | Died 1 month post-op | [4] |
Establishing the histopathological differentiation between metastatic disease and other tumours such as primary gastrointestinal stromal tumours (GIST) is essential in determining the appropriate treatment [9].

Laparoscopic wedge resection is the treatment of choice for isolated small/medium gastric tumours (<7 centimetres) near the greater curvature of the stomach as it is associated with quicker recovery in comparison to open procedures [10]. Saidi et al. (2007) report one case where this resection technique was used in a patient with an isolated gastric metastasis of RCC origin, after which they remained disease-free 18 months following surgery. Our patient is one of the longest surviving patients after laparoscopic wedge resection for isolated gastric RCC metastasis and remains disease-free 8 years post-surgery.

Subtotal and total gastrectomies are more frequently reported and are used to treat larger tumours or those which are localised within the antral or fundal regions of the stomach [2,11]. In the cases reviewed, all patients who underwent wedge resection in the absence of metastases to other organs were disease-free after 2-18 months with no evidence of further bleeding.

Endoscopic clipping is used to achieve haemostasis in upper GI bleeding, although it is also a technique used to localize gastric or oesophageal tumours to aid external beam radiotherapy [12]. Radiotherapy to gastric tumours is primarily utilised to palliatively treat symptoms of bleeding, pain and dysphagia [13,14]. To the best of our knowledge, there are no case reports on gastric metastases from renal carcinoma in which radiotherapy has been used as a treatment modality for cessation of bleeding.

Given the relatively small number of patients who develop gastric metastases from RCC, it would not be feasible to conduct trials to determine which interventions have the best outcomes. Hence, based on our experience and our literature review, we propose the following paradigm for treating gastric metastases from RCC primary (Figure 4)

| Sugasawa et al. 2010 | 69 | M | Melaena | 19 | Fundus | Single | Ulcer | Wedge Rx | None | Disease free after 12 months [43] |
| Tiwari et al. 2010 | 58 | F | Haematemesis & Melaena | 0 | Antrum | Single | Polypoid | Subtotal Gx | Lung | Died 2 months post-op [7] |
| Palade et al. 2011 | - | - | Melaena | 8 | - | Single | Ulcer | Partial Gx | Lung, brain, bone | - [44] |
| Cruz et al. 2011 | 56 | F | Melaena | 6 | Antrum | Single | Tumour | Subtotal Gx | Lung, brain | - [45] |
| Eslick et al. 2011 | 65 | M | PR Bleeding | 9 | Body | Single | Ulcer | Endoscopic polypectomy | None | Alive after 6 years [2] |
| Rodrigues et al. 2012 | 45 | F | Haematemesis | 9 | Body | Single | Ulcer | Sunitinib | Lung, ovary | Died after 4 months [46] |
| Namikawa et al. 2012 | 65 | M | Mass on CT | 23 | Body | Single | Polypoid | Wedge Rx | None | Disease free after 2 months [9] |
| Gómez-de-la-Cuesta et al. 2012 | 87 | F | Melaena | 4 | Body | Multiple | Polypoid | Palliative | Lung, pancreas | - [10] |
| Sripoorna et al. 2012 | 71 | M | Anaemia | 3 | - | Single | Polypoid | Endoscopic mucosal resection | None | Disease free after 15 months [47] |
| Kim et al. 2012 | 79 | M | Abdominal pain | 0 | Body | Single | Ulcer | Endoscopic submucosal dissection | None | Disease free after 6 months [6] |
| Thoufek et al. 2012 | 59 | F | Dyspepsia | 3 | Fundus | Single | Polypoid | Sunitinib | Brain | - [48] |
| Onorati et al. 2013 | 80 | - | - | 20 | - | - | - | - | - | - [49] |
| Sakurai et al. 2014 | 61 | M | Melaena | 2 | Body | Single | Polypoid | Partial Gx | Lung, bone, brain | Died 4 months post-op [50] |
| Ikari et al. 2014 | 64 | M | - | 22 | - | Single | Tumour | Endoscopic submucosal dissection | None | Disease free after 30 months [51] |
Gastric Metastases from Primary RCC: Treatment

Patient with known RCC + Upper GI Bleed

Upper GI Endoscopy + Biopsy

RCC Metastasis to Stomach

Non-RCC Metastasis or Gastric Primary

MDT Discussion

CT/PET Scan +/- Bone Scan

Evidence of other metastases?

Yes*

Palliative Radiotherapy

Interventional Endoscopic Therapy

Palliative Embolization

No

Surgery

Lesion <7cm in the gastric body

Lesion >7cm or within antrum or fundus

Wedge Resection

Subtotal/Total Gastrectomy

*Depending on available expertise

RCC: Renal Cell Carcinoma; MDT: Multidisciplinary Team; CT: Computed Tomography.

Figure 4: Treatment Paradigm for Management of Bleeding Gastric RCC Metastases.
Discussion of such cases in a multi-disciplinary setting is critical. It is thought that oncology patients who are discussed at such meetings often have better outcomes [15,16].

Conclusion

Gastric metastases in RCC are uncommon, but not as rare as once thought. They can cause significant haemorrhage and are generally associated with poor prognosis. Treatment should be patient-tailored depending on general condition at time of presentation, presence of extra-gastric metastases and the available resources and expertise. However, based on both our experience and the literature, we suggest that surgical intervention has good therapeutic and prognostic benefit in patients with isolated metastatic disease to the stomach. On the other hand, for those with widespread metastatic disease, other management options, if available, including embolization therapy, endoscopic submucosal resection and chemotherapy, should be considered. Furthermore, we advise that radiotherapy should also be considered as a viable option in the management of patients with bleeding lesions and concurrent metastases.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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