Renal cell carcinoma metastases to gallbladder

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ABSTRACT

A 74-year old man underwent a radical cholecystectomy for presumed gallbladder cancer. The histology of the resected specimen in fact revealed the lesion to be metastatic renal cell carcinoma from his resected right nephrectomy performed 14 years previously.

KEYWORDS

Gallbladder polyp – Gallbladder cancer – Renal cell cancer – Metastasis

Accepted 12 March 2013; published online 1 November 2013

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Case history

We present an unusual case of renal cell carcinoma metastasising to the gallbladder 14 years after a nephrectomy for the primary tumour. A 74-year-old man presented initially to his general practitioner with symptoms consistent with biliary colic. His liver function tests were deranged at the time with a bilirubin level of 52µmol/l, an alanine aminotransferase level of 331iu/l and an alkaline phosphatase level of 152iu/l. While awaiting ultrasonography, he was admitted to his local hospital with a further attack of symptoms although this time he had developed biliary pancreatitis that was treated conservatively. Ultrasonography at the time was inconclusive and repeat imaging was arranged three weeks later. This revealed a vascular polypoid lesion measuring 22mm x 23mm x 27mm in the gallbladder (Fig 1).

At this time, the patient was continuing to suffer from attacks of biliary colic, and had developed concerning symptoms of lethargy and night sweats. It was felt that this lesion was suspicious for malignancy and he was referred to the regional hepatobiliary centre for consideration of surgery. Following discussion at the specialist multidisciplinary team meeting, it was felt that it was appropriate to offer the patient a radical cholecystectomy for suspected gallbladder malignancy. He was relatively fit despite significant ischaemic heart disease requiring a quadruple coronary artery bypass graft in 1995 and subsequent coronary stenting in 2011. He had also undergone a right nephrectomy for renal cell carcinoma in 1998, which was noted on computed tomography (CT) (Fig 2).

Due to the patient's previous surgery, it was felt an open approach was more appropriate than a laparoscopic one and he underwent an uncomplicated resection, making an uneventful recovery. He was fit enough to leave hospital on the seventh postoperative day.

Histological examination of the resected specimen confirmed complete excision with a tumour that extended into the muscle but did not breach the serosa. Surprisingly, the tumour was not of biliary origin but was confirmed to be renal clear cell carcinoma, presumed to be spread from the primary tumour resected 14 years previously (Fig 3).

The lesion was confirmed to display the classical findings of a well defined, unencapsulated nodule consisting of nests of clear cells in rich vascular stroma. No obvious mitotic lesions were seen. Immunohistochemistry was positive for vimentin, CAM 5.2, AE1/3, MNF116 and CD10, and negative for synaptophysin, chromogranin, CD56 and S100. A singular focus of vascular invasion was seen. Interestingly, blood clots were found in the gallbladder and cystic duct lumen. It is possible that an embolus of part of these clots could be the cause of the episode of pancreatitis prior to diagnosis. No other lesions were found on CT of the thorax, abdomen and pelvis, and at the latest follow-up appointment the patient remains alive and well.

Discussion

Gallbladder polyps are relatively common and found in up to 5% of the adult population.¹ Most polyps are benign in the form of cholesterol polyps or adenomas but a small percentage are malignant. There remains debate regarding the optimal treatment of gallbladder polyps, with a Cochrane review from 2009 finding no good evidence to guide practice but noting that general consensus is to presume polyps over 1cm in size may be malignant and should be treated as such.¹

Primary gallbladder cancer is the fifth most common gastrointestinal tumour with an incidence of 1.2 cases per 100,000 population in the US.² It is associated with a poor

Figure 1 Ultrasonography showing the presence of a polypoid lesion in the gallbladder

Figure 2 Computed tomography showing gallbladder polyp and also previous right nephrectomy

prognosis and only a small percentage of patients with the disease are suitable for potentially curative radical resection.

Patients with gallbladder cancer fall into one of two main groups: those where the tumour is identified at histological examination of a specimen removed for biliary symptoms, and those in whom preoperative imaging was suspicious for malignancy and who then underwent radical resection. The survival rate in the former group is usually favourable, with stage I and stage II disease having five-year survival rates of 60–90% and 58–80% respectively.⁵ For those in the latter group, it is much less favourable, with stage III and stage IV

Figure 3 Histology showing renal cell carcinoma (left) invading the gallbladder mucosa (right)

disease giving five-year survival rates of 15–40% and 5–10% respectively.

In a large retrospective series from the Memorial Sloan-Kettering Cancer Center in New York, Fong *et al* showed that median survival in non-operated cases was only 5.4 months while in those patients who underwent primary procedures with curative intent the median survival was 26 months, with a 5-year survival rate of 38%.⁴ This highlights the importance of good preoperative imaging and a planned radical resection where malignancy is suspected. Although primary biliary tumours are by far the most commonly found gallbladder cancers, metastases from other tumours have been described.

As many as a third of patients presenting with a new renal cell carcinoma present with synchronous metastases.⁵ In addition, up to 50% will develop metachronous metastases at some point in their life. The most common sites of metastases are the lung, bone, liver, adrenal glands and brain although unusual sites have been described. Involvement of the gallbladder is rare (as few as 0.4–0.6% of cases).⁶ A review from the US in 2012 by Chung *et al* found only 33 cases in the published literature.⁵ The median time for metachronous metastases was 4 years as opposed to the 14 years in our case. Chung *et al* also showed that in the 33 cases described, the gallbladder was the sole site of metastases in only 39% of cases.

Long-term survival data for gallbladder metastases are not available as there are so few cases reported but a large study, again from the Memorial Sloan-Kettering Cancer Center, looked at survival after metastectomy for all renal cell carcinoma metastases.⁷ Patients who had a curative resection of metastases had a five-year survival rate of 44%. They showed that favourable features for survival were a disease free interval greater than 12 months versus 12 months or less (55% vs 9% 5-year overall survival [OS] rate, $p < 0.0001$), solitary versus multiple sites of metastases (54% vs 29% 5-year OS rate, $p < 0.001$) and age younger than 60 years (49% vs 35% 5-year OS rate, $p < 0.05$).

Conclusions

The outcome from gallbladder cancer continues to be poor and radical surgery remains the only hope of long-term survival. Preoperative suspicion led to a referral to a tertiary liver unit for consideration of this surgery. In patients with a history of renal cell carcinoma, no matter how long ago, the presence of gallbladder metastases should be considered as resection of even large lesions can have excellent long-term survival.

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