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ONLINE CASE REPORT

*Ann R Coll Surg Engl* 2011; **93:** e96–e98
doi 10.1308/147870811X591134

# Metachronous bilateral adrenal metastases following curative treatment for colorectal carcinoma

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**ABSTRACT**

A delayed, metachronous presentation of bilateral adrenal metastases following colorectal cancer has never previously been reported. We describe the case of a 68-year-old man who underwent curative surgery and adjuvant chemotherapy for a locally invasive sigmoid adenocarcinoma, only to be diagnosed with metachronous bilateral adrenal metastasis necessitating further resection and chemotherapy. We discuss the literature surrounding this pathology and highlight the importance of continual, vigilant radiological surveillance of the adrenal glands after curative treatment of colorectal carcinoma with or without subsequent adrenal metastasis.

**KEYWORDS**

Metachronous metastasis – Bilateral adrenal metastasis – Colorectal carcinoma – Surgical resection – Adjuvant chemotherapy

Accepted 16 January 2011; published online 25 August 2011

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## Case history

A 68-year-old man presented with a six-month history of an altered bowel habit and weight loss. Flexible sigmoidoscopy demonstrated a sigmoid tumour, the biopsies of which confirmed an adenocarcinoma. No evidence of metastatic disease was noted on staging computed tomography (CT) of the thorax, abdomen and pelvis. At laparotomy, a locally advanced T4 tumour was found, involving the appendix and vault of the bladder. A sigmoid colectomy, appendicectomy and wedge resection of the bladder was performed. Histology was consistent with a moderately differentiated infiltrating adenocarcinoma with surgical resection margins free of tumour. Dukes B staging was established after 15 lymph nodes identified no metastatic disease.

Twenty-eight weeks of adjuvant chemotherapy was commenced with 650mg 5-fluorouracil (5-FU) and 25mg folinic acid. The patient received external beam radiotherapy to his pelvis with 6MV photons of 45Gy in 25 fractions over 5 weeks, which was sandwiched into his chemotherapy schedule. Following the completion of the adjuvant chemotherapy and radiotherapy, exit CT revealed a right adrenal metastatic deposit with no evidence of disease elsewhere in the thorax, abdomen or pelvis. Twelve months following initial surgery, a right adrenalectomy was performed without complication. Histology was consistent with a 6cm x 5cm x 2cm multinodular adrenal mass demonstrating foci of a moderately differentiated adenocarcinoma, with 'dirty necrosis' (typically seen in metastases of colorectal origin) that was morphologically identical to the primary tumour. Immunostaining of the specimen was positive for CK20, carcinoembryonic antigen (CEA) and CDX2 but negative for CK7 and TTF1, in keeping with a colorectal metastasis.

Seven months following this, surveillance CT identified an isolated metachronous left adrenal metastasis that was operated on successfully following second-line chemotherapy with irinotecan, 5-FU and folinic acid. Histology revealed a 6.5cm x 5cm x 2.5cm adrenal mass containing multiple small white nodules that demonstrated a moderately differentiated adenocarcinoma with features of 'dirty necrosis', similar to the previous adrenalectomy specimen. Immunostaining patterns were also identical to those of the previous specimen.

Over the entire course of our patient's follow-up, his serum CEA levels were consistently within the normal range (0–7.0µg/l). Nine years following his sigmoid colectomy, our patient is currently free of metastatic and recurrent disease on imaging. He also demonstrated no sequelae of adrenal insufficiency at his last follow-up appointment, having received a standard regimen of steroid replacement therapy (30mg hydrocortisone and 300µg fludrocortisone daily).

## Discussion

Adrenal metastases from a primary malignancy are not uncommon. The most common primary tumours to metastasise to the adrenal glands originate in the lung, breast and kidney. The incidence of adrenal metastases from any primary malignancy ranges from 8.6% to 27.0%, while that of adrenal metastases specifically from a colorectal carcinoma ranges from 1.9% to 17.4%.[1] The lower end of this range may indeed be attributed to adrenal metastases being mistaken for lymph node metastases adjacent to the aorta. Fortunately, the detection of clinically silent adrenal metastases has improved with the widespread use of abdominal imaging modalities including CT, magnetic resonance imaging (MRI) and positron emission tomography (PET) CT.

An American study reported that 8 of 47 patients (17%) who underwent an adrenalectomy for metastatic cancers had an adrenal metastasis from colorectal cancer.[2] Another study addressing fine needle aspiration of adrenal masses revealed that 5 of 39 cases (12.8%) of adrenal metastases from malignant lesions were derived from colorectal cancer.[3] Despite variations in reported incidences, it is conceivable that adrenal metastases from colorectal cancers are not unusual. A number of studies have found that the vast majority of autopsy cases with adrenal metastases also included several other sites of metastases. Metachronous unilateral lesions have been described in association with liver metastases.[4]

With solitary adrenal metastases, the resection of the affected adrenal gland usually carries a good prognosis. It is therefore important to consider the possibility of adrenal metastases from colorectal cancer during follow-up after primary surgery since the early detection of solitary adrenal metastases may result in a second curative operation. Never has a case been described with bilateral adrenal metastases presenting separately that have been successfully operated on.

The spread of adrenal metastases from a colorectal carcinoma is believed to occur along the portal venous, arterial and lymphatic routes. A plausible means of haematogenous metastasis from the primary lesion via the lungs to the adrenals has also been described. In concordance with this, a few reports have described lung metastasis becoming evident some time after the initial adrenal metastases, raising the possibility of latent and silent lung metastasis having already occurred at the time of detection of the adrenal metastases.[1] In contrast, our patient had no other metastases detected with either of his adrenal metastases, nor did he develop any signs of them over the subsequent years.

Serum CEA is a useful indicator for the presence of adrenal metastases after colorectal cancer surgery. In synchronous bilateral lesions, adrenal insufficiency has been described as a presenting feature, accompanied by raised levels of serum CEA.[5] In our patient, serum CEA had always remained within normal limits.

In a series of radiological studies evaluating adrenal metastases, ultrasonography and CT were the most popular modalities because of their widespread availability and non-invasive nature. CT is a cost-effective means of identifying adrenal metastases compared with normal adrenal morphology on prior scans. In the context of the follow-up of a known malignancy, any new adrenal mass on CT, as was evident in this case, should be considered metastatic. MRI is another effective means of evaluating adrenal masses and is vital in differentiating between adenomas, carcinomas and metastases in cases of 'adrenal incidentalomas'.

The advent of PET-CT for staging and surveillance has allowed for earlier detection, more accurate localisation and a better characterisation of the metabolic activity (eg in determining functional status of incidentalomas) of adrenal lesions, tremendously facilitating treatment planning. It is undoubtedly effective in characterising adrenal masses as benign or malignant in the absence of previous comparison scans and is also recommended fully to exclude metastatic disease elsewhere prior to a potentially curative adrenal resection. Compared with standalone CT and MRI, PET-CT has consistently demonstrated greater sensitivity, specificity and accuracy in differentiating between benign and malignant adrenal lesions. A review of such diagnostic efficacies of PET-CT in the recent literature revealed sensitivities ranging from 93% to 100% (vs standalone CT: 61–100%; MRI: 79–100%), specificities ranging from 80% to 100% (vs standalone CT: 82–97%; MRI: 82–100%) and accuracies ranging from 92% to 100% (vs standalone CT: 81–99%; MRI: 89–100%).[6]

Despite these promising figures, it should be noted that false-positive findings occur in 5% of adrenal lesions identified as positive with PET. These include inflammatory and infectious lesions, adenomas and endothelial cysts. False-negative findings may also be seen in adrenal metastatic lesions with haemorrhage or necrosis, small (<10mm) metastatic nodules and metastases from certain pulmonary or carcinoid tumours.[6]

It is foreseeable that the role of the other imaging modalities, as well as that of riskier techniques (eg fine-needle aspiration) in characterising adrenal masses, may eventually be assumed by the less invasive and more accurate PET-CT. However, it may currently not be reasonable to recommend PET-CT as a means of routine follow-up imaging in lieu of CT as this would not prove cost-effective. PET-CT should be reserved as a problem solver or, as mentioned above, to provide further staging prior to a potentially curative metastatic resection.

Although adrenal metastases are usually found as part of a widespread metastasis, some reports have described a curative resection of solitary adrenal metastases from colorectal cancer.[7–9] It is generally accepted that a solitary metastasis should be resected to achieve a good prognosis although the incidence of truly resectable lesions is low. Despite a lack of evidence in the literature, our case suggests that solitary, metachronous metastases in both adrenal glands may also respond well to consecutive surgical resection, chemotherapy and vigilant follow-up.

## Conclusions

The incidence of adrenal metastases from colorectal cancer is not rare in autopsy series but separate, bilateral, metachronous lesions, as occurred in our patient, have yet to be described. Despite the liver and lung being the most common metastatic sites for colorectal cancer, adrenal metastases should be looked out for as early detection and subsequent surgical intervention is the key to a good prognosis.

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