Adrenocortical carcinoma: a diagnostic and treatment dilemma

Introduction

Laparoscopic adrenalectomy is the gold standard for treatment of adrenal tumours, but it is not indicated for a tumour of any size when invasion of surrounding tissues is clearly detected by preoperative imaging. Although laparoscopic adrenalectomy for metastatic adrenal malignancy is feasible, in the case of primary adrenal malignancy it should be done very carefully by a highly skilled laparoscopic surgeon.

Discussion

This case highlights some interesting and important features:

1. Port site metastasis following laparoscopic adrenalectomy
2. Difficulty in discerning malignancy in an adrenocortical neoplasm preoperatively
3. A tumour being reported as adrenocortical adenoma which later metastasized.

Port site metastasis after laparoscopic adrenalectomy is rare, with an incidence between 0.8 and 21%. However, metastatic seeding of tumour cells is one of the most feared complications following biopsies or surgical removal of malignancies (Iino et al, 2000). The possibility of port site metastasis must be considered in patients who undergo laparoscopic surgery for large and potentially malignant tumours. Efforts must be made to minimize tumour spread, such as minimal tumour manipulation, avoidance of tumour boundary violation, avoidance of gas leakage, avoidance of morcellation, and use of an impermeable bag for specimen retrieval (Saraiva et al, 2003).

Dr Sheraz Khan *is Specialist Registrar in Diabetes and Endocrinology in the Diabetes Centre, Manchester Royal Infirmary, Manchester M13 0JE and* **Dr Komal E Imtiaz** *is Consultant Physician in Diabetes and Endocrinology, Chorley and South Ribble District General Hospital, Chorley*

Correspondence to: Dr S Khan

The initial computed tomography scan indicated that the tumour was likely to be malignant, so was it safe to proceed to a laparoscopic rather than an open approach? Unfortunately it is difficult to determine the malignant potential of adrenal neoplasms because there is no reliable preoperative diagnostic test. The size of adrenal neoplasms has been used by some investigators to predict the risk of malignancy for adrenal incidentalomas but no consensus exist. Generally most centres

Case Report

A 61-year-old woman was referred by her GP with a 12-month history of weight gain, facial puffiness, difficulty climbing stairs and the tendency to bruise easily. On clinical examination she had a moon face, bruising all over the body and a raised blood pressure of 170/100 mmHg. Routine haematological and biochemical tests were normal apart from a raised glucose level of 16 mmol/litre. 9am cortisol was raised on three consecutive occasions: 698, 842 and 716 nmol/litre (normal range 119–618 nmol/litre). A simultaneous adrenocorticotropic hormone was undetectable at <5 ng/litre (normal range <50 ng/litre). 24-hour urine cortisol excretion was raised on three consecutive occasions 1643, 2130 and 1918 nmol/24 hours (normal range 33–286 nmol/24 hours). Computed tomography scan of the abdomen and chest revealed a 5 cm mass with heterogeneous enhancement in the right adrenal gland. The liver, both kidneys and spleen were normal and the lung fields were clear. The report stated that the size of the tumour and enhancement characteristics were more in keeping with a malignant rather than benign neoplasm.

The patient was commenced on metyrapone and underwent right laparoscopic adrenalectomy. The tumour was removed intact and histopathology revealed features of adrenocortical adenoma with no convincing evidence of malignancy. She made a good clinical and biochemical recovery postoperatively and cortisol levels in the blood and urine returned to normal.

Ten months later she developed swellings at the site of entrance of the laparoscope and at the site of the drain. On examination she had 2 cm diameter mobile subcutaneous nodules at three of the port sites. Computed tomography of the abdomen revealed a normal adrenal bed but three subcutaneous masses lying in the right upper quadrant, leading to suspicions of metastasis. The masses were excised and histology confirmed them to be cancerous and morphologically similar to the tumour excised from the adrenals. However, they had acquired more worrying histological features (higher mitotic and apoptotic rate, as well as focal necrosis) and were regarded as being of uncertain malignant potential.

The patient made a good recovery from the operation and remained well for the next 2 years with no clinical or biochemical evidence of recurrence of the disease. However, she again developed a puffy face, difficulty going upstairs and her blood pressure became more difficult to control. Her 9am cortisol was raised (679 nmol/litre) with undetectable adrenocorticotropic hormone. 24-hour urine cortisol was raised (2704 nmol/litre), and a computed tomography of the abdomen revealed a 5.4 x 3.6 cm right para-aortic/infrahepatic mass – a 1.1 cm para-aortic lymph node was also noticed. She was commenced on metyrapone and mitotane and referred for debulking surgery. The patient was aware that the surgery would not be curative but would make her Cushing's easier to manage and improve her response to subsequent chemotherapy.

She underwent debulking surgery for intra-abdominal metastasis. Part of her right kidney, lymph nodes and appendix were removed. She had hypoadrenalism following debulking surgery. Her mitotane and metyrapone was stopped and she was commenced on high-dose steroid replacement which was gradually tapered off. The patient responded very well to the surgery and her general health improved greatly. Six months after surgery a routine computed tomography scan of the abdomen showed a 2.4 x 2 cm hepatic metastasis. She was referred for surgical ablation but died of a massive cerebral haemorrhage.

have used adrenal tumour size of 5–6 cm or greater as an absolute contraindication for resection because the risk of malignancy is high (35–98%). It is unclear, however, at what size an adrenal neoplasm should be resected by means of an open approach or a laparoscopic approach. Some surgeons have laparoscopically resected adrenal tumours up to 15 cm in size (Kebebew et al, 2001). Adrenal imaging (computed tomography, magnetic resonance imaging, metaiodobenzylguanidine; MIBG) characteristics (e.g. high attenuation, irregularity, heterogeneity, signal intensity) are not accurate enough to diagnose or exclude primary adrenal cancer or metastasis preoperatively.

Do adrenocortical carcinomas arise from benign adenomas? In this patient the tumour was reported to be benign histologically. Biopsies from the port site metastasis showed that the tumour had acquired more worrying histological features and was regarded as being of uncertain malignant potential. However, one has to assume that the initial tumour was malignant as it metastasized to the lymph node and liver. This case supports the hypothesis that, at least in some tumours, there is a multistep tumourigenesis, with sequential progression from normal to adenomatous cells and eventually to malignant cells (Bernard et al, 2003).

Conclusions

This case illustrates that laparoscopic adrenalectomy should not be performed if there is any possibility of adrenocortical malignancy in the course of preoperative evaluation, especially in large tumours. It also suggests that adrenocortical carcinoma may evolve from a benign adenoma, via the 'multistep tumourigenesis hypothesis', at least in some adrenal cancers. **BJHM**

Bernard MH, Sidhu S, Berger N et al (2003) A case report in favour of a multistep adrenocortical tumorigenesis. *J Clin Endocrinol Metab* **88**(3): 998–1001

Kebebew E, Siperstein AE, Duh Q-Y (2001) Laparoscopic adrenalectomy: the optimal surgical approach. *J Laparoendosc Adv Surg Tech A* **11**: 409–13

Iino K, Oki Y, Sasano H (2000) A case of adrenocortical carcinoma associated with recurrence after laparoscopic surgery. *Clin Endocrinol* **53**(2): 243–8

Saraiva P, Rodrigues H, Rodrigues P (2003) Port site recurrence after laparoscopic adrenalectomy for metastatic melanoma. *Int Braz J Urol* **29**(6): 520–1