Multi-modal approach to treatment in advanced adrenocortical carcinoma

L Hall1, C Perry1, N Reed2, E Leen3, H Wasan4, M Freeli

1 Endocrine Unit, Western Infirmary, Glasgow 2 Beatson West of Scotland Cancer Centre, Glasgow 3 Dept. of Radiology, Imperial College London 4 Dept. of Medical Oncology, Hammersmith Hospital, London

Introduction
A 38 year old HR manager presented in 2008, 9 months post partum with acne, facial hirsutism and upper abdominal discomfort. On examination she was normotensive, virilised and with an easily palpable mass arising from the right upper quadrant.

Biochemistry

Androstenedione 93.9 nmol/l
DHA 37.7 umol/l
17 OHP 13 nmol/l
Testosterone 13.7 nmol/l
Oestradiol 157 pmol/l
LH, FSH undetectable
SHBG 53 nmol/l
ODST cortisol <25 nmol/l

U&E normal (K 3.3 mmol/l)
Alk phos 174 µ/l, alb 26 g/l
TSH 2.5 mU/l, FT4 13 pmol/l
Glu 6.7 mmol/l
CRP 100 mg/l
Ca²⁺(adj) 2.49 mmol/l
AFP 7 KU/l

Imaging
• Large heterogeneous right adrenal tumour (18x12x10cm)
• Similar mass right lobe of liver
• Compression of IVC with extensive IVC + femoral vein thrombus

Immediate management
• IVC filter
• Mitotane chemotherapy (+hydrocortisone)

Pathology revealed adrenocortical carcinoma

Surgical mananagement
• Right adrenalectomy with extended right hepatectomy
• Common bile duct excision
• Portal vein reconstruction + IVC excision/ replacement allogetic iliac vein graft

Further mananagement
• 1st cycle chemotherapy with doxorubicin, cisplatin + etoposide in addition to mitotane October 2008
• Chemo R adrenalectomy
• Extended R hepatectomy
• Common bile duct excision
• Portal vein reconstruction + IVC excision/ replacement, allogetic iliac vein graft

Progress
• Difficulty achieving therapeutic serum levels of mitotane because of toxicity
• Recurrence in May 2010 with 2 hepatic metastases
• Surgical exploration revealed multiple hepatic metastases, so further resection not attempted
• Tumour sample sent to Portsmouth hospital for in vitro culture, but no growth occurred
• Radiofrequency ablation (RFA) to liver metastases in June 2010

References

Discussion
Adrenocortical carcinoma (ACC) is a rare aggressive tumour with a median five year survival of 10-25% when it presents with advanced stage disease1, and in most cases metastatic disease is fatal within 1 year, although there are a small number of case reports of long-term responses to chemotherapy +/- mitotane2,3.

Surgical resection, when possible, is the mainstay of treatment and a 2007 European retrospective analysis supported the use of adjuvant mitotane4, which is now frequently used. Adjuvant radiotherapy is not thought to be beneficial, although there is a lack of RCT evidence investigating its efficacy in patients with resected ACC. It is not known whether cytotoxic chemotherapy alone or in combination with mitotane is more effective than mitotane alone. There are also little published data on RFA in metastatic ACC, but 2 small studies (both n = 8) have demonstrated safety and short-term efficacy in terms of tumour shrinkage5, and median survival of 1.9 years post RFA6 respectively.

Pre-clinical studies exploring the use of the multi-targeted receptor tyrosine kinase inhibitor sunitinib in ACC are promising7 although the few published cases and a small clinical trial of use of sunitinib in metastatic ACC report variable outcomes8,9. This is a highly unusual case of prolonged survival in aggressive ACC with the use of multiple therapeutic modalities, many of which have a paucity of clinical evidence.

Figures 3. RFA tools and 4. post RFA appearance

Figure 6. Gross pathology and histology

Figure 1. CT of abdomen

Figure 2. CT of abdomen

Figure 5. CT of abdomen