Adrenocortical carcinoma

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Definition ACC is a rare aggressive malignancy that arises from the adrenal cortex. The prognosis is variable but is generally poor, in part owing to its tendency to present at a late stage. Although most ACCs are sporadic, a minority occur as part of genetic tumour syndromes such as multiple endocrine neoplasia type 1 (MEN /uni00A0 1), familial adenomatous polyposis and the Li–Fraumeni and Lynch syndromes. Optimal surgery remains the best way of curing the patient and so preoperative diagnosis and planning are key in ensuring this outcome. Incidence Estimated incidence is one or two cases per 1 000 000 popu lation per year and, in keeping with benign adrenocortical tumours, a female predominance is observed (1.5:1). Don H Nelson , 1925–2010, Professor of Medicine, University of Utah, Salt Lake City , UT , USA Frederick Pei Li , 1940–2015, Professor of Clinical Cancer Epidemiology , Harvard, USA Joseph F Fraumeni Jr , b. 1933, Director of the National Cancer Institute Henry T Lynch , 1928–2019, Professor of Cancer Research, Creighton University School of Medicine, Omaha, NE, USA. Lawrence M Weiss , contemporary , pathologist, Aliso Viejo, Ca, USA. fourth and fifth decades. Pathology Tumours are often large (>10 /uni00A0 cm) with a cut surface that ranges - from orange to brown (Figure 57.7). Necrosis is usually present. Distinguishing between benign and malignant adrenocortical tumours may be di ffi cult, with the presence of local invasion or - distant metastasis being the only definitive criteria. If neither are present, the modified Weiss histopathological system may be used to guide management. It comprises five criteria: >6 mitoses/50 high-power fields, ≤ 25% clear tumour cells in cytoplasm, abnormal mitoses, necrosis and capsular invasion. If a criterion is absent, it is scored 0; if present, it scores 2 for the first two criteria and 1 each for the last three. A total score ≥ 3 is suggestive of malignant behaviour. More recently the use of the Ki-67 proliferation index has been advocated, with increasing count suggesting poorer prognosis. Clinical presentation Patients may present with hormonal excess (50–60%) or symptoms of an abdominal mass such as abdominal or back pain (30–40%). Around one in six ACCs present as adrenal incidentalomas. Those that are hormonally active usually cause Cushing’s syndrome or a mixed picture of Cushing’s and virilisation in women. Mineralocorticoid excess is rare, as is feminisation in male patients. Diagnosis Although radiological investigations are critical in diagnosis, the presence of autonomous secretion of glucocorticoids, sex hormones and steroid precursors should also be carefully evaluated. Phaeochromocytoma (PCC) must also be excluded. - , MD, USA.

Figure 57.7 Adrenocortical carcinoma that caused Cushing’s

syn

drome and virilisation in a female patient.

Radiology ACC is often readily diagnosed on CT or MRI (Figure 57.8 where size (>6 /uni00A0 cm), heterogeneous appearance and presence of necrosis are suggestive and local invasion and metastatic disease are diagnostic. Common sites of metastases are the lungs and liver, so staging should include the thorax. FDG-PET scanning is complementary and is advised to exclude occult metastatic disease in suspicious lesions. A maximum standard unit value (SUVmax) >40 or 1.5 times higher than the liver 11 both suggest malignant tumours. The use of C-metomidate PET may improve diagnostic accuracy but is not widely avail able. In terms of tissue diagnosis, adrenal biopsy is discouraged and fine-needle aspiration cannot distinguish benign from malignant tumours. Biopsy may have a role in patients with widespread metastatic disease at presentation to guide pallia tive systemic trea tment. Biochemistry Glucocorticoid excess should be excluded by careful history and examination, followed by low-dose overnight DST . Serum levels of adrenal androgens (DHEAS, androstenedione, testosterone, 17-hydroxyprogesterone) and serum oestradiol in men and postmenopausal women should also be measured. In patients who are hypertensive, the aldosterone–renin ratio should be measured along with the serum potassium. Steroid precursors can be measured in 24-hour urine collections and may demonstrate a particular pattern on mass spectrometry although use is not widespread at present. Lastly , 24-hour urine or plasma metanephrines should be measured in all patients to exclude PCC. Treatment Surgery Successful R0 resection of the tumour should be the aim of surgery and o ff ers the best chance of cure for the patient. Preoperative assessment should therefore focus on determin ing whether any adrenal tumour is potentially malignant as this will guide the operative strategy . Treatment should take treating this rare disease. Patients with cortisol excess should be given perioperative hydrocortisone. At presentation, ther e are three common scenarios: /uni25CF Indeterminate or probably malignant tumour <6 /uni00A0 cm : laparoscopic adrenalectomy may be feasible in this situation, but if there is evidence of local invasion on imaging or suspicion of it at laparoscopy open surgery is mandated. /uni25CF Indeterminate or probably malignant tumour >6 /uni00A0 cm : laparoscopic surgery is not advised. In this scenar - io open radical resection must be undertaken, if necessary en bloc with involved adjacent organs (see Surgery of the adrenal glands). /uni25CF Indeterminate or probably malignant tumour <6 /uni00A0 cm with synchronous metastatic disease . For limited metastatic disease , open resection of the tumour and intra-abdominal metastases is advised. For distant disease, resection of the primary followed by adjuvant systemic or surgical treatment of metastases is appropriate. For widespread metastatic disease , initial surgery is), no longer routinely advised. Instead, palliative treatment with mitotane with or without chemotherapy should be pursued. If there is significant disease regression after 3–6 months, surgery may then become an option. More rarely , patients present with locally advanced disease with tumour extension into the great vessels. In this situation, it is recommended that such patients are referred to centres with experience of treating these cases. - Oncological treatment Patients at high risk of recurrence (size >5 /uni00A0 cm, Ki-67 >10%, tumour rupture at surgery , tumour thrombus) and those with metastatic disease should commence mitotane therapy as soon - as possible (for up to 5 years) as this has been shown to improve disease-free and overall survival. Palliative EDP (etoposide– doxorubicin–cisplatin) chemotherapy may also be an option if there is disease

progression despite mitotane therapy . Unless there is ongoing steroid excess, all patients treated with mito - tane should receive oral hydrocortisone replacement therapy . According to the European Network for the Study of Adrenal Tumours (ENSAT) classification, the 5-year, disease - specific survival rates for ACC are: 82% in stage I (tumour <5 /uni00A0 cm; T1N0M0), 61% in stage II (tumour size >5 /uni00A0 cm; T2N0M0), 50% for stage III (tumour of any size with at least one of the following factors: tumour infiltration in surrounding tissues [T3], tumour invasion into tumour thr ombus in the vena cava or renal vein [T4], positive lymph nodes [N1] but no distant metastases) and 13% for stage IV (distant metastases) (see Further reading).

Figure 57.8 Magnetic resonance imaging of adrenocortical carcinoma (arrow) in a patient with cortisol and testosterone excess.

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