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Case Report

Secondary hypertension in pregnancy due to an adrenocortical carcinoma

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Introduction

Severe hypertension that occurs in the first and second trimesters of pregnancy should alert the clinician to the possibility of secondary hypertension. Adrenal tumours that are associated with hypertension in pregnancy include pheochromocytoma, adrenal cortical adenoma, adrenal cortical carcinoma and other lesions. In normal pregnancy, there is an elevation of basal serum cortisol and urinary free cortisol. There may be a failure to suppress serum cortisol following an overnight dexamethasone suppression test. This can render the diagnosis of Cushing's syndrome difficult in this context. We report a lady with severe hypertension at 18 weeks of gestation in whom adrenal carcinoma was the cause.

Case report

A 30-year-old housewife, a secundagravida at 18 weeks' gestation, presented with localised left loin pain, headache and dizziness of 2 months duration. Her blood pressure was 210/130 mmHg. There was no history of palpitations, weight loss, visual disturbances, syncope or haematuria. Ultrasound imaging of the abdomen revealed a large adrenal mass that measured 16 cm × 9.6 cm × 8.6 cm, thrusting the left kidney inferiorly. She was referred to our hospital with a probable diagnosis of pheochromocytoma complicating pregnancy.

Examination revealed grade 2 hypertensive changes in the optic fundus. System examination was otherwise normal with no evidence of virilisation. Initial investigations revealed severe hypokalaemia (serum potassium of 2.2/2.7 mmol/L) with kaluresis (24 h urine potassium of 117 mmol/24 h) and mild alkalosis (31 mmol/L). Plasma glucose levels were deranged (fasting plasma glucose: 7.3 mmol/L, post-prandial plasma glucose: 16.2 mmol/L). The serum cortisol measurement taken at 8.00 a.m. was 1026 nmol/L (193–690 nmol/L, chemiluminiscent immunoassay, Diagnostic Products Corporation, Los Angeles, USA) and was elevated above the normal level for early second trimester of pregnancy. Serum dehydroepiandrosterone sulphate was 2.55 mmol/L (0.95–11.7 mmol/L) and serum aldosterone was 269.2 pmol/L (27.7–444 pmol/L, radioimmunoassay; Diagnostics Products Corporation) both being lower than expected for pregnancy (which could be up to five times the cited reference intervals). Twenty-four hour urinary vanillylmandelic acid levels were reported to be normal on three separate samples (3/4.3 per 1 mg in 24 h, range: 1–8 mg/day; Biorad Columns, Hercules, CA, USA). As this patient had severe hypertension and hypokalaemia, high dose dexamethasone suppression tests were not carried out. The low dose test would not have been meaningful considering the fact that the patient was pregnant and had an adrenal mass. Electrocardiogram showed U waves and left ventricular hypertrophy, which was confirmed by 2-D echocardiogram.

The blood pressure was difficult to control with prazosin, phenoxybenzamine, alpha methyldopa, amlodipine and atenolol on maximal doses and remained at 180–190/120–110 mmHg. The treatment options were discussed at length with the couple. One option was to surgically excise the tumour and continue her pregnancy, but the risk of spontaneous abortion and placental abruption was explained to them. In view of the large size of the tumour, the chance of it being a malignant adrenal tumour was great. Bearing this in mind, the couple opted for medical termination of pregnancy and to subsequently proceed with surgical excision of the tumour. Medical termination of pregnancy was performed using misoprostol under intravenous glyceryl trinitrate cover.

Computerised tomography of the abdomen revealed a well defined mass measuring 13 cm × 11 cm, in the left suprarenal region with heterogenous enhancement following intravenous contrast (Fig. 1). She underwent surgery under parenteral hydrocortisone cover. At the time of surgery, the tumour appeared to be well defined and thrusting the left kidney inferiorly. There was no adenopathy or obvious local invasion. The tumour was entirely removed. The immediate postoperative period was uneventful. Histopathology was suggestive of an adrenocortical carcinoma with capsular invasion. She was advised mitotane (1,1-dichloro-2-(0-chlorophenyl)-2-(p-chlorophenyl) ethane) therapy and was discharged with two antihypertensive agents. Her electrolytes normalised in the postoperative period. She was placed on

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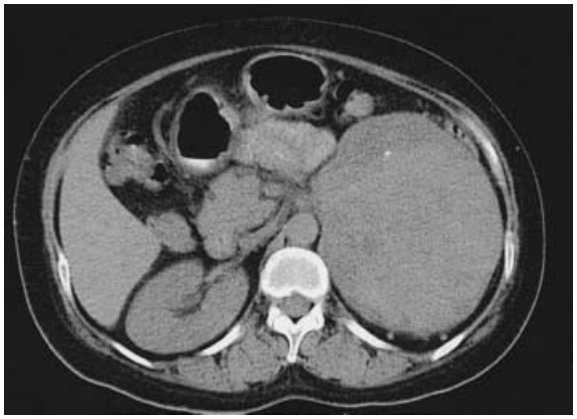

Figure 1 Computerised tomography of the abdomen showing a left adrenal mass with a speck of calcification.

oral steroid replacement as the opposite adrenal was expected to be functionally suppressed for at least 6 months.

Discussion

Making a clinical diagnosis of Cushing's syndrome during pregnancy is a difficult task. Both Cushing's syndrome and pregnancy may be associated with s triae, weight gain, oedema, centripetal obesity, glucose intolerance and hypertension.[1] The recent onset of hirsutism and acne may give a clue to excessive androgen production which can occur in Cushing's syndrome. Cortisol levels rise progressively over the course of gestation, to reach levels two- to threefold more than the pregestational values by term.[2] This is as a result of an increase in cortisol-binding globulin levels under the effect of oestrogen. However, the normal circadian rhythm is maintained. Low dose dexamethasone suppression tests often yield false negative results in pregnancy, but a failure to suppress serum cortisol with high dose dexamethasone may be helpful in diagnosing adrenal tumours causing Cushing's syndrome.

Less than 70 cases of Cushing's syndrome in pregnancy have been reported. In one of the largest series that have been described, 45% of them were because of adrenal adenomas, 45% were a result of pituitary adenomas and 10% were caused by adrenal carcinomas. One patient with an ectopic adrenocorticotrophic hormone producing tumour has also been reported.[3] In a series of 22 pregnant women with Cushing's syndrome, the onset of hypercortisolism occurred during pregnancy in 68% and in the post-partum period in 22%. Of those with adrenal tumours, 50% had an adrenal carcinoma.

Cushing's syndrome in pregnant mothers is complicated by hypertension in 54% and diabetes and pre-eclampsia in 13%. In the infant, maternal Cushing's syndrome can lead to prematurity, adrenal insufficiency and stillbirth. Successful pregnancy outcomes have been reported after laparoscopic adrenalectomy at 22–30 weeks of gestation.[4,5] In our patient, severe hypokalemic alkalosis, kaliuresis and basal cortisol values beyond the range expected for the early second trimester of pregnancy[2] strongly suggest that the adrenal tumour was overproducing cortisol. The normalisation of hypokalaemia in the postoperative period in our patient supported this hypothesis. While deoxycorticosterone acetate producing tumours can cause hypokalaemia, kaliuresis, alkalosis and hypertension, they are usually much smaller in size and rare. They demonstrate suppression of cortisol and aldosterone levels. In our patient, elevated cortisol levels and suppressed aldosterone levels point towards a cortisol producing tumour. The current case report illustrates some of the difficulties involved in diagnosing endogenous Cushing's syndrome in pregnancy, and also the fact that large adrenal masses, in spite of being functional, may be malignant.

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