An elderly lady in shock

Mathew J, Menon PS, Shah NS

A 62-year-old lady was referred to endocrine services for investigation of bilateral adrenal masses. Eight days prior to admission she was admitted elsewhere with extreme exhaustion and breathlessness following a febrile illness and was treated with intravenous fluids. On admission, she had a blood pressure of 84/60 mm Hg and pulse rate of 124/minute. She was distinctly pigmented, short (147 cm, < 5th percentile), hirsute and had androgenic alopecia (Hamilton Norwood IV). She was afebrile and the systemic examination was otherwise within normal limits.

What are the possible causes of shock in this lady?

In the presence of pigmentation, primary adrenal insufficiency should be kept first in the list of differential diagnoses. Presence of a febrile illness preceding the episode of shock points to septic shock as a possible differential. Having detected bilateral adrenal masses in the abdomen, retroperitoneal haemorrhage from an adrenal mass lesion should also be considered. Cardiogenic shock is unlikely in the absence of other findings.

What are the relevant investigations at this point?

Considering the above differential diagnosis, the investigations would include estimation of haemoglobin concentration, complete blood counts, estimation of serum levels of (random) cortisol, electrolytes and 17-hydroxyprogesterone, blood and urine cultures, urine microscopy, chest radiograph and electrocardiogram.

The patient was started on intravenous hydrocortisone after sending the blood and urine samples for the investigations listed above. Pending reports of cultures, a broad-spectrum antibiotic was also started. The results of the investigations were as follows: Serum sodium: 128 mEq/L, serum potassium: 5.2 mEq/L, serum cortisol: 13 µg/dl (Normal >15 µg/dl), Dehydroepiandrosterone (DHEAS): 866 µg/dl (Normal: 50 - 250 µg/dl), 17-hydroxyprogesterone: 300 ng/ml (Normal: 0.5-3.5 ng/ml in luteal phase, 0.2-1 ng/ml in follicular phase) Blood and urine cultures were sterile, chest radiograph was normal and electrocardiogram showed sinus tachycardia.

How is this value of cortisol interpreted? Is an ACTH stimulation test necessary?

In a patient with acute severe illness, serum cortisol of 13 µg/dl is suggestive of hypocortisolemia. An ACTH-stimulated cortisol is not required to substantiate a diagnosis of hypocortisolemia in patients with random cortisol values below 15 µg/dl. Adrenal insufficiency is unlikely with cortisol measurements greater than 34 µg/dl. For persons with cortisol values between these values, an ACTH stimulation test is necessary.[1]

What is the possible diagnosis in this setting?

In the presence of adrenal deficiency and hyperandrogenism with elevated 17-hydroxyprogesterone measurements, a block in the cortisol synthetic pathway with overproduction of androgens is to be considered. Since she never had a history of salt wasting crisis prior to this, she most likely has a simple virilizing type of congenital adrenal hyperplasia (CAH) due to 21 hydroxylase deficiency.

The patient improved gradually and blood pressures normalized. Since the patient had an adrenal mass, a computed tomography of the abdomen was performed (Figure 1).

Figure 1: Bilateral large adrenal myelolipomas
What is the differential diagnosis of the CT scan shown in the figure?

The figure shows heterogeneously enhancing hypodense masses in the suprarenal region measuring 11 x 12 x 10 cm on the left side and 6 x 4 x 5 cm on the right side. The mass had a fat density of -84 HU. The differential diagnosis of these masses with fat density includes retroperitoneal lipomas, teratoma, exophytic renal angiomyolipoma, liposarcoma, and myelolipoma.\[2\] Retroperitoneal lipomas and liposarcomas are usually unilateral. Since the adrenal glands are not seen separate from the mass, renal angiomyolipoma is unlikely. Bilateral large adrenal myelolipomas have been reported in association with previously unsuspected CAH. Three of these were in patients with CAH due to 21-hydroxylase deficiency\[1,4\] and one due to 7-α-hydroxylase deficiency.\[5\] Inadequately treated patients with CAH can also develop myelolipomas.\[6,7\] Other causes of bilateral adrenal masses presenting with adrenal insufficiency are tuberculous adenitis, fungal infections, lymphoma, haemorrhage and metastatic tumours.\[8\]

Percutaneous fine needle aspiration cytology was attempted, but was unsuccessful.

How are adrenal myelolipomas managed?

The treatment for these lesions, if asymptomatic, is conservative unless there is a possibility that they may be confused with necrotic adrenal carcinoma. Tumour progression or haemorrhage is uncommon.\[9\] Adrenal carcinoma in association with CAH has been reported only in four cases.\[1\] The major indications for the resection of this predominantly conservatively treated lesion include presence of pain, significant mass effect or haemorrhage, and inability to clearly differentiate the lesion from liposarcoma on imaging.\[2\]

What are the common clinical presentations of congenital adrenal hyperplasia?

The common clinical presentations of 21-hydroxylase deficiency CAH include salt wasting crisis, ambiguous genitalia, postnatal virilization, and premature pubarche depending on the sex of the patient and severity of enzyme deficiency.\[10\]

The birth history and childhood growth of the patient was not available. She had attained menarche at the age of 16 years, following treatment. Since then, she complained of progressive pigmentation of the body, hair growth over the chin and upper lip and androgenic balding. She underwent a genital surgery at the age of 18 years and got married at the age of 20 years. She was probably diagnosed to have CAH and had conceived at the age of 30 years following treatment with Prednisolone, details of which are not available. Since her treating endocrinologist expired, no further follow-up or treatment was undertaken.

What are the problems associated with CAH during adulthood?

Women in the reproductive age group can have progressive virilization, late onset of menarche, anovulation with polycystic ovaries and infertility.\[11\] Older individuals with CAH had significantly lower lumbar spine and femoral neck bone mineral density compared with controls, inversely related to the higher dose of glucocorticoids.\[12\] Obesity and insulin resistance are also more common in older individuals with CAH. There is an increased prevalence of adrenal incidentalomas in CAH, especially in non-compliant patients.\[11\] Adrenal myelolipomas are also rarely associated with CAH.\[13\]

Our patient has been under constant follow-up for the last 18 months. Repeat imaging of the lesion does not show any increase in size.

How will the patient be managed on a long-term basis?

After the acute episode is over, the patient needs to be started on glucocorticoid replacement. Since, patients with simple virilizing CAH have aldosterone secretion disturbance, fludrocortisone is added to maintain normal levels of plasma renin activity and reduce the dose of glucocorticoid.\[14\] The dose of glucocorticoid is titrated to maintain testosterone in the normal range (Normal: <1 ng/ml in women) and 17-hydroxyprogesterone between 1 to 10 ng/ml.\[10,13\] The dose of fludrocortisone is titrated by plasma renin activity and electrolyte measurements. The patient should be monitored for adverse effects of glucocorticoids (Cushingoid features, osteoporosis, impaired glucose tolerance, hypertension) and mineralocorticoids (hypertension, oedema). Appropriate increases in oral glucocorticoid dosage or conversion to intravenous replacement are required during stressful conditions.

Hirsutism can be managed by antiandrogens. Ongoing hyperandrogenemia unresponsive to medical methods should lead to bilateral adrenalectomy.\[10,13\]

Our patient was started on treatment with Prednisolone 7.5 mg and Fludrocortisone 50 micrograms daily. The dose of Prednisolone was reduced to 5 mg daily since the patient developed Cushingoid features.

Treatment of CAH extends beyond childhood and adolescence. Patients with CAH are vulnerable to several long-term effects of over and under-treatment. The importance of ongoing care and follow-up should be highlighted to patients during their transition from paediatric to adult endocrine care.

References

3. Ravichandran R, Lafferty F, McInnisse MJ, Taylor HC. Congenital adrenal hyperplasia presenting as massive adrenal incidentalomas in the sixth decade of life; re-