Spontaneous resolution of bilateral avascular necrosis of femoral head following cure of Cushing syndrome secondary to primary pigmented micronodular adrenal disease.

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Introduction

Atraumatic avascular necrosis of the hip is typically associated with exogenous glucocorticoid treatment. To date there have been less than twenty reports where avascular necrosis was the presenting feature of endogenous cortisol excess. It has been promulgated that, if left untreated, avascular necrosis leads to a complete collapse of the femoral head necessitating hip replacement in up to 70% of patients. The majority of the described patients with avascular necrosis due to endogenous hypercortisolism were treated surgically.

Case description

A 36 year old female was admitted for investigations of right leg pain. She had an L4/L5 lumbar disectomy two years previously for similar symptoms with very good initial clinical outcome. Her repeat lumbar spine MRI showed a left para-central disc herniation at L4/L5 level. She underwent L4/L5 revision disectomy with modest symptomatic improvement. Incidental findings of an early L1 compression fracture and multiple rib fractures were made.

Given the fractures in a young lady, an endocrinology opinion was sought. The patient reported significant weight gain, easy bruising, amenorrhoea of two years duration and recent onset of facial hirsutism. On examination, she had abdominal adiposity with violaceous striae, facial plethora and hirsutism, atrophic skin, multiple ecchymoses and proximal muscle weakness in keeping with Cushing’s syndrome. She had never used exogenous steroids.

Her biochemical investigations confirmed cortisol excess with cortisol post 1 mg dexamethasone suppression test of 747 nmol/l and cortisol following a low dose 48-hour dexamethasone suppression test of 607 nmol/l. Two 24 hour urine collections showed free cortisol of 1263 nmol/l and 1443 nmol/l (reference range up to 290 nmol/l/24 hours). ACTH was suppressed at <5.0 pg/ml consistent with an ACTH-independent source of Cushing syndrome.

Non-contrast dedicated CT adrenal glands showed possible subtle hypotrophy of the left adrenal gland and a normal right adrenal gland.

The diagnosis of micronodular hyperplasia was considered and the patient underwent Liddle’s test (Table 1) but failed to demonstrate a paradoxical rise in urinary free cortisol at the end of the test. She underwent a laparoscopic left adrenalectomy but remained hypercortisolemic following the surgery: morning cortisol on day four post surgery was 283 nmol/l, cortisol post one milligram dexamethasone suppression test was 306 nmol/l. Post-operatively her right leg pain worsened and she developed left leg pain affecting her ability to ambulate. MRI of her hips showed bilateral avascular necrosis of the femoral heads with early bone fragmentation on the left (Figures 1a and 1b). It was elected to defer surgical core decompression of the left femoral head until right sided adrenalectomy was performed. Histology of the adrenal glands showed multifocal nodular hyperplasia and brown pigment consistent with the diagnosis of primary pigmented micronodular adrenal disease.

The patient went on to have a right laparoscopic adrenalectomy with excellent biochemical response: morning cortisol at day four post surgery was <10 nmol/l. Following bilateral adrenalectomy the patient commenced on glucocorticoid and mineralocorticoid replacement. Within 4 months of adrenalectomy her bilateral leg pain had resolved and she was able to walk 6 kilometres daily as well as attend the gym regularly. Repeat MRI showed marked improvement in the high signal intensity abnormalities in both femoral heads, consistent with spontaneous healing of avascular necrosis (Figures 2a and 2b).

Radiological findings

Additional investigations

<table>
<thead>
<tr>
<th>Day</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Day 5</th>
<th>Day 6</th>
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<tbody>
<tr>
<td>24 hour urinary free cortisol (nmol)</td>
<td>1443</td>
<td>1700</td>
<td>1626</td>
<td>1071</td>
<td>945</td>
<td>877</td>
</tr>
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Table 1: Liddle’s test: 24 hour urine free cortisol measured at baseline (day 1 and 2), during low dose dexamethasone suppression test (day 3 and 4) and during high dose dexamethasone suppression test (day 5 and 6). In 69-75 percent of patients with cortisol excess due to primary pigmented nodular adrenocortical disease there is a paradoxical percent rise in 24 hour urinary cortisol excretion on day six of the test.

CONCLUSIONS

We report a case of a 36 year old woman with Cushing’s syndrome due to primary pigmented nodular adrenocortical disease, presenting with symptomatic avascular necrosis of both hips. This was managed conservatively from an orthopaedic surgery perspective and the patient’s hypercortisolism was cured following bilateral adrenalectomy. With this approach she went on to have an excellent functional recovery, and marked improvement in radiological findings on magnetic resonance imaging. She remains symptom-free four years post adrenalectomy and attends the gym regularly with excellent functional ability of both hips. In this case, similar to other cases reported in the literature, the initial presenting symptoms were attributed to another pathology. Avascular necrosis frequently evades early diagnosis and a high index of clinical suspicion is required for its accurate identification. It is important to remember that avascular necrosis can be a presenting feature of hypercortisolism, both endogenous and exogenous, and as such should prompt consideration of a work-up for same. This case is the first to report a favourable outcome over a long-term follow up period of a patient with bilateral avascular necrosis of the hip which reversed with treatment of endogenous hypercortisolism.