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 hypercortisolaemia were treated surgically.

Case description

A 36 year old female was admitted for investigations of right leg pain. She had an L4/L5 lumbar discectomy 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 discectomy 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 807 nmol/l. Two 24 hour urinary collections showed free cortisol of 1263 nmol and 1443 nmol (reference range up to 290 nmol/24 hours). ACTH was supressed at <5.0 pg/ml consistent with an ACTH-independent source of Cushing syndrome.
Non-contrast dedicated CT adrenal glands showed possible subtle hypertrophy 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 hypercortisolaemic following the surgery : morning cortisol on day four post surgery was 293 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 was 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

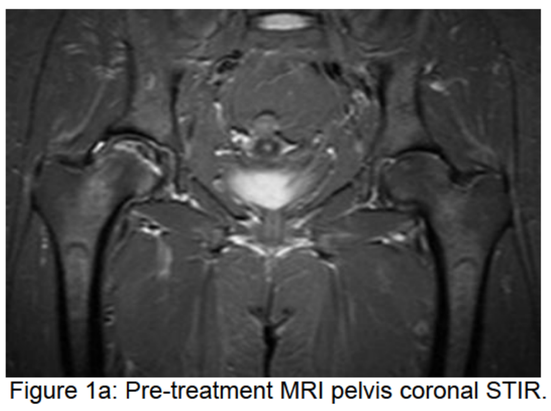

Figure 1a: Pre-treatment MRI pelvis coronal STIR.

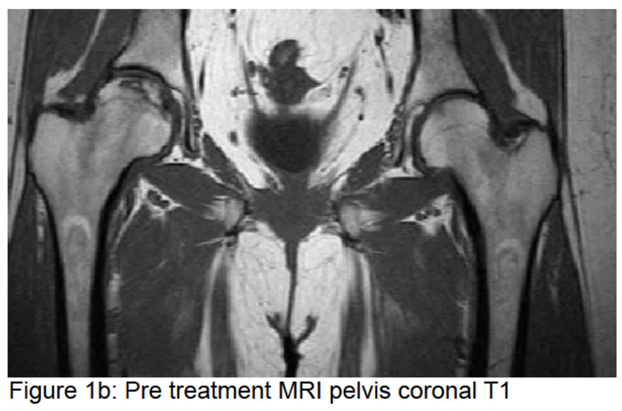

Figure 1b: Pre treatment MRI pelvis coronal T1

Figure 1: MRI Pelvis – Pre-treatment (a) Coronal STIR (b) Coronal T1. Right femoral head inner bright hyper-intense and outer dark hypo-intense signal lines on the STIR sequence and dark hypo-intense signal line on the T1 sequence compatible with osteonecrosis

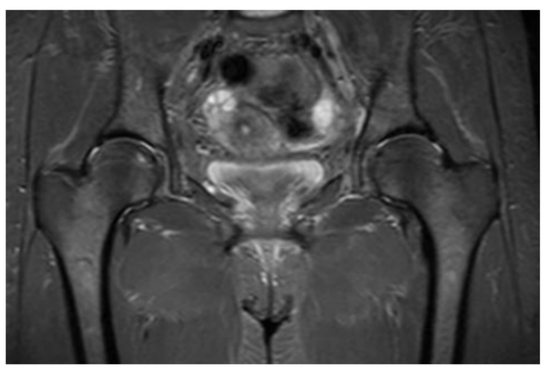

Figure 2a: Post-treatment MRI pelvis coronal STIR

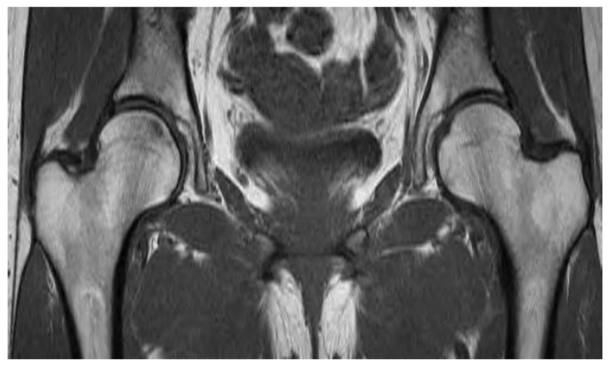

Figure 2b Post-treatment MRI pelvis coronal T1

Figure 2: MRI Pelvis – Post-treatment (a) Coronal STIR (b) Coronal T1. Near-complete resolution of right femoral head pre-treatment signal abnormality with now only a small residual bright hyper-intense STIR sequence and dark T1 sequence hypo-intense signal focus. No evidence of cortical collapse.

Additional investigations

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6
24 hour urinary free cortisol (nmol)	1443	**1700**	**1526**	**1071**	**945**	**877**

Table 1. Liddle's test : 24 urinary free cortisol measured at baseline (day 1 and 2), during low 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 50 percent rise in 24 hour urinary cortisol excretion on day six of the test.

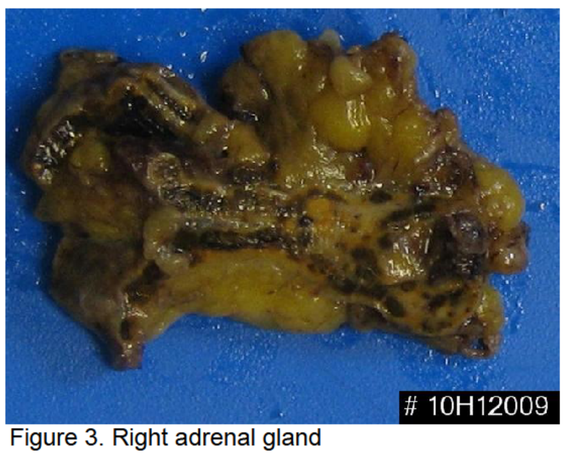

Figure 3. Right adrenal gland

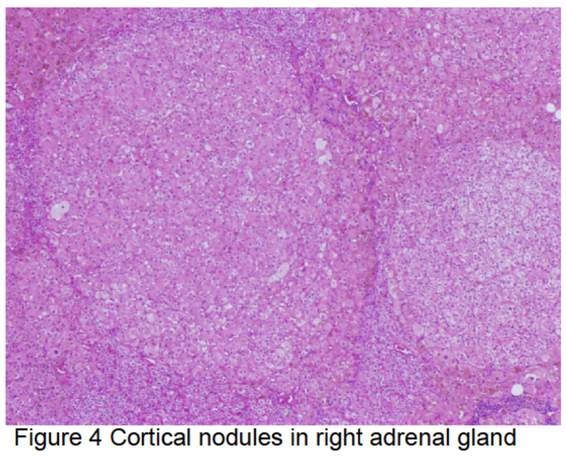

Figure 4 Cortical nodules in right adrenal gland

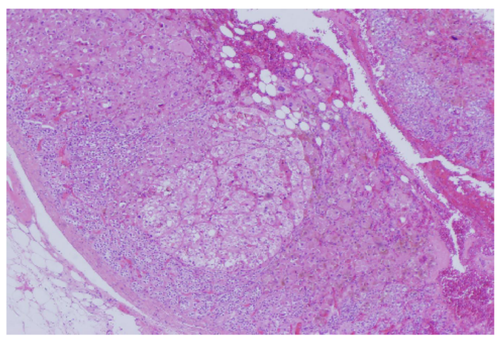

Figure 5 Mild hyperplasia with focal nodules in the left adrenal gland

Examination of the adrenal glands demonstrated features of multifocal nodular cortical hyperplasia; in addition, focal aggregates of cortical cells with cytoplasmic accumulation of brown pigment (lipofuscin) were identified

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 hypercortisolaemia 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 hypercortisolaemia, 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 hypercortisolaemia.

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