Hip pain - a symptom to be vigilant in hypercortisolism…

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A 64-year-old female with background history of hypertension presented with proximal myopathy, pigmentation and easy bruising. She also complained of left sided hip pain which was worse with movement. There was no preceding history of fever. Examination revealed a BMI of 20.2 kg m⁻², central obesity with thin extremities. There was round facies, facial plethora and thin skin. There were patches of ecchymoses and pigmented extremities with hyperpigmented nails (figure 1A, 1B). Blood pressure was 150/90 mmHg. She had an antalgic gait. Examination of the hips revealed painful hip movements on left hip as well as right hip. Laboratory investigations were significant for hypokalemia (serum Potassium 3.3 mmol/L) and overnight dexamethasone test was not suppressed (416 nmol/L). X-ray hips showed left sided crescent sign (figure 2). Magnetic Resonance Imaging of bilateral hips were done after orthopedic opinion which showed bilateral T1 hypo intensity and T2 heterogeneous hyperintensity and double line sign at the femoral heads (figure 3). Further evaluation revealed an ACTH of 23.2 ng/dL suggestive of ACTH dependent Cushing. Inferior petrosal sinus sampling confirmed pituitary dependent ACTH hypersecretion (table 1), unfortunately lateralization was not possible. MRI pituitary revealed a left sided pituitary microadenoma (figure 4).

Figure 1: Patient’s external appearance and pigmented extremities
Figure 2: X-ray bilateral hip joints AP view

Figure 3: MRI imaging of bilateral hips

Figure 4: MRI pituitary post contrast imaging showing 10x 7x 8mm lesion on the left side of the pituitary
Table 1. Results of inferior petrosal sinus sampling
(Prolactin central to peripheral ratio: Right side 1.86, left side 1.44; Central to peripheral
ACTH ratio: Right side 2.74, Left side 2.52)

<table>
<thead>
<tr>
<th>Site</th>
<th>ACTH (pg/mL)</th>
<th>Cortisol (nmol/L)</th>
<th>Prolactin (mU/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>R/ Inferior Petrosal sinus</td>
<td>91.91</td>
<td>476.5</td>
<td>610.8</td>
</tr>
<tr>
<td>L/ inferior petrosal sinus</td>
<td>86.6</td>
<td>560.1</td>
<td>471.2</td>
</tr>
<tr>
<td>R/ Internal Jugular Vein</td>
<td>68.6</td>
<td>539</td>
<td>489.2</td>
</tr>
<tr>
<td>L/ Internal Jugular Vein</td>
<td>38.53</td>
<td>512.8</td>
<td>320.8</td>
</tr>
<tr>
<td>Femoral vein</td>
<td>33.57</td>
<td>493.9</td>
<td>326.9</td>
</tr>
</tbody>
</table>

1. What is the Endocrinological diagnosis of this patient?
ACTH dependent Cushing syndrome secondary to pituitary adenoma is the most possible diagnosis of this patient with the presentation and investigations.

2. What is the cause for bilateral hip pain?
X-ray AP view of bilateral hips shows presence of crescent sign and MRI findings are suggestive of bilateral avascular necrosis. Avascular necrosis of the hips are commonly caused by trauma or micro trauma\(^1\). Exogenous steroids are the commonest cause for non-traumatic avascular necrosis of the hip. However, even though uncommon, untreated endogenous hypercortisolism is also known to cause avascular necrosis of the hip as in this patient. Avascular necrosis occurs either due to intraluminal obstruction of the blood vessels by microthrombi, emboli or extraluminal obstruction due to marrow oedema\(^2\). Femoral head is more susceptible to avascular necrosis due to the limited blood supply through the artery of ligamentum teres\(^3\). The exact mechanism of in hypercortisolism is not clear. It is hypothesized that decreased bone remodeling that occurs in cortisol excess leads to impaired bone formation increasing the risk of necrosis of bone.

3. How would you manage this patient?
She was immediately referred for transsphenoidal surgery for resection of pituitary adenoma. Bilateral hip replacement was scheduled to be done after achieving eucortisolism.

Hip pain should not be neglected in patients with features of hypercortisolism. MRI of hip joints are the preferred diagnostic method as X-ray is often normal. Sensitivity of X-ray in detecting early stages of avascular necrosis is as low as 41\(^4\).

References
