Review Article

A diagnostic approach towards patients with hirsutism - screening for sinister causes

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Abstract

Hirsutism is a common problem which has many causes. Fortunately, the majority of them are benign. However, a more sinister cause may be sometimes present. The investigations to rule out all possible causes are tedious and expensive. A correct diagnostic approach taking into consideration history, signs of virilisation, and relevant investigation can help identify the important causes and prevent unnecessary workup of such patients.

Key words

Hirsutism, diagnostic approach.

Hirsutism is a very common problem. Its causes are many, ranging from idiopathic to relatively benign conditions, like polycystic ovary syndrome, through to more serious ones e.g. androgen secreting tumours. The investigations needed to thoroughly evaluate the patient for all possible causes of hirsutism are expensive and time consuming. Also, some causes are relatively common while others are not so common and still others, rare. Therefore, it is neither possible nor necessary to perform all these tests in all patients. The question now arises is what preliminary tests should be performed in all patients and which patients need to be evaluated further.

More than 90% of women with hirsutism have the relatively benign conditions of idiopathic hirsutism (IH) or polycystic ovary syndrome (PCOS). Although exact guidelines for a practical approach towards a patient with hirsutism have not been established, it is the clinical assessment and correct interpretation of preliminary investigations that leads a clinician towards a diagnostic possibility. The importance of a thorough medical history and clinical examination in this context cannot be stressed enough. The clinical presentation of IH/PCOS is characteristic with mild symptoms arising in the decade between 15-25 years with gradual progression usually requiring years before coming to medical attention. If hirsutism is occurring outside this decade, especially with rapid progression and signs and symptoms of virilisation, this needs to be further investigated (see Table 1).

Measurement of serum androgen levels particularly testosterone (T), in association with sex hormone binding globulin (SHBG),
Table 1 Presenting features in patients with different causes of hirsutism.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Time of onset</th>
<th>Menstrual disturbances</th>
<th>Virilisation</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>IH</td>
<td>15-25 yrs</td>
<td>-</td>
<td>-</td>
<td>Acne may be present</td>
</tr>
<tr>
<td>PCOS</td>
<td>15-25 yrs</td>
<td>+</td>
<td>Rare</td>
<td>Obesity 40%; enlarged ovaries may be palpable</td>
</tr>
<tr>
<td>CAH</td>
<td>Congenital</td>
<td>+</td>
<td>+</td>
<td>Small stature, evidence of intrauterine androgen excess</td>
</tr>
<tr>
<td>Cushing’s syndrome</td>
<td>Any time</td>
<td>+</td>
<td>Unusual</td>
<td>Evidence of glucocorticoid excess</td>
</tr>
<tr>
<td>Androgen secreting tumour</td>
<td>Any time</td>
<td>+</td>
<td>+</td>
<td>Palpable mass may be present</td>
</tr>
</tbody>
</table>

is helpful for at least two reasons. First the finding of only mildly elevated androgen values provides the investigator and the patient with an assurance that other disorders such as a tumour or congenital adrenal hyperplasia are not lurking in a cryptic form. Secondly a baseline androgen value against which to compare subsequent values is necessary to assess the early impact of treatment. Levels of testosterone 100% above the normal range or T/SHBG ratio three times above normal should certainly be regarded as highly suspicious and warrant additional investigations. A case may also be made for measurement of leutinising hormone LH, follicle stimulating hormone FSH and an LH/FSH ratio as a preliminary investigation. The normal ratio is below 1 and ratio is above 2 in most cases of PCOS.

Abdominal and pelvic ultrasonographic examination for adrenals and ovaries as a preliminary investigation is a relatively inexpensive and non invasive test. It is not however very sensitive for detecting PCOS and other ovarian pathologies. A transvaginal scan (TVS) is more sensitive for this purpose but it cannot be routinely done in all patients because of its unacceptability especially in unmarried patients.

Among patients with hirsutism an adrenal tumor is unlikely if the patient has normal basal serum concentration of testosterone and dehydro-epiandrosterone sulphate (DHEAS). If testosterone levels are markedly elevated the next investigation to go for would be DHEAS levels. If DHEAS is also increased a virilising tumour is to be suspected. To rule it out a dexamethasone suppression test is indicated. A virilising tumour is unlikely if serum DHEAS and 17 ketosteroid excretion are within the normal range and serum cortisol concentration is less than 3.3 µg/dl after administration of dexamethasone for 5 days. If it is higher, the role of imaging techniques like CT abdomen and MRI, then come into play for localisation of the tumor.

Studying hirsute women for the more ominous causes of hirsutism requires that we strike a balance between initiating a major diagnostic exercise in too many women and doing so little that we fail to diagnose disorders that are both treatable and more serious than IH or PCOS. Screening procedures that rely mainly on clinical evaluation may be as sensitive as the hormone based evaluation for the diagnosis of causes of hirsutism. Androgen producing malignant tumours is the most sinister cause
Figure 1 An algorithm for investigations of hirsutism

Serum androgen levels

- Normal
  - LH/FSH ratio
    - Normal
    - ↑ or ↑↑
    - ↑↑ (100% above normal)
  - Abnormal (>2)
    - USG & other tests for PCOS

- Abnormal
  - T/SHBG ratio
    - Normal
    - IH
    - Abnormal

- DHEAS levels
  - Normal
  - Adrenal pathology unlikely
  - Tests for ovarian tumour localisation

- LH/FSH ratio
  - Normal
  - Abnormal (increased)
    - IH
    - Dexaemethasone suppression test for five days
      - Cortisol < 3.3 µg/dl
        - Tumour not likely
        - Tests for CAH
      - Cortisol > 3.3 µg/dl
        - CT/MRI for localization of adrenal tumour

†, mild elevation; ††, moderate elevation; †††, marked elevation CAH, congenital adrenal hyperplasia; DHEAS, dehydro-epiandrosterone sulphate; FSH, follicle stimulating hormone; IH, idiopathic hirsutism; LH, leutinising hormone; PCOS, polycystic ovary syndrome; T, testosterone; SHBG, sex hormone binding globulin.
of hirsutism. Imaging procedures are reserved for the rare occasion when hormonal evaluation suggests the presence of tumour. By these means the most important causes of hirsutism can be efficiently identified and unnecessary work up can be avoided.

References