Database analysis of women with tumor-level serum testosterone

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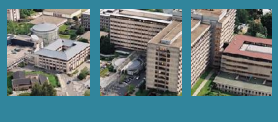


INTRODUCTION

In female hyperandrogenism, total testosterone assay is the recommended first-line test, as it is the best laboratory predictive marker among androgens of an androgen-producing tumour. A total testosterone serum level above twice the upper normal value by direct assays requires exclusion of an androgen producing tumour (virilizing ovarian / adrenal tumour).

OBJECTIVE

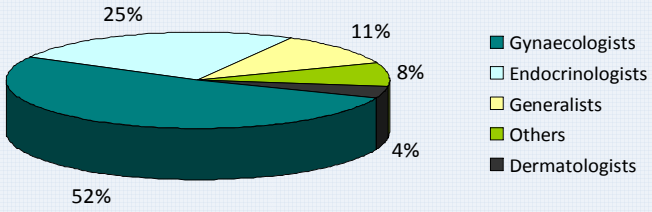
The aim of our work was to evaluate the number, the final diagnosis and the quality of care of women with an elevation of total testosterone ≥ 1.6 ng/ml measured by direct RIA assay (normal range: 0.2 - 0.8 ng/ml).

PATIENTS AND METHOD

Analysis of the lab database (between 2004 and 2013) identified 132 women with an elevated total testosterone ≥ 1.6 ng/ml.

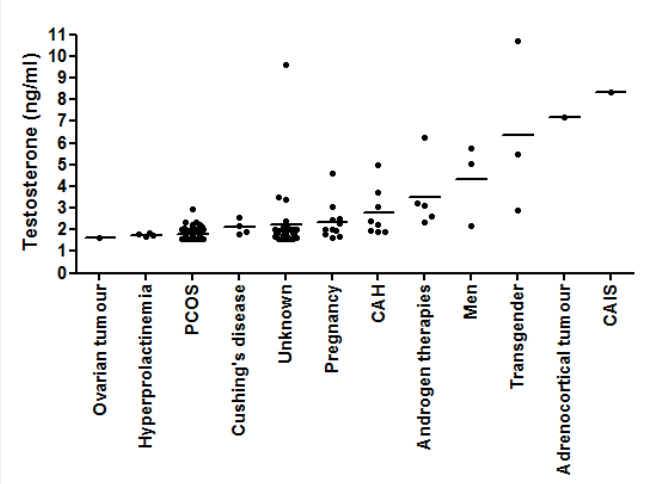
Total Testosterone > 0.8 ng/ml 1057 patients → **Total Testosterone > 1.6 ng/ml 132 patients**

Testosterone measurement was asked by endocrinologists (25%), gynaecologists (52 %) and others (23 %).



RESULTS

In ascending order of total testosterone values, associated diagnosis were: ovarian tumour (n = 1), hyperprolactinemia (n = 4), PCOS (n = 63), Cushing's disease (n = 4), unknown (n = 28), pregnancy (n = 11), congenital adrenal hyperplasia (CAH) (n = 8), androgen therapies in post-menopausal women (n = 5), men misclassified as women by data processing (n = 3), transgender patients (n = 3), adrenocortical tumour (n = 1) and androgen insensitivity syndrome (CAIS) (n = 1).

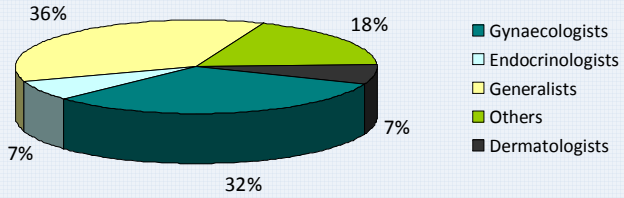


In the PCOS group, the mean value of total testosterone was 1.8 ng/ml (SD ± 0.2) and the maximal value was 2.9 ng/ml. PCOS group concerns almost 50 % of patients and corresponds probably to a severe form of PCOS. The diagnosis of PCOS was based on the presence of at least two out of three criteria of the revised 2003 consensus of Rotterdam.

RESULTS

Diagnosis was not established in 20 % of patients (n = 28).

The following pie-chart displays the percentage of specialists who first prescribed the testosterone assay.



Six of the 28 patients had elevated SHBG (Sex Hormone Binding Globulin) with normal free testosterone index.

The following table shows the characteristics of the 22 remaining patients.

Patient characteristics	Value (mean ± SD)	Normal value	n (number of patients)
Age (years)	43 ± 22		22
Total testosterone (ng/ml)	2.3 ± 1.7	0.2 - 0.8	22
SHBG (ng/ml)	9.8 ± 5.6	8.7 - 26	14
Free testosterone index	27.0 ± 13.1	0.4 - 9.1	14
DHEA-s (ng/ml)	2054 ± 1059	900 - 3500	13
Δ_4Androstenedione (ng/ml)	2.9 ± 1.6	0.2 - 3.1	10

In patients without diagnosis, ovarian ultrasonography was performed in 30% while adrenal imaging in 15%.

DISCUSSION

If serum levels of total testosterone are elevated, a focused history and physical examination should be performed in order to exclude the diagnosis of an androgen producing tumour.

The Polycystic Ovary Syndrome (PCOS) is the most frequent cause of hyperandrogenism, especially in young women. Nevertheless, PCOS is a diagnosis after exclusion of other hyperandrogenic disorders.

A simple screening panel of endocrine tests (basal 17-hydroxyprogesterone, DHEA-s, morning plasma cortisol, Prolactin, TSH, IGF-1) and a pelvic and adrenal ultrasound should also be performed.

In our group of undiagnosed patients, the level of serum DHEA-s was within normal values and that orientated the source of androgen excess mostly towards an ovarian origin. However, only 30% of these patients underwent a pelvic ultrasonography.
The initial screening included a basal 17-hydroxyprogesterone measurement in 4 patients. One of these patients had also an ACTH stimulating test while a 24-h urine cortisol assay was performed in only 1 patient.
No sufficient clinical data concerning hirsutism and dysmenorrhea were available.

CONCLUSION

In conclusion, analyzing a hospital lab database is a way to create a registry of uncommon diseases. It permits also to assess and improve the quality of care of patients with a rare disease or with lab values that require further assessment.

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