Review Article

Interpretation of Thyroid function tests

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ABSTRACT

Thyroid function tests (TFTs) are amongst the most commonly requested laboratory investigations in both primary and secondary care. Interpretation of thyroid function tests is generally straightforward due to considerable improvement in TSH, T3 & T4 assays. If the reverse relationship between TSH & thyroid hormone maintained then usually the cause is thyroid gland related. If the reverse relationship not maintained than the cause other than thyroid gland should be thought & evaluated accordingly.

Thyroid function tests (TFTs) are amongst the most commonly requested laboratory investigations in both primary and secondary care. Interpretation of thyroid function tests is now generally straightforward due to considerable improvement in TSH, T3 & T4 assays, and more than 90% of people investigated are diagnosed with normal thyroid gland function. However, there remain a few situations in which the results of TSH, T4, and T3 assays tend to point in different directions, as well as cases in which thyroid function test results seem clear cut but are in fact misleading.

Thyroid function tests :

Highly sensitive TSH assay (second or third generation, with a limit of detection < 0.1 mIU/L) alone is used for initial screening. TSH alone can be considered as initial screening with some limitations, it can be misleading in some conditions like recent treatment of thyrotoxicosis, pituitary disease, non-thyroidal illness, TSH-secreting pituitary tumour & thyroid hormone resistance. Combining total or free thyroid measurement along with TSH can be used to address these limitation with increased cost. Discussing different assays for measurement TSH, thyroid hormone assays is beyond the scope of this article.

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Our discussion on thyroid function interpretation is pertaining to six clinical scenario commonly encountered in practise. ***Figure 1*** showing schematic diagram of different pattern of TFT & their causes.

1) Low TSH, raised T3 or T4 :

30 year old non pregnant female presented with palpitation, anxiety, tremors & weight loss since 4-5 month. On clinical evaluation patient found to have tachycardia, fine tremors & diffuse thyroid enlargement. Biochemical evaluation found to have T3 - >3 00 ng/dl (80-180), T4 - 24 ug/dl (4.5 - 12.5) & TSH - < 0.001u IU/l (0.4-4.5). Technetium thyroid scan showed uniform increased uptake & diagnosis made as Grave's disease.

Other differential diagnosis for similar thyroid function are multinodular goitre (MNG), or toxic nodule & thyroiditis. Clinical & further evaluation can usually separate these conditions. Multiple palpable thyroid nodules & technetium scan showing toxic nodules favours MNG. Thyroiditis can be differentiated from the other conditions by short duration of symptoms, technetium scan showing decreased uptake & unusually rapid response to antithyroid drugs (< 2wks).

Rarely this clinical scenario can be caused by trophoblastic disease in pregnancy (↑ HCG), Struma ovary & activating mutations of TSH receptor. Drugs like amiodarone & lithium can cause thyrotoxicosis.

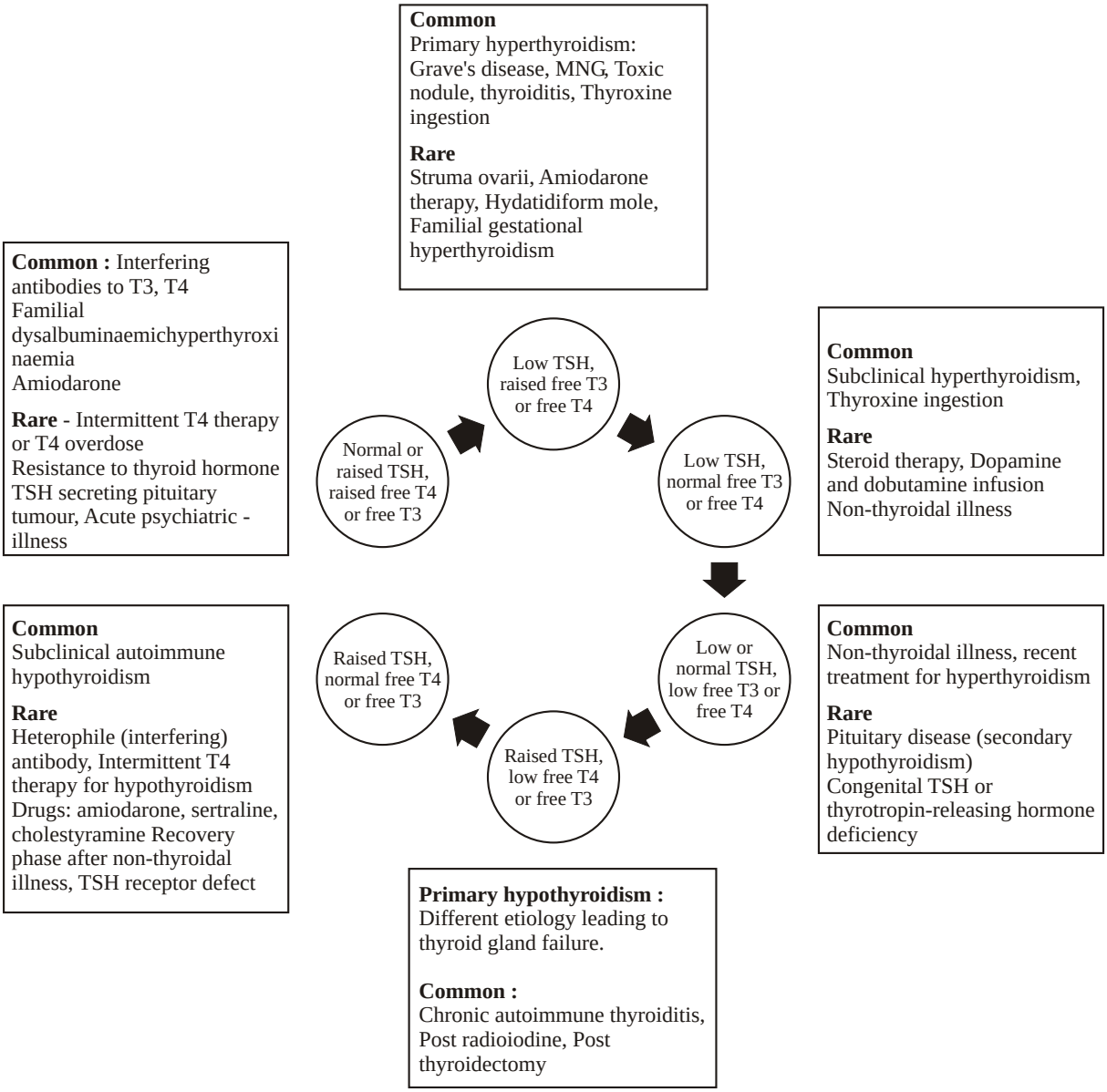

Figure 1 : **Schematic diagram of different pattern of Thyroid function tests**

2) Low TSH, normal T3 or T4 :

This pattern is seen in subclinical thyrotoxicosis, all above mentioned conditions can present with this pattern in mild state.

40 year old female patient evaluated for anterior neck swelling with no symptoms of thyroid dysfunction. On clinical examination MNG was evident & TSH was supressed (0.001uIU/l) with normal T3, T4 (T3 - 155ng/ml, T4 - 8.5Ug/dl). Technetium thyroid scan showed focal areas of increased uptake with suppressed normal thyroid consistent with diagnosis of subclinical thyrotoxicosis of MNG. This situation can require treatment since the risk of atrial fibrillation and osteoporosis is increased.

Similar TFT can be seen among patients in hospital, high-dose steroid or dopamine and dobutamine infusions, both of which can suppress pituitary TSH release, or non-thyroidal illness should be considered. Repeat thyroid function tests showing a return to normal after recovery should confirm these diagnoses.

3) Low or normal TSH, low T3 or T4 :

36 year old female patient came with history of lethargy, amenorrhea since 1yr. On clinical examination patient had dry skin with a dull look typical of hypothyroidism. On enquiry patient gives history of severe post-partum hemorrhage in last delivery 2 years back. TFT showed normal TSH (3.5 uIU/ml) & low T3 (80 ng/dl), T4 (2.1 ug/dl). Further evaluation showed low morning serum cortisol (2.1 ug/dl). With this biochemical feature the possibility of central hypothyroidism kept & MRI pituitary done which showed empty sella consistent with diagnosis of Sheehan's syndrome.

This clinical scenario is also caused bynon-thyroidal illness (NTD), D commonly associated with low T3, low TSH & normal T4, in late stages T4 can be decrease, but T3 will be disproportionately low compared to T4. In central hypothyroidism T4 decreases more compared to T3 but mixed picture can be seen.

The diagnosis of central hypothyroidism is important, because it may associated with unsuspected large pituitary tumour or Sheehan's syndrome or pituitary or cranial irradiation, even 20 years previously, can cause central hypothyroidism. Patient needs to be treated for other pituitary hormones especially ACTH cortisol which can be life threatening.

4) Raised TSH, low T4 or T3 :

This clinical scenario mainly caused by the primary hypothyroidism. Primary hypothyroidism is caused by

Common : Chronic autoimmune thyroiditis, Iodine deficiency, Post radioiodine, Post thyroidectomy, Hypothyroid phase of transient thyroiditis

Rare : (anti-TPO negative, no radioiodine or surgery) Post external-beam irradiation to the neck, Drugs : amiodarone, lithium, interferons, interleukin-2, Iodine excess, Amyloid goitre (large, firm goitre with systemic amyloidosis) Riedel's thyroiditis, Congenital - thyroid tissue absent, Thyroid dysgenesis possibly associated with TSH-receptor, PAX-8, and, TTF2 mutations, Congenital - thyroid tissue present, Iodine transport defects - low radioiodine uptake or saliva iodine, Iodine organification defect, Congenital - high radioiodine uptake, positive perchlorate discharge, Thyroglobulin synthetic defect low thyroglobulin concentration, TSH-receptor defects, Resistance to TSH with other (unspecified) defects

5) Raised TSH, normal T4 or T3 :

A 28 year female married since 8 years, during evaluation for primary infertility patient found to have grade II goiter with no symptoms of thyroid dysfunction. Serum TSH was elevated 9.5 uIU/l and anti-microsomal antibody titer was 476. So diagnosis was kept as subclinical hypothyroidism & started her on thyroxine. Not all patients with subclinical hypothyroidism need treatment. If the patient has a goiter or if thyroid antibodies are present or the presence of symptoms are compatible with hypothyroidism, infertility, pregnancy or imminent pregnancy it favors treatment.

In some clinical circumstances the possibility of other than this should be suspected were the TSH is abnormally high (> 20 mIU/ml) & T3, T4 are normal & TSH levels remains elevated in spite of adequate dose of thyroxine. This clinical scenario is usually associated with the presence of a heterophile-eg, antimouse immunoglobulin-interfering with the TSH assay. Repeat estimation, with a different assay, or the addition of blocking agents such as mouse serum, can be helpful. A same clinical scenario in patient with previously controlled well with thyroxine should raise suspicion of malabsorption. Amiodarone can lead to elevated TSH in first 3 month of therapy due to excess iodine load. Rarely in the paediatric age groups Pandred syndrome can present like this.

6) Normal or raised TSH, raised free T4 or free T3 :

42 year old female patient presented with palpitation & anterior neck swelling, on examination diffuse goiter & mild coarsening of face were present. On biochemical evaluation, TSH was normal (3.2 uIU/l) with elevated T3 & T4. IGF 1 level done in the view of facial coarsening which was elevated (647 ng/ml) & MRI pituitary showed macro adenoma.

Diagnosis was kept as pituitary macro adenoma cosecreting GH & TSH. Post surgery TFT were improved.

This pattern of thyroid function is commonly seen in many condition leading to increased TBG (eg. pregnancy, estrogen excess, acute hepatitis, familial dysalbuminaemichyperthyroxinaemia), free thyroid hormone measurement is help full in these condition. Drugs like amiodarone can lead to this pattern of TFT by inhibiting peripheral conversion of T4 to T3 & increasing free T4. Acute psychiatric conditions mainly schizophrenia can cause elevated free thyroid hormone but it rarely lasts beyond 14 days of illness. Rarely interfering antibody to T3 & T4 assay can lead to similar TFT.

Patient with thyroid hormone resistance present with mild toxic symptoms with elevated free T3, T4 & normal or elevated TSH. These patient need detailed family history for the diagnosis & MRI pituitary should be done to rule out pituitary adenoma.

Thyroid function tests in pregnancy :

In pregnancy the total thyroid hormone can be increased due to increased thyroid binding globulin (TBG) so the assessment of free thyroid hormone is important in pregnancy. The level of TSH range also change in pregnancy due HCG, in first trimester TSH ranges from 0.1-2.5 uIU/L & in second & third trimester TSH ranges from 0.2-3uIU/L. In first trimester due to HCG, patient can have supressed TSH & normal or mildly raised free thyroid hormone which will not require any treatment. This gestational thyrotoxicosis can be differentiated from Grave's by presence of goitre & ophthalmic signs, TSH receptor antibody can help in the differentiation of these two conditions.

Conclusion :

Ultra-sensitive TSH can be used as initial test for the evaluation of thyroid dysfunction with above limitations keeping in mind. If the reverse relationship between TSH & thyroid hormone maintained then usually cause is thyroid gland related. If the reverse relationship not maintained than the cause other than thyroid gland should thought &evaluating accordingly.

References :

1. Koulouri O, Moran C, Halsall D, Chatterjee K, Gurnell M. Pitfalls in the measurement and interpretation of thyroid function tests. Best Pract Res ClinEndocrinolMetab; 2013 Dec [cited 2014 Oct 26];27(6):745-62.
2. Dayan CM. Interpretation of thyroid function tests. 2001;357:619-24.
3. Biondi B, Wartofsky L. Treatment with thyroid harmone. Endocr Rev.2014;35:433-512.