Interpreting thyroid function tests

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This endocrine education section uses case scenarios to educate doctors on the best approach to the diagnosis and management of patients with different endocrine problems.

PART 1. WHAT IS THE CORRECT DIAGNOSIS?

Below are brief summaries of patient profiles. What do you think is the most likely diagnosis for each case described?

Case 1.

A 40-year-old woman requests routine thyroid function tests because she feels particularly tired and has had irregular, lighter periods. She has a 6-month-old baby. She has a family history of 'thyroid problems' (her mother and aunt, who are both middle aged). She has no goitre. You order thyroid function tests and the results show that her thyroid-stimulating hormone (TSH) level is undetectable and her free thyroxine (T_4) and triiodothyronine (T_3) levels are elevated.

Which one of the following is the most likely diagnosis?

a. Postpartum thyroiditis
b. Hashimoto's disease
c. Graves' disease
d. Iodine deficiency

Discussion

The patient's symptoms suggest hyperthyroidism. Postpartum thyroiditis is common after pregnancy, occurring in approximately 5% of pregnancies. The onset is typically within two to four months of delivery and the condition is usually self-limiting. Usually thyroid peroxidase (TPO) antibodies are present but, unlike Graves' disease, there is low radioactive uptake on scanning (if this is carried out as the brief radiation precautions can disrupt breastfeeding). Hypothyroidism may also occur in this condition, in the recovery phase.

Hashimoto's disease is indistinguishable from the hypothyroid phase of postpartum thyroiditis clinically and pathologically. Women who have positive TPO antibodies before pregnancy have a 50% chance of developing postpartum thyroiditis. Both are autoimmune conditions and most cases are probably a spectrum of the same disease.

Autoimmune thyroid disease can also present as Graves' disease (with hyperthyroidism) and this can present for the first time in the postpartum period. Graves' ophthalmopathy and a large goitre may differentiate this condition clinically from other autoimmune hyperthyroid conditions. Radioactive uptake is usually increased on the thyroid nuclear uptake scan.

Iodine deficiency results in hypothyroidism. The patient's test results confirm hyperthyroidism, as do her symptoms.

Answer

The answer is therefore a. Postpartum thyroiditis (hyperthyroid phase) is the most likely diagnosis given the patient's test results.

Case 2.

A 70-year-old man has been on thyroxine therapy for six months after he was noted to have a small multinodular goitre and mild hypothyroidism at diagnosis. His recent test results show that his TSH level is undetectable, his free T_3 and T_4 levels are normal and his antithyroid antibodies are negative.

Which one of the following is the most likely diagnosis?

a. Reduced adherence to thyroxine therapy
b. Thyroid autonomy in a multinodular goitre
c. Hashimoto's thyroiditis
d. Over-treatment with thyroxine therapy

Discussion

Excess thyroxine treatment could certainly cause the biochemical results shown in this patient.

Reduced adherence to thyroxine therapy would normally result in hypothyroidism.

A patient with hypothyroidism in the past is unlikely to develop thyroid autonomy, so although this is not absolutely impossible, it is very unlikely.

Hashimoto's thyroiditis is uncommon in men, usually presents in a younger age group and is antibody positive. The hypothyroid

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phase occurs when the gland is damaged, usually to the point of being unable to make thyroid hormone, although spontaneous recovery of the gland can occur (at least temporarily).

Answer

The answer is therefore d. Over-treatment with thyroxine therapy is the most likely diagnosis for this patient.

Case 3.

A young woman aged 24 years presents with a tender neck and shotty lymphadenopathy. She has recently had an influenzal illness. Her TSH level is below normal but detectable, her free T_4 level is elevated and her free T_3 is at the upper limit of the normal range.

Which one of the following is the most likely diagnosis?

a. Hashimoto's disease
b. Graves' disease (hyperthyroid phase)
c. Subacute thyroiditis
d. Toxic multinodular goitre

Discussion

Subacute thyroiditis, also known as De Quervain's thyroiditis, is classically granulomatous on histology. It occurs commonly after viral infections. Typical cases require no investigation other than thyroid function tests, although a nuclear thyroid scan is wise as a definitive diagnosis. The thyroid gland releases thyroid hormone in the acute phase; however, hypothyroidism may follow. The condition is usually self-limiting and may only require symptomatic treatment in the hyperthyroid phase and thyroid replacement hormone therapy if hypothyroidism is symptomatic or persists.

Hashimoto's disease presents clinically with a more gradual onset and very little discomfort. Lymphadenopathy is absent and TPO antibodies are positive.

Graves' disease is possible but unlikely, given the patient's history and the T_4/T_3 ratio. Antibody testing would be positive and there would be high uptake on a radionuclide scan.

A patient with a toxic multinodular goitre would not present clinically with thyroid tenderness.

Answer

The answer is therefore c. Subacute thyroiditis is the most likely diagnosis in this case.

Case 4.

A 16-year-old girl is brought to you because her mother is concerned she is developing anorexia. You carry out thyroid function tests and these reveal that, although her TSH and free T_4 levels are normal, her free T_3 level is below normal.

Which one of the following is the most likely diagnosis?

a. Sick euthyroid syndrome
b. Graves' disease
c. Subacute thyroiditis
d. Hypothyroidism

Discussion

Sick euthyroid syndrome fits with the history of this patient. Carbohydrate deprivation inactivates enzymic T_4 to T_3 conversion, as may occur in patients with a severe illness. This pattern can be seen in patients with anorexia nervosa.

Graves' disease is not consistent with the results of the patient's thyroid function tests. Clinically, there is often a goitre.

Subacute thyroiditis with hyperthyroidism is not confirmed by this patient's thyroid function tests because T_4 and T_3 levels would be elevated and the TSH level suppressed, even if the T_4/T_3 ratio is high.

Hypothyroidism is not confirmed by this patient's thyroid function tests because free T_4 levels would be low and TSH levels raised in patients with primary hypothyroidism, and free T_4 levels would be low in those with secondary hypothyroidism.

Answer

The answer is therefore a. Sick euthyroid syndrome is most likely in this scenario biochemically.

PART 2. WHAT INVESTIGATIONS ARE MOST USEFUL?

Below are brief summaries of patient profiles. For each case, what do you think is the clinically most useful investigation to help confirm a diagnosis or aid clinical care?

Case 1.

A 55-year-old man has a palpable single thyroid mass on examination. His blood TSH level is normal.

What is the most useful investigation to confirm a diagnosis?

Answer

Fine-needle aspiration thyroid biopsy, usually under ultrasound guidance, is the most useful investigation for this patient. If the nodule is palpable, ultrasound guidance may not be necessary, but helps to pick up impalpable nodules elsewhere in the gland. This investigation is needed to exclude thyroid cancer. If the nodule is cystic and the aspiration is nondiagnostic, a repeat biopsy is usually unhelpful. However, if the nodule is solid, then an adequate specimen must be obtained and this is possible at the initial aspiration.

Case 2.

A 65-year-old woman has increased lethargy, unexplained weight gain and hypersomnolence. Her TSH level is four times the normal upper level, her free T_4 level is low and her free T_3 level is at the lower limit of normal. She has a small asymmetric and firm goitre on palpation.

What is the most useful investigation to confirm a diagnosis?

Answer

The most likely diagnosis is primary hypothyroidism and the most common cause is autoimmune thyroid disease (Hashimoto's disease). Anti-TPO and antithyroglobulin antibodies could be considered to help diagnose Hashimoto's thyroiditis. This would not change the initial hormone management (thyroid replacement hormone therapy).

Case 3.

A 35-year-old man has had a recent upper respiratory tract infection. He now complains of an extremely painful anterior neck and marked lethargy but is afebrile. He is very tender over the right lobe of the thyroid. His C-reactive protein (CRP) level is 10 times the upper normal level. His TSH level is undetectable, and his free T_4 and free T_3 levels are both mildly elevated.

What investigation would you carry out next?

Answer

A technetium-labelled thyroid uptake scan would be the most appropriate investigation to carry out next. The most likely diagnosis is postviral painful thyroiditis, also known as subacute thyroiditis. Technetium uptake on the symptomatic side should be low and may also be low on the initially unaffected side also.

Case 4.

A 67-year-old man is on an appropriate dose of thyroxine therapy for papillary thyroid cancer, which was recently treated by total thyroidectomy and radioactive-iodine. Six months later, his neck ultrasound shows no residual thyroid or any other disease.

Is there another test you would consider at this time?

Answer

Measurement of the serum thyroglobulin level with antithyroglobulin antibody to validate accuracy of the thyroglobulin assay could be considered at this time. In the absence of residual normal thyroid tissue (i.e. after surgical and radioiodine ablation), thyroglobulin is a marker of residual or recurrent papillary or follicular thyroid cancer. Optimal follow up of patients with thyroid cancer is in conjunction with a thyroid specialist. **ET**