Endocrinology
L:2

د. حازم اسماعيل غزاي

Consultant In Internal Medicine

Anbar Medical College

Medical Department

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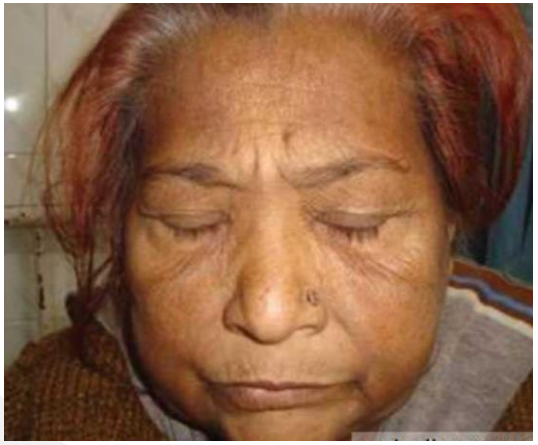
HYPOTHYROIDISM

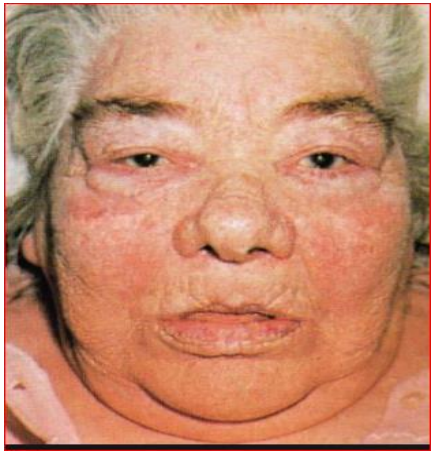
-The prevalence of primary hypothyroidism is 1:100, but increases to 5:100 if patients with subclinical hypothyroidism (normal T4, raised TSH) are included.

-The female: male ratio is approximately 6:1.

-There are various causes of primary hypothyroidism, but autoimmune disease (Hashimoto's thyroiditis) and thyroid failure following 131I or surgical treatment of thyrotoxicosis, account for over 90% of cases in those parts of the world which are not significantly iodine-deficient

Hypothyrodism :Clinical assessment





- Clinical features depend on the duration and severity of the hypothyroidism.
- In the patient in whom complete thyroid failure has developed insidiously over months or years many of the clinical features are likely to be present.
- A consequence of prolonged hypothyroidism is the infiltration of many body tissues by the mucopolysaccharides, hyaluronic acid and chondroitin sulphate, resulting in a low-pitched voice, poor hearing, slurred speech due to a large tongue, and compression of the median nerve at the wrist (carpal tunnel syndrome).
- Infiltration of the dermis gives rise to non-pitting oedema (i.e. myxoedema) which is most marked in the skin of the hands, feet and eyelids. The resultant periorbital puffiness combined with facial pallor due to vasoconstriction and anemia, or a lemon-yellow tint to the skin due to carotenaemia, purplish lips and malar flush, the clinical diagnosis is simple.
- Most cases of hypothyroidism are not so obvious, however, tiredness, weight gain, depression or carpal tunnel syndrome, an opportunity for early treatment will be missed

Physical signs of hypothyroidism

include the following:

- Dull facial expression
- Coarse facial features
- Periorbital puffiness
- Weight gain
- Slowed speech and movements
- Dry skin
- Jaundice
- Pallor
- Coarse, brittle, straw-like hair
- Loss of scalp hair, axillary hair, pubic hair, or a combination
- Macroglossia
- Goiter (simple or nodular)
- Hoarseness
- Decreased systolic blood pressure and increased diastolic blood pressure
- Bradycardia
- Pericardial effusion
- Abdominal distention, ascites
- Hypothermia (only in severe hypothyroid states)
- Nonpitting edema (myxedema)
- Pitting edema of lower extremities
- Hyporeflexia with delayed relaxation, ataxia, or both

Investigations

- Primary hypothyroidism resulting from an intrinsic disorder of the thyroid gland, serum T4 is low and TSH elevated, usually in excess of 20 mU/l. Serum T3 concentrations do not discriminate reliably between euthyroid and hypothyroid patients and should not be measured.
- - In the rare secondary hypothyroidism there is atrophy of normal thyroid gland caused by failure of TSH secretion in a patient with hypothalamic or anterior pituitary disease, e.g. pituitary macroadenoma. Serum T4 is low but TSH may be low, normal or even slightly elevated .
- -In severe prolonged hypothyroidism the electrocardiogram classically demonstrates sinus bradycardia with low voltage complexes and ST segment and T wave abnormalities.
- Measurement of thyroid peroxidase antibodies is helpful, but further investigations are rarely required
- Other investigations : CBC , Lipid profile ,ECG, Cx ray , Echo study

Abnormalities in the complete blood count and metabolic profile that may be found in patients with hypothyroidism :

- Anemia (megaloblastic anemia)
- Dilutional hyponatremia
- Hyperlipidemia
- Reversible increases in creatinine
- Elevations in transaminases and creatinine kinase

Management

- Most patients will require life-long thyroxine therapy. It is customary to start slowly and a dose of 50 µg per day should be given for 3 weeks, increasing thereafter to 100 µg per day for a further 3 weeks and finally to a maintenance dose, usually 100-150 µg per day.

- Thyroxine has a half-life of 7 days so it should always be taken as a single daily dose and at least 6 weeks should pass before repeating thyroid function tests and adjusting the dose.
- Patients feel better within 2-3 weeks. Reduction in weight and periorbital puffiness occurs quickly, but the restoration of skin and hair texture and resolution of any effusions may take 3-6 months.
- -The correct dose of thyroxine is that which restores serum TSH to within the reference range. To achieve this, serum T4 will usually be in the upper part of the normal range or even slightly raised
- - Some patients remain symptomatic despite normalisation of TSH and may wish to take extra thyroxine which suppresses TSH values. However, there is evidence that suppressed TSH is a risk factor for osteoporosis and atrial fibrillation (; subclinical thyrotoxicosis) so this approach cannot be recommended .
- It is important to measure thyroid function every 1-2 years

Thyroxine replacement in ischaemic heart disease

- Hypothyroidism and IHD are both common, sometimes occur together.
- Although angina may remain unchanged in severity or disappear with restoration of metabolic rate, exacerbation of myocardial ischaemia, infarction and sudden death are well-recognised.
- In patients with known IHD , thyroxine should be introduced at low dose and increased very slowly under specialist supervision.
- Approximately 40% of patients with angina cannot tolerate full replacement therapy despite the use of β-blockers and vasodilators; coronary artery surgery or balloon angioplasty can be performed safely in such patients and, if successful, allow full replacement dosage of thyroxine in the majority

Hypothyroidism in pregnancy

- Most pregnant women with primary hypothyroidism require an increase in the dose of thyroxine of 50 μg daily to maintain normal TSH levels. This may reflect increased metabolism of thyroxine by the placenta and increased serum thyroxine-binding globulin during pregnancy, resulting in an increase in the total thyroid hormone pool to maintain the same free T4 and T3 concentrations.
- Serum TSH and free T4 should be measured during each trimester and the dose of thyroxine adjusted to maintain a normal TSH

EFFECTS OF HYPOTHYROIDISM IN PREGNANCY

- On mother :Anemia and CHF, Pre-eclampsia , Post partum hemorrhage, Myopathy,
- On fetal :Cognitive impairment, Congenital Hypothyroidism, Hyperbilirubinemia. Respiratory distress

Myxoedema coma

- Myxoedema coma is a medical emergency and treatment must begin before biochemical confirmation of the diagnosis.

- This is a rare presentation in which there is a depressed level of consciousness, usually in an elderly patient. Core Body temperature may be as low as 25°C, convulsions are not uncommon.
- The mortality rate is 50% and survival depends upon early recognition and treatment of hypothyroidism and other factors, e.g. drugs such as phenothiazines, cardiac failure, pneumonia, dilutional hyponatraemia and respiratory failure.
- Thyroxine is not available for parenteral use so triiodothyronine is given as an intravenous bolus of 20 μg followed by 20 μg 8-hourly. In survivors there is a rise in body temperature within 24 hours and, after 48-72 hours, it is usually possible to substitute oral thyroxine in a dose of 50 μg per day.
- Unless it is apparent that the patient has primary hypothyroidism, e.g. thyroidectomy scar or goitre, the thyroid failure should be assumed to be secondary and treatment given with hydrocortisone 100 mg i.m. 8-hourly.
- Other measures include slow rewarming, cautious use of intravenous fluids, broad-spectrum antibiotics and high-flow oxygen. Occasionally, assisted ventilation may be necessary.

ASYMPTOMATIC ABNORMAL THYROID FUNCTION TEST RESULTS

- One of the most common problems in medical practice is how to manage patients with abnormal thyroid function test results who have no obvious signs or symptoms of thyroid disease.
- Subclinical thyrotoxicosis
- Subclinical hypothyroidism
- Non-thyroidal illness ('sick euthyroidism)

Subclinical thyrotoxicosis

- TSH is undetectable and the serum T3 and T4 lie in the upper parts of their respective reference ranges.
- This combination is most often found in older patients with multinodular goitre.
- These patients are at increased risk of atrial fibrillation and osteoporosis and hence such patients have mild thyrotoxicosis and require therapy, usually with 131I.
  - Annual review is essential as the conversion rate to overt thyrotoxicosis with elevated T4 and/or T3 concentrations is 5% each year .

Subclinical hypothyroidism

- TSH is raised and the serum T3 and T4 concentrations are usually in the lower part of their respective reference ranges.
- It may persist for many years, although there is a risk of progression to overt thyroid failure, particularly if antibodies to thyroid peroxidase are present in the serum or if the TSH rises above 10 mU/l.
- In patients with non-specific symptoms a trial of thyroxine therapy may be appropriate. In those with positive autoantibodies or TSH > 10 mU/l it is better to treat the thyroid failure early rather than risk of subsequent presentation with profound hypothyroidism.
- Thyroxine should be given in a dose sufficient to restore the serum TSH concentration to normal

Non-thyroidal illness (sick euthyroidism)

- In patients with systemic illness (e.g. myocardial infarction, pneumonia, Liver Disease ,CKD) there is decreased peripheral conversion of T4 to T3 and alterations of binding proteins and their affinity for thyroid hormones. Elevated reverse triiodothyronine (rT3)which is metabolically inactive.
- Serum TSH may be subnormal as a result of the illness itself or the use of drugs such as dopamine or corticosteroids.
- The most common combination is a low serum TSH, raised T4 and normal or low T3, high rT3 .But many patterns of thyroid function tests can be seen. Usually normalizes as the underlying illness recovers.
- Biochemical assessment of thyroid function should not be undertaken in patients with non-thyroidal illness, unless there is good evidence of concomitant thyroid disease, e.g. goitre, exophthalmos.
- Treatment with Thyroid Hormone Replacement is controversial.

Solitary thyroid nodule

- It is important to determine whether the nodule is benign, e.g. cyst or colloid nodule, or malignant.
- It is rarely possible to make this distinction on clinical grounds alone.
- A solitary nodule presenting in childhood or adolescence, particularly if there is a past history of head and neck irradiation, or presenting in the elderly should raise the suspicion of a primary thyroid malignancy .
- Very occasionally, a secondary deposit from a renal, breast or lung carcinoma presents as a painful, rapidly growing solitary thyroid nodule.

Investigations :

- T3, T4 and TSH should be measured in all patients with a solitary thyroid nodule. The finding of undetectable TSH is very suggestive of an autonomously functioning thyroid follicular adenoma.
- For euthyroid patients, the most useful investigation is fine needle aspiration of the nodule.. Aspiration may be therapeutic in the small proportion of patients in whom the swelling is a pure cyst, recurrence is an indication for surgery.
- Cytological examination will differentiate benign (80%) from suspicious or definitely malignant nodules (20%) .
- The limitations of fine needle aspiration are that it cannot differentiate between follicular adenoma and carcinoma.

Rx:

- Solitary nodules with a solid component in which cytology either is inconclusive or shows malignant cells are treated by surgical excision. ---Those in which malignancy is confirmed by formal histology are then treated.
- Benign lesions are sometimes excised, e.g. if they are growing, but the majority of patients can be reassured

THYROID NEOPLASIA

- Primary thyroid malignancy is rare, accounting for less than 1% of all carcinomas, ,
- It can be classified according to the cell type of origin. More common in women than men

Papillary carcinoma

This is the most common of the malignant thyroid tumours and accounts for 90% of irradiation-induced thyroid cancer.

It may be multifocal and spread is to regional lymph nodes. Some patients present with cervical lymphadenopathy and no apparent thyroid enlargement; in such instances, the primary lesion may be less than 10 mm in diameter.

Follicular carcinoma

This is always a single encapsulated lesion. Spread to cervical lymph nodes is rare. Metastases are blood-borne and are most often found in bone, lungs and brain.

Management:

This is usually by total thyroidectomy followed by a large dose of 131I in order to ablate any remaining thyroid tissue, normal or malignant.

Thereafter, long-term treatment with thyroxine in a dose sufficient to suppress TSH (usually 150-200 μg daily) is important, as thyroid carcinomas is TSH-dependent.

Follow-up is by measurement of serum thyroglobulin, which should be undetectable in patients whose normal thyroid has been ablated and who are taking a suppressive dose of thyroxine.

Detectable thyroglobulin is suggestive of tumour recurrence or metastases, which may respond to further radio-iodine therapy.

Prognosis

Most patients have an excellent prognosis when treated appropriately.

Those under 50 years of age with papillary carcinoma can anticipate a near-normal life expectancy if the tumor is less than 2 cm in diameter, confined to the thyroid and cervical nodes, and of low-grade malignancy.

Even for patients with distant metastases at presentation, the 10-year survival is approximately 40%.

TUMOUR OF THYROID GLAND

RELATIVE INCIDENCE	PERCENTAGE
PAPILLARY CARCINOMA	60
FOLLICULAR CARCINOMA	20
ANAPLASTIC CARCINOMA	10
MEDULLARY CARCINOMA	5
MALIGNANAT LYMPHOMA	5

ANAPLASTIC CARCINOMA AND LYMPHOMA

These two conditions are difficult to distinguish clinically.

-Patients are usually elderly women.

-The goitre is hard and symmetrical. There is usually stridor due to tracheal compression and hoarseness due to recurrent laryngeal nerve palsy.

There is no effective treatment of anaplastic carcinoma, although radiotherapy may afford temporary relief of mediastinal compression.

-The prognosis for lymphoma, which may arise from pre-existing Hashimoto's thyroiditis, is better. External irradiation often produces dramatic goitre shrinkage

MEDULLARY CARCINOMA

Medullary carcinoma of the thyroid (MTC) accounts for 5% of thyroid cancer. MTC arises from the parafollicular C cells of the thyroid, which do not accumulate radioiodine, and it secretes calcitonin ,Sporadic, or isolated, MTC accounts for 75% of cases and the remaining 25% are part of multiple endocrine neoplasia type 2 (MEN2)

- In addition to calcitonin, the tumour may secrete 5-hydroxytryptamine (5-HT, serotonin), ACTH and prostaglandins..

-Patients usually present in middle age with a firm thyroid mass. Cervical lymphadenopathy is common, but distant metastases are rare initially.

-Serum calcitonin levels are raised and are useful in monitoring response to treatment.

May associated with decrease in calcium serum levels.

-Treatment is by total thyroidectomy with removal of affected cervical nodes.

-Since the C cells do not concentrate iodine, there is no role for 131I therapy.

-Prognosis is very variable, some patients surviving 20 years or more and others less than 1 year.

RIEDEL'S THYROIDITIS

-This is not a form of thyroid cancer, but the presentation is similar and the differentiation can usually only be made by thyroid biopsy.

-It is a rare condition of unknown aetiology in which there is extensive infiltration of the thyroid and surrounding structures with fibrous tissue.

-There may be associated mediastinal and retroperitoneal fibrosis.

-Presentation is with a slow-growing goitre which is irregular and stony-hard. There is usually tracheal and oesophageal compression necessitating partial thyroidectomy.

-Other recognised complications include recurrent laryngeal nerve palsy, hypoparathyroidism and eventually hypothyroid