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A Case Series

Diverse Manifestation of Hypothyroidism: A Case Series Study

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Abstract

Hypothyroidism is a condition in which thyroid gland does not produce enough thyroid hormones. Thyroid irregularities adversely affect the overall health of the affected person. Even though physical examination helps to suspect hypothyroidism clinically, only advanced laboratory technique can accurately confirm it. In this case series we report three hypothyroidism cases which give a broad view of manifestation of hypothyroidism and its clinical associations. Early diagnosis and prompt treatment can prevent, detect, or treat hypothyroidism and it will improve the quality of life.

Keywords: Acquired hypothyroidism, Cholesteryl ester transfer protein, Cretinism, Hypothyroidism, Hypothalamic-pituitary disease, Myxedema coma, OSA

Introduction

Hypothyroidism has become common endocrine disorder over the last few years globally. It is a condition in which thyroid gland does not produce enough thyroid hormones. Causes of hypothyroidism can be categorized into two [1] congenital cases and [2] acquired causes. Causes for congenital hypothyroidism include hormonal defect and thyroid dysgenesis. Symptoms of congenital hypothyroidism include decreased activity, intolerance to cold temperatures, Gaining weight, increased sleep, feeding difficulty and prolonged jaundice. Acquired hypothyroidism happens due to hormonal resistance or autoimmunity. It can also be result of thyroid surgery or ingestion of anti-thyroid medications.

Thyroid irregularities adversely affect the overall health of the affected person. Hypothyroidism manifest may be missed due to its rare presentation, therefore even subclinical hypothyroidism needs special attention. Even though physical examination helps to suspect hypothyroidism clinically, only advanced laboratory technique can accurately confirm it. Tests for hypothyroidism include blood tests and imaging tests.

Complications of hypothyroidism include goiter, heart problem, infertility and metal health issues. Early treatment and medications in correct doses can prevent patient with hypothyroidism even from life threatening complications.

In this study we report three hypothyroidism cases which give a broad view of manifestation of hypothyroidism and its clinical associations. So early diagnosis and prompt treatment can prevent, detect, or treat hypothyroidism and it will improve the quality of life.

Clinical Features

Clinical manifestations of hypothyroidism may be influenced by factors such as coexisting non thyroidal illness. If hypothyroidism is caused by hypothalamic-pituitary disease, the manifestations of associated endocrine deficiencies such as hypogonadism and adrenal insufficiency may mask the manifestations of hypothyroidism. History of thyroid dysfunction or thyroid surgery and also previous medication provide manifestations of hypothyroidism.

Symptoms of hypothyroidism includes lethargy, dryness of skin, hair loss, cold intolerane, confusion, constipation, weight gain, hoarseness of voice and amenorrhea. Cold clammy extremities, puffiness of face, bradycardia, delayed tendon reflex and peripheral edema are common signs appear during examination.

Etiology

Hypothyroidism can be classified into two (1) Primary hypothyroidism and (2) Secondary hypothyroidism. Hypothyroidism can be caused by the thyroid itself is called primary hypothyroidism, or by the malfunction of the pituitary gland or hypothalamus is called secondary hypothyroidism. Primary hypothyroidism can be congenital (Hypoplasia & mal-descent of thyroid and Familial enzyme defects) or acquired through iodine deficiency or autoimmunity. Whereas, secondary hypothyroidism can be due to hypopituitarism. Occurrence of hyperthyroidism and /or hypothyroidism during the postpartum period in women who were euthryroid during pregnancy is called Post-partum thyroiditis. Subclinical hypothyroidism is a condition in which peripheral thyroid hormone levels are within normal range but TSH levels are mildly elevated. Patient who are in high risk group with subclinical hypothyroidism should be treated timely.

Hypothyroidism should also be suspected with association of other comorbid conditions like autoimmune diseases (diabetes mellitus, Rheumatoid arthritis, sjogrens syndrome) pernicious anemia and addison disease [18]. It should be screened for multiorgan involvement such as in Pedred and Schimdt syndrome (PGS1).

Lab / Imaging

In hypothyroidism, T3 and T4 are low and reciprocally TSH will be high. Deranged lipid profile and transaminitis are associated findings of hypothyroidism. ECG usually shows low voltage and bradycardia. In hypothyroidism, cardiomegaly and pleural effusion can be diagnosed by X-ray. Limb X ray can facilitate the diagnostic of delayed bone age or epiphyseal dysgenesis. Anti-TPO antibody can have prognostic significance [19]. Thyroid radio-isotope scan, ultrasound and CT /MRI scan has its own indication for detailed thyroid evaluation.

Treatment

One of the causes for hypothyroidism is iodine deficiency and it is most common preventable cause of mental retardation in children as well. Daily iodine requirement is around150- 200mcg. Treatment for hypothyroidism involves the use of levothyroxine daily. This oral medication restores adequate hormone levels. It also reversing the signs and symptoms of hypothyroidism. Lifelong levothyroxine replacement therapy is very affordable treatment option to improve hypothyroidism symptoms. Dose calculated as 1.6 mcg/kg/day for normal population and upto 2.2 mcg/kg /day for pregnant women. Targeted TSH value ranges should be between 0.5 to 5 mU/L and for pregnant women stricter control is advisable with TSH value from 0.2 to 3

mU/L for reducing the risk of pre-eclampsia and pre-term birth. Cardiac patients shall start with minimal dose possible and increase it gradually and appropriately.

Urgent treatment is required for linear growth due to hypothyroidism. Early diagnosis and treatment hypothyroidism is crucial for mental and intellectual development. Treatment for hypothyroidism also helps by preventing associated complications and negative effects on other organs. It helps to control total cholesterol, triglyceride and low density lipoproteins. Levothyroxine is effective for hypothyroidism, additionally decreased carotid intima media thickening was observed in patients after long-term levothyroxine treatment [20].Preventing precipitating factors like infection, trauma, stroke, hemorrhage and avoiding use of diuretic,–can minimise risk of myxedema coma in background of hypothyroidism. High dose levothyroxine, steroids and volume management are available treatment modality for myxedema coma.

Treatment of myxedema coma involves ICU admission for close monitoring, high doses of levothyroxine (300-500mcg), triiodothyronine (30-50mcg IV), antibiotics (for underlying infection), Oxygen supplement, IV hydrocortisone, passive warming, careful volume management, adequate glycemic control and ventilator support if required.After initiation of therapy or dosage change there shall be a follow up of 6 to 8 weeks for monitoring clinical progress and hormones level (TSH levels).

First Case:

A 40 year old gentleman attended the outpatient department with complaint of facial puffiness and generalized anasarca, which were progressively increased over last three months. The patient also noticed that he gained weight over last few months. He complained of easy fatigability and breathlessness on walking for few meters. Occasionally climbing 2 flights of stairs he had chest discomfort which subsides spontaneously. Snoring by patient at night was also confirmed.

On physical examination bilateral pedal edema and abdominal distension were observed, body mass index (BMI) was 28 Kg/m2, however bradycardia and blood pressure were within normal range (120/70 mmHg). There were no pallor, icterus or clubbing.

After admission, further investigation suggested very high TSH (383.3McU/ml) and deranged lipids (Triglyceride 2869mg/dl, total cholesterol -1113mg/dl). However complete blood count (CBC), random blood sugar, liver and renal profile and serum cortisol level were within normal range.

Image 1: Pinkish hue of collected blood sample

ECG demonstrated low amplitude waves in all leads without any ischemic changes, 2dEcho was suggestive of concentric Left ventricular hypertrophy (LVH) with global hypokinesia. Chest x-ray was within normal range.Patient was treated for severe hypothyroidism and associated dyslipidemia, congestive heart failure and obstructive sleep Apnea. Patient responded positively to high dose thyroxine (starting 300mcg then tapered), high dose statins and cardiac medications. He was referred to Pulmonologist for sleep study and management of Obstructive sleep apnea (OSA).

Second Case:

A 65-year-old elderly male was admitted in emergency department. The Patient was drowsy at the time of admission. Patient's decreased daily activities and low urine output were also reported. He had a history of hypertension and hypothyroidism, but his medication was irregular. It was reported that, pedal edema was developed 15 days ago and he was suffering from low grade fever for last 5 days. On examination, it was observed that the patient was drowsy, however he was responding to pain stimuli. He had tachycardia with feeble pulse and blood pressure of 80/60 mmHg. Temperature was recorded as 99 F. Laboratory tests showed anemia with high leucocyte counts and high serum creatinine (3.9mg/dl). serum TSH was very high (383 mU/L) and FT4 was 0.03 ng/dl , Serum sodium was 132 mEq/L , serum potassium was 4.2 mmol/L , random blood glucose sugar was 143mmol/LUrine routine showed 60 – 80 pus cells hence urine culture was sent which turned out profuse E coli growth.

Other workup including ECG was normal; chest x ray showed blunting of left costophrenic angle. Therefore he was diagnosed with severe hypothyroidism with Urosepsis precipitating Myxedema Coma. He was treated with injectable antibiotics and IV fluids, ionotropes along with IV steroids and high dose thyroxine (300mcg). The patient responded positively to the treatment and recovered well.

Third Case:

A 36-year-old woman came with menorrhagia & generalized tiredness for 10 days. Loss of appetite was also noticed. Yellowish discoloration of her skin was also noticed. Patient had a history of hypothyroidism in childhood for which she took medication for few months. Her height was 98cm and weight was 18 kg. On examination, it was observed that she had pallor and yellowish tinge of skin. She had coarse facies and features of Dwarfism.

Oral examination showed that she has Macroglossia. Laboratory investigations confirmed high serum TSH -120 mU/L (normal 0.5- 5.5), low T3 – 0.33 (normal 1.2-2.4), T4 -1.1 µg/dL (normal 2.8-11.4) with negative anti thyroid peroxidase Antibody and anti-thyroglobulin antibodies. CPK total (1842 U/L) was very high and she also had very high leucocyte counts and low hemoglobin of 7 gm. /dl.Ultrasonography of neck showed normal thyroid gland. Chest x ray showed dextrocardia. Congenital hypothyroidism was diagnosed, which leads to dwarfism (infantile proportion) and mental retardation. She was treated with IV iron supplements and high dose of thyroxine

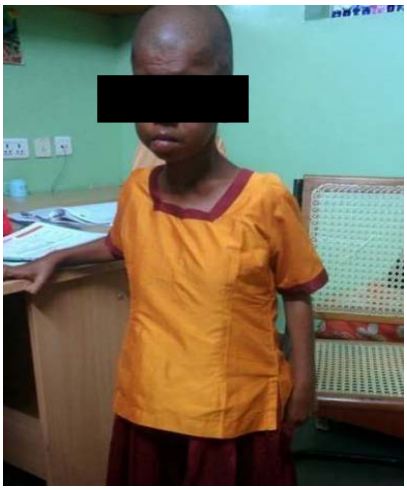

Image 2: dwarfism due to thyroid insufficiency (cretin)

Discussion:

Hypothyroidism is a condition in which thyroid gland does not produce enough thyroid hormones. It has varied manifestation and should not be ignored. It may lead to systemic complications. If it is not treated timely, it can cause a lot of health problems including obesity, joint pain, infertility and heart disease. Early diagnosis and timely treatment can prevent, detect, or treat hypothyroidism and it will improve the quality of life.

First patient had typical symptoms of hypothyroidism. Diagnosis reports for many years were not available. He had high BMI, Anasarca and OSA. Thyroid related hypertriglyceridemia was also developed in his case due to which his blood sample had slightly pinkish tinge.

Hypothyroidism is associated with dyslipidemia as thyroid hormone stimulates HMG-CoA reductase enzyme. HMG-CoA reductase enzyme is the rate limiting enzyme for cholesterol biosynthesis [1]. Decreased thyroid hormone leads to high triglycerides and increased LDL-C levels [2], additionally low hepatic lipase is likely to affect VLDL catabolism and increase non-HDL component of blood [3]. Thyroid hypo-function increases total cholesterol, LDL and triglycerides but it rarely affects HDL level. High VLDL and chylomicrons are converted to LDL through lipoprotein lipase, which lead to hypertriglyceridemia [4].T3 and T4 act on lipoprotein lipase which converts triglycerides and VLDL to LDL [5]. It also helps to decrease Triglycerides (TG) by converting it to HDL. Thyroid hormones also stimulate CETP (Cholesteryl ester transfer protein) which help interconversion of HDL and non-HDL [6]. T3 and T4 decreases oxidation of LDL by inducing more LDL receptors and LDL expression in peripheral cells and liver, which stops macrophage to transform into foam cell, due to which atherogenesis hinders[7]. T3 and T4 also act on PCSK9 causing dysfunction of LDL receptor and elevate blood LDL levels [8].Thyroid hormones increases bile acid which in turn increase bile synthesis through 7-alpha hydroxylase enzyme [9].All this are mechanism by which hypertriglyceridemia predominant in hypothyroidism.

OSA in hypothyroidism occurs due to muco-protein deposition in upper airways. This deposition decreases neural output which weakens muscular tone leading to abnormalities in ventilatory control [10, 11].Mechanism of bradycardia in hypothyroidism is unknown, potential cause include altered autonomic nerve activity or intrinsic remodeling of sinus node (disturbing ion channel). Low T3 affect cardiac function by vasoconstriction with decreased ionotropism and

chronotropism [12]. Severe hypothyroidism cause decrease myocardial contractility and reduced cardiac output which leads to hypotension. Conduction abnormalities like flattened T wave, low voltage, bundle branch blocks and complete heart blocks are commonly seen on ECG [13].Patient was also having cardiac hypo-function as combine effect of high viscosity of blood, decreased cardiac contractility and high pulmonary pressure due to OSA.

Treating the patient with levothyroxine, retrospectively proved that in this case hypothyroidism was responsible for most of symptoms.

In the second case the patient has known hypertension and was on irregular treatment, hence he was a high risk patient. He had urinary tract infection which triggered underlying severe hypothyroidism and leads the patient to myxedema coma. Myxedema is extreme manifestation of severe hypothyroidism. It triggers deterioration of mental status which may lead to coma. Symptoms of myxedema includes hypothermia, hypotension and hypoventilation. Investigation wise elevated creatine phosphokinase (CPK), hyperlipidemia, hypoglycemia and transaminitis can be present in such cases. Also low neurovascular sensitivity to hypoxia and hypercapnia with respiratory muscle dysfunction, obesity, pleural effusions and reduced lung volume can lead to hypoventilation [14]. In a study by V Mathew et al demonstrated that macroglossia and myxedema of nasopharynx and larynx increases frequency of aspiration pneumonia in specific population [15]. Another study by S Khalid et al showed that altered vascular permeability leads to effusion and anasarca. Glycosaminoglycan deposition also plays an important role in formation of anasarca [16].Decreased gluconeogenesis, adrenal insufficiency and occult infection can trigger hypoxemia, hyponatremia and hypoglycemia which ultimately leads to myxedema coma.

Third case was reported with congenital hypothyroidism. The patient was not treated well with thyroid mediction in her childhood which caused limited mental as well as physical growth. Stunted growth and mental subnormalities are well seen in cretins. Lack of awareness regarding condition and lack of treatment in early years lead to cretinism. Carotenemia in hypothyroidism occurs due to decrease conversion of carotene into vitamin A [17].Although we treated patient with thyroxine supplement, she had symptomatic improvement in lethargy and return of appetite.

Conclusion:

Thyroid irregularities adversely affect the overall health of the affected person. Hypothyroidism manifest may be missed due to its rare presentation, therefore even subclinical hypothyroidism needs special attention. Even though broad clinical manifestations of hypothyroidism helps to suspect hypothyroidism, only advanced laboratory technique can accurately confirm it. In this study we report three hypothyroidism cases which give a broad view of manifestation of hypothyroidism and its clinical associations. Early diagnosis and prompt treatment can prevent, detect, or treat hypothyroidism and it will improve the quality of life. High risk population including elderly, patient with OSA, psychiatric illness, dyslipidemia, post radiation therapy and patients having family history and associated other autoimmune diseases should be screened and also suspicion of thyroid abnormalities should be raised upon identifying manifestations of hypothyroidism.

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