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HASHIMOTO'S THYROIDITIS INSTIGATES MYXEDEMA PSYCHOSIS – A REVIEW

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Abstract:
Thyroid dysfunction is one of the universal commonest endocrine disorders. According to a recent projection, it has been estimated that about 42 million people in India suffering from thyroid diseases. Province of thyroid is essential in the regulation of metabolic process throughout the body by secretion of their respective hormones. A healthy thyroid plays a vital part in brain chemistry. Inadequate thyroid function has been long associated with mainly with psychiatric symptoms. Decompensation into myxedema coma occurs when the hypothyroid patient's homeostatic mechanisms are disrupted only when the patient has begun to decompensate do these neurovascular mechanisms fail. L-triiodothyronine role in central nervous system, specifically regulating of glutamate uptake and consequently by promoting neuronal development and neuro protection, so Hashimoto's thyroiditis is a rare condition associated mainly with neurological symptoms it has been recognized that thyroid disease may give rise to psychiatric disorders that can be corrected by reestablishment of normal thyroid function. Thyroid function should be monitored periodically by following the guidelines to detect hypothyroidism in all children and adolescents to prevent development of psychiatric symptoms.

Keywords: *Hypothyroid, Hashimoto's thyroiditis, Myxedema psychosis, Selnocysteine enzyme.*

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INTRODUCTION:

History of thyroid and psychiatric disorders

In 1874, Queen Victoria's court physician Sir William Withey Gull writes down the very first description of the clinical features of adult hypothyroidism (1,2). Gull describe that "hypothyroidism" was termed myxoedema or myxedema signify "mucus" & edema signify "swelling" from ancient Greek in 1878 by William Ord(2,3). In 1888, hypothyroidism was first related to psychosis by the Committee on Myxoedema of the Clinical Society of London. Based on 198 patients with myxoedema, the committee reported half the cases presented with delusions and hallucinations, mainly in cases where the disease was advanced. They also revealed that mental disturbances including acute or chronic mania, dementia, melancholia, suspicion, and agoraphobia (4,5). It 1949 Asher initiated the term "myxoedema madness". Overall fourteen cases of myxoedema patients revealed psychosis "madness", ten admitted to mental observation wards with non-myxoedema diagnoses.

Thyroid gland

Thyroid gland is a small, butterfly-shaped gland responsible for the production of T4 L-thyroxine (tetraiodothyronine) and T3 L-triiodothyronine, which are requisite for the regulation of metabolic process all over the body. Iodine is an essential component of the thyroid hormones comprising 65% of T4's weight and 58% of T3's. Inadequate amount of iodine lead to deficient amount of thyroid production, increased TSH secretion and thyroid stimulation and goiter in an attempt to compensate (6). A healthy thyroid plays a vital part in brain chemistry, but thyroid problems don't just cause physical symptoms; they can make you feel mental, too (7) through a variety of mechanisms: modulation of gene expression of several group of proteins, some of them with known physiopathological indication in mood disorders and the influence on serotonin and noradrenergic neurotransmission, known to be one of the mode of action of anti depressant (8). Hypothyroidism is most common abnormality of thyroid function in children and adolescents. The prevalence of thyroid dysfunction between 11 to 18 years is 1% and the most common cause of acquired hypothyroidism is chronic lymphocytic throiditis (hashmoto's thyroiditis), with a 2:1 female predominance and second endemic goiter due to iodine deficiency.

Psychosis

Psychosis is a condition that acts on the way that brain processes information. It causes to lose touch with reality. Psychosis is a symptom, not an illness. Early intervention could stop a psychosis-related condition from worsening (9). Young people are mostly to get it. Even before what doctors call the first episode of psychosis (FEP), you may show modest switch in the way you act or think called the prodromal period. Symptoms of a psychotic episode are Hallucinations, Delusions. The model course of a psychotic episode (fig 1) can be thought of as having three phases: Prodrome Phase, Acute Phase, and Recovery Phase (10, 11). It is an autoimmune disease in which the thyroid gland is infiltrated by lymphocytes which charge and pull down the functioning of thyroid cells called thyrocytes (26). Myxedema refers to a severe form of hypothyroidism than can happen when the condition is left untreated or is not treated adequately (9, 26). Distribution is four times more common in women than in men; 80 percent of case of myxedema coma occurs in females. Decompensation into myxedema coma occurs when the hypothyroid patient's homeostatic mechanisms are disrupted (12). Some of the most common precipitating factors include infection, particularly pneumonia and urosepsis, and certain medication (amiodarone, anesthesia, barbiturates and β blockers). Only when the patient has begun to decompensate do these neurovascular mechanisms fail.

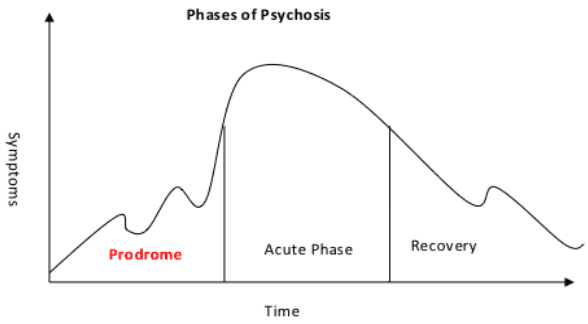

figure 1: Phase of Psychosis

THYROIDITIS CAUSE OF MYXEDOMA PSYCHOSIS

The connection between the action of thyroid hormone and neuropsychiatric function is intricate, and some mechanisms of thyroid hormone hold into brain tissues, hormone operates, and impacts on neurotransmitter generation have been recognized. Neuropsychiatric manifestations activated by thyroid dysfunction likely respond well to reestablishment of the euthyroid state. Thyroid hormones have been shown to regulate the levels of dopamine receptors and the activity of tyrosine hydroxylase, the rate- limiting enzyme of cathecolaminergic pathway. Moreover, it has been suggested that dopamine may be inhibitory of TSH secretion, as treatment with dopamine blockers lead to increase in TSH level or to subclinical hypothyroidism, and that hypothyroidism can lead to increased dopamine receptor sensitivity (13, 14). The rise in dopaminergic activity was hypothesized to influence the pituitary secretion, and decreased β adregenic activity was deducing as consequence of reduced serum TSH concentration. The role of T3 in the CNS, specifically on regulation of glutamate uptake, showed an increased neuronal viability against toxicity when neurons were cultured in the presence of T3-treated astrocytes. Also T3 is efficient of managing extracellular glutamate levels by modulating the astrocytic glutamate transporters and accordingly by promoting neuronal development and neuroprotection (19).

Deiodinases are selenocysteine enzymes that eliminate iodine molecules from thyroid hormones. Three types of deiodinases have been recognized (24, 33). Deiodinase 1 (D1) is found mostly in liver and kidney, because deiodinase 2 (D2) is found in adipose tissue, brain, and pituitary gland. Both D1 and D2 plays role in the conversion of T4 to T3. Deiodinase 3 (D3) inactivates T4 by altering it into reverse T3 and converts T3 to diiodothyronine (T2). Brain concludes most of its T3 from the conversion of T4 to T3 from D2 enzyme activity. Single-nucleotide polymorphisms (SNPs) have been recognized in the deiodinase genes. One such polymorphism identified is related to D2 coding and is cited as the Thr92Ala polymorphism. This SNP is seen often in various ethnic groups. This polymorphism has been delibrately for an association of any changes in well-being and neurocognitive functioning, as well as to certainlly identifies a preference for combined LT4 and LT3 therapy for treatment of hypothyroidism, with mixed results. Under hypothyroid conditions, it has been suggested that the D2 enzyme with this polymorphism may deiodinate less effectively and therefore shows diminished levels of local T3 production and, perhaps, an increased dependence on circulating T3 to maintain optimal brain T3 levels (37).

RESULTS AND DISCUSSION:

Treatment and Guidelines of myxedema coma is as follows (7):

- Intravenous (IV) LT4 at a dose of 4 µg/kg of lean body weight, or approximately 200-250 µg, as a bolus in a single or divided dose, depending on the patient's risk of cardiac disease
- After 24 hours, 100 µg LT4 IV, then 50 µg/day IV
- Stress doses of IV glucocorticoids
- Subsequent adjustment of the LT4 dose can be based on clinical and laboratory findings

Medication in the drug class thyroid products are used in the treatment of hypothyroidism (7):

- Levothyroxine (LT4) is normally considered to be the treatment of choice for patients with hypothyroidism.
- Liothyronine (LT3) is a synthetic form of the natural thyroid hormone (T3) converted from

T4. It is not intended for use as sole maintenance therapy, but in rare cases it can be used together with LT4 in small doses (5-15 µg/day).The recommended ratio of T4 to T3 is 10-14:1. T3 has a short duration of activity (half-life, 12-24 hours), which allows quick dosage adjustments in the event of over dosage.

Hypothetically, LT3 may be preferred when gastrointestinal (GI) absorption is defective 95% of this hormone is engaged, compared with 50-80% of T4 or if peripheral conversion is defaced. Dosage recommendations are for short-term use in special conditions (eg, myxedema coma), under the guidance of an endocrinologist. Dosage should be determined in consultation with an endocrinologist. Indian Thyroid Society (ITS) recommends screening of TSH levels in all Pregnancy Women at the time of their first visit, ideally during pre-pregnancy evaluation or as soon as pregnancy is confirmed Medical management: When and how to initiate Levothyroxine therapy and titration of dose When and how to administer Levothyroxine tablets specially in relation to meals Importance for regularity and Compliance.

CONCLUSION:

For more than 125 years it has been recognized that thyroid disease may give rise to psychiatric disorders that can be corrected by reestablishment of normal thyroid function. More than 60 years ago we know that patient with profound hypothyroidism may present with depressive psychosis individuals with positive antithyroid peroxide antibodies with symptoms of anxiety and depression more common than in control. Hashimoto's thyroiditis is a rare condition associated mainly with neurological symptoms. It contains an abundant amount of auto – antibodies in the blood. The natural course of juvenile autoimmune thyroiditis is quite variable, and thyroid function should be monitored periodically to detect hypothyroidism in all children and adolescents. With reports on glutamate and other endogenous excitatory aminoacids have ability to regulate the secretion of anterior piyuitary hormones as well as in the neuroendocraine regulation of hypothalamic – pituitary axis. deregulation of the pituitary-TH axis continue to be of interest given the interaction between the pituitary-thyroid axis and dopaminergic, serotonergic, glutamatergic and GABAergic systems, together relationship with myelination and proinflammatory response, which strongly implicated in myxedema madness. Finally the idendification of SNPs in genes coding for types 1 and 2 deiodinase as well as the organic anion – transporting polypeptide may be useful in predicting the degree of symptoms associated with thyroid dysfunction, and may be useful in predicting the response to various medication and combination when appropriately controlled prospective studies are completed in future.

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