

Case Report / Olgu Sunumu

Macro-TSH: Bir Tanı Zorluğu
Macro-TSH: A Diagnostic Dilemma

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Abstract: Macro-TSH, nadir görülen bir laboratuvar interferansı olup özellikle pediatrik hastalarda tanı açısından zorluklar oluşturur. Bu yazıda, hipotiroidizm belirtileri olmaksızın yüksek tiroid uyarıcı hormon (TSH) seviyeleriyle karakterize edilen makro-TSH'lı 5 yaşındaki bir erkek hastanın vakası sunulmaktadır. Normal serbest tiroksin (fT4) seviyelerine rağmen, klinik bulgular ile TSH seviyeleri arasındaki uyumsuzluk daha fazla araştırmayı gerektirmiştir. Polietilen glikol (PEG) ile işlenen serum örnekleri, TSH seviyelerinde belirgin bir azalma göstermiş ve makro-TSH varlığını doğrulamıştır. Bu vaka, TSH ve fT4 seviyeleri arasında uyumsuzluk olduğu durumlarda klinik ve laboratuvar bulgularının dikkatli bir şekilde değerlendirilmesinin önemini vurgulamaktadır. Makro-TSH'nin tanınması, gereksiz tetkik ve tedavilerin önlenmesine ve böylelikle hastaların yönetiminde iyileşmeye yol açabilir.

Keywords: Thyroid Stimulating Hormone, False Positive Reaction, Pituitary Adenoma

Özet: Macro-TSH, a rare laboratory interference, poses a diagnostic challenge, especially in pediatric patients. We present a case of a 5-year-old male patient with macroTSH, characterized by elevated thyroid-stimulating hormone (TSH) levels without symptoms of hypothyroidism. Despite normal free thyroxine (fT4) levels, the discrepancy between clinical findings and TSH levels prompted further investigation. Serum samples treated with polyethylene glycol (PEG) revealed a significant decrease in TSH levels, confirming the presence of macro-TSH. This case underscores the importance of clinical and laboratory findings in discordant TSH and fT4 levels. Recognition of macro-TSH can prevent unnecessary investigations and treatments, improving patient management.

Anahtar Kelimeler: Tiroid Uyarıcı Hormon, Yanlış Pozitif Reaksiyon, Hipofiz Adenomu

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1. Introduction

Thyroid-stimulating hormone (TSH) plays a crucial role in evaluating thyroid dysfunctions. When elevated TSH accompanies an average level of free thyroxine (fT4), it commonly indicates the existence of subclinical hypothyroidism. However, it can also, though infrequently, signal other conditions, including thyroid hormone resistance (Refetoff syndrome), biologically inactive TSH, laboratory interferences, and TSH-producing pituitary adenomas. Macro-TSH is a rare laboratory interference that can disrupt the measurement of TSH, leading to spuriously high results (1-3). In this study, we aim to underscore the significance of evaluating clinical and laboratory findings in cases where free thyroxine (fT4) values are discordant with thyroid stimulating hormone (TSH) levels. This approach helps prevent delays in diagnosing conditions such as macro-TSH, as observed in our case, and, more importantly, aids in avoiding unnecessary investigations and treatments.

2. Case Report

A neurosurgeon examined the 5-year-old male patient after imaging revealed a microadenoma in the pituitary gland. Further inquiry into the patient's medical history revealed that routine pre-school tests had shown elevated thyroid stimulating hormone (TSH) levels, which led to the initiation of L-thyroxine treatment. The patient had no significant prior medical history, and the family did not report any history of thyroid disorders. During the physical examination, the patient appeared healthy, conscious, and cooperative. His height measured 117 cm (standard deviation +1.3), and his body weight was 19 kg (standard deviation +0.11). Systemic examination revealed no additional pathologies, and the thyroid examination yielded expected results. Genital examination indicated a stretched penile length of 5 cm and bilateral testicular volumes of 2 ml. Complete blood count, kidney function tests, and transaminase levels were within normal ranges, and the patient did not present with any complaints or physical manifestations

suggestive of thyroid dysfunction. Laboratory analyses indicated free triiodothyronine levels of 4.1 pg/mL (within the normal range of 2.3-4.2), free thyroxine levels of 1.2 ng/dL (within the normal range of 0.88-1.3), and a significantly elevated TSH level of 53.4 μ IU/mL (outside the normal range of 0.63-4.82). We conducted these tests twice to validate the findings. The tests for anti-thyroglobulin antibodies, anti-thyroid peroxidase antibodies, and TSH receptor-activating antibodies all returned negative results. Although the patient was referred from an external center with a preliminary diagnosis of pituitary adenoma, we considered the anterior pituitary hormone measurements to be normal. When serum was combined with an equal volume of 25% polyethylene glycol (PEG) to address the discrepancy between high serum TSH levels and FT4, the γ -globulin fraction precipitated. Subsequently, the TSH concentration in the supernatant notably decreased from 53.4 μ U/mL to 1.2 μ U/mL (PEG precipitation rate: 97.8%).

3. Discussion

In this study, we present a rare case of macro-TSH in childhood, characterized by elevated TSH levels without symptoms of hypothyroidism, posing a diagnostic challenge in pediatric patients. Symptoms and signs of thyroid dysfunction, such as hyperthyroidism and hypothyroidism, often lack specificity and may be ambiguous or absent. The measurement of thyroid stimulating hormone (TSH), free thyroxine (fT4), and free triiodothyronine (fT3) is crucial for diagnosing overt and subclinical thyroid disorders. The assessment of serum thyroid-stimulating hormone (TSH) stands as a critical diagnostic measure in the assessment of thyroid disorders. When the fT4 level is within the normal range despite elevated TSH levels, we should consider the possibility of macro-TSH, which is an infrequent phenomenon, especially in children (4). Patients with macro-TSH typically exhibit elevated TSH levels, normal thyroid hormone levels, and a lack of clinical indications of

thyroid dysfunction. Although plasma TSH levels are frequently reported as significantly elevated, in certain instances, as observed in our patient, they may only be slightly raised (5,6).

The mechanisms of macro hormone production are influenced by various factors and result from the combination of hormones with immunoglobulins (Ig). Specifically, macro-TSH is formed when monomeric TSH, typically 28 kDa in its biologically active form, combines with IgG, leading to a substantial increase in molecular weight, approximately 150 kDa. This increased molecular weight significantly reduces the renal clearance of macro-TSH, allowing it to circulate in the bloodstream for a longer duration (7). However, it has also been demonstrated that macro-TSH may not only originate from IgG but also from IgA binding. For instance, in an asymptomatic Japanese patient, macro-TSH bound to IgA was identified. This finding suggests that in cases where there is a discrepancy between thyroid function test results and clinical symptoms, it is essential to consider that macro-TSH can be caused by both IgG and IgA binding (8). These mechanisms are crucial considerations in the diagnosis and management of macro hormone-related conditions.

Biochemically, macro-TSH resembles subclinical hypothyroidism and can result in inappropriate LT4 therapy. Likewise, our patient received treatment for hypothyroidism. Such cases, which typically do not respond to hypothyroidism treatment, are often diagnosed during further investigation due to unresponsiveness to treatment and laboratory-clinical incompatibility. After observing no response to hypothyroidism treatment, we conducted MRI imaging with the suspicion of a TSH-secreting adenoma. TSH-secreting adenoma in childhood is exceedingly rare.

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Although reported in a case report, this uncommon condition is more often seen in older age groups than in childhood. The microadenoma detected in our patient was deemed non-secretory. While different studies report various rates for childhood cases, they report microadenomas less frequently in children than in adults. Although Rathke's cleft cyst is the most common mass observed in the pediatric age group, the MRI appearance in our patient was indicative of a microadenoma. Surgical or medical intervention is typically not recommended managing such microadenomas. Instead, experts recommend follow-up without treatment as the most suitable approach in these cases (9).

Macrohormones have high molecular weight. Existing literature predominantly focuses on prolactin when discussing macrohormones. Polyethylene glycol (PEG) mediated precipitation is widely used to screen for macroprolactinemia. This method relies on measuring the recovery level of monomeric prolactin after PEG treatment. Macro-TSH, a rare phenomenon that has gained attention in recent years, is characterized by elevated levels of TSH, with no corresponding increase in thyroid hormones, and patients typically remain euthyroid, indicating minimal or negligible biological effects of macro-TSH (5,6,10). In our case, the TSH value measured after PEG was within normal limits.

4. Conclusion

Researchers rarely report macro-TSH in childhood. Recognizing this condition, especially when TSH levels do not align with the patient's clinical presentation, can help avoid unnecessary investigations and treatments.

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Ethics

Informed Consent: The authors declared that informed consent form was signed by the patient.

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