group are shown in Fig. 1. In those with CAD or MyD, cTnI was detectable in 69.2% of patients and undetectable in the remainder. In the control group (Con), cTnI was detectable in 26.2% and undetectable in 73.8% of the patients. Of the detectable values, 87.5% were ≤0.07 μg/L (the 99th percentile value) in the CAD and MyD groups; the remainder were between 0.07 and 0.1 μg/L (8.3%) or >0.1 μg/L (4.2%). In the control group, all detectable values were ≤0.07 μg/L. The ROC curve analysis suggested that a cTnI cutoff concentration of 0.02 μg/L best distinguished persons with ischemic (CAD) or nonischemic (MyD) myocardial impairment (area under the curve, 0.74; 95% confidence interval, 0.66–0.83) from those with milder disease. Regression analysis showed that the only variable that correlated with cTnI was left ventricular ejection fraction \( r^2 = 0.097; r = -0.311; P < 0.001 \). In all 12 patients with an ejection fraction <50%, cTnI concentrations were detectable [median (75th–25th percentiles), 0.045 (0.0275–0.06) μg/L].

Our data suggest a difference in cTnI concentrations between groups of cardiovascular outpatients with more severe disease compared with less severely affected patients. These differences are all below the 99th percentile of a reference interval. The mechanisms responsible for measurable cTnI values of this type are unclear. The group data are intriguing and suggest that when better assays permit evaluation of low values, there appears to be additional information that can be used to evaluate patients.

Fig. 1. cTnI values in the control group (Con; \( n = 42 \)), in patients with CAD (\( n = 80 \)) or noncoronary myocardial impairment (MyD; \( n = 24 \)), and in patients with CAD or MyD together (\( n = 104 \)). Boxplots are shown with medians (lines inside boxes), first and third quartiles (limits of boxes), and 1.5 interquartile ranges (whiskers). ● denote outlying points. Dashed lines indicate the limit of detection (line A), the 99th percentile (line B), and the decision limit based on the requirement of a CV <10% (line C).

References


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Response to Newman et al. (March 2006): Factitious Increase in Thyrotropin in a Neonate Caused by a Maternally Transmitted Interfering Substance

To the Editor:

Newman et al. (1) have described a factitious increase in thyrotropin in 2 infants and their mothers, detected by newborn screening using a blood-spot thyroid-stimulating hormone (TSH) assay. The authors do not positively identify the cause of this increase in TSH, but they describe its disappearance from one infant’s serum as consistent with an immunoglobulin. Most cases of a factitious increase in TSH in newborns are attributable to the presence in sera of heterophilic antibodies. Equipment manufacturers, to protect their assays from these effects, include non-immune serum or immunoglobulin in their reagents, giving a very low incidence of TSH increase. Newman et al. suggest that their case is unusual because no treatments were administered to the mother that would account for the increased TSH, and she had not been exposed to animals.

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A similar case of an infant and her mother was identified in the Wales congenital hypothyroid screening program (2). The infant’s blood-spot TSH was 104 mIU/L at 7 days after birth, and on recall 7 days later, her serum free thyroxine (FT4) was 14 pmol/L, and TSH was 48 mIU/L. Because of these discrepant results of FT4 and total T4 within the reference intervals with an increased TSH that appeared to increase on dilution, thyroid function tests were done on the mother. Maternal serum FT4 was 14 pmol/L, total T4 was 180 nmol/L, and TSH was 33.1 mIU/L, with all pituitary hormones within the reference intervals or at appropriate postpartum concentrations. TSH of the infant and maternal sera, measured after serial dilutions, showed nonparallelism, with reference TSH in both an RIA and an IRMA. Maternal TSH concentrations did not return to reference intervals with the addition of nonimmune sera. Purified IgG from the mother bound human but not bovine TSH, and this binding was inhibited by the addition of excess TSH. At age 7 months, the infant’s TSH concentrations were within the reference interval, whereas the mother’s TSH remained increased, and in 2 subsequent pregnancies, both infants had increased but factitious serum and blood-spot TSH concentrations. The cause of the increased TSH concentrations was concluded to be an IgG to TSH in the mother’s serum, which was acquired transplacentally by the infants.

Serum immunoglobulins that bind TSH have been described (3-10), but they are rare, and only 1 case report of an antibody binding to follicle-stimulating hormone has been documented (11). In contrast, IgG binding to prolactin (macroprolactin) is common and well described, accounting for up to 26% of all cases of hyperprolactinemia (12). The prevalence of macroprolactinemia depends on the assay system, with some having only low reactivity, whereas others have a much higher reactivity with prolactin. TSH complexes with IgG may be very rare or may go unidentified because of low reactivity in TSH assays. It is intriguing to speculate that the prevalence of these complexes is higher than is supposed, accounting for some cases of a typical FT4 with an increased TSH, so-called subclinical hypothyroidism. In a community study from the north of England, long-term follow-up over a period of 20 years of a cohort of randomly selected individuals revealed that the annual risk of developing hypothyroidism in women is 4.3% both when antithyroid antibodies are present and when TSH is increased (13). However, not all individuals with increased TSH develop hypothyroidism, and this group may include individuals who have TSH-IgG complexes in their sera. Thus, screening for TSH-IgG complexes in subclinical hypothyroid patients might be valuable.

In screening for congenital hypothyroidism by detecting factitious increases in TSH attributable to TSH-IgG complexes, heterophilic antibodies, or other immunoglobulin effects (14), it is imperative that in the follow-up of an increased blood-spot TSH, a serum sample from the mother be collected and analyzed at the same time as a sample from the infant (15) to detect any real, but transient, increase in TSH in the infant attributable to transplacentally acquired thyrotropin receptor-blocking antibody.

References


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False-Negative Pregnancy Test in Hydatidiform Mole

To the Editor:

A 16-year-old girl (gravida 0, para 0) presented to the emergency department with a 2-week history of nausea, vomiting, vaginal spotting, and lower leg edema. On examination we found a palpable lower abdominal mass. The patient acknowledged recent sexual activity but denied having any sexually transmitted diseases.