Can prolonged pregnancy complicate hypothyroidism?

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To The Editor: Women with primary hypothyroidism may have either oligo-, or amenorrhea, or menorrhagia. These menstrual changes often result in decreased fertility. If pregnancy does occur there is an increased likelihood for early abortion or premature labor [1]. Post term pregnancies (PP) have not been reported before. However, it has been hypothesized that prolonged pregnancy is a possible complication of hypothyroidism due to some sort of myometriopathy [2].

Case report
A pregnant Libyan patient, 37 years old, gravida 10, para 9 with a history of one previous caesarean section (because of antepartum hemorrhage), previously healthy and under regular antenatal follow up, presented on her 39th week of pregnancy with one month's history of gradually worsening lower limbs weakness and aching pain, which became worse in the last week.

On examination she was looking well with pink cheeks, the power at hips and knees was 4/5, both on flexion and extension with tenderness over the two quadriceps muscles and a delayed relaxation phase of the deep tendon jerks at the ankles. Gower's sign was positive. The power at the ankles and at the upper limbs was normal, the sensory examinations were also normal.

Laboratory findings: creatinine phosphokinase (CPK):82 U/L, S.Ca²+: 8.2 mg/dl, S.K+: 4.7mmol/L, alkaline phosphatase: 337U/L, thyroid stimulating hormone (TSH) >100 mIU/L (0.47-4.68 mIU/L), FT4: 7.9 pmol/L (12-22 pmol/L) FBS: 55mg/dl. The neck ultrasonography showed a normal size thyroid with low echogenesity, and a nine millimeters nodule at the left lobe. Anti thyroid peroxidase (anti-TPO) antibodies were >600 IU/ml.

Based on the above findings she was diagnosed as a case of hypothyroid myopathy and was started on 100ug L-thyroxin daily but after 3 weeks she was still having the same complaint with the same examination findings and she was already post term (42 weeks + 1 day), and this was the first time for her to have a prolonged pregnancy. She was subjected to an elective caesarean section in the next day along with tubal ligation, and she delivered a normal male baby weighing 3Kgs who had a normal thyroid function test.

Three weeks later she was seen in the endocrinology clinic. She was feeling well and her neurological examination was almost normal with normal power and reflexes. Her TSH was 8 m IU/L so the L-thyroxin dose was increased to 125ug/day.

Discussion
The standard internationally-recommended definition of prolonged pregnancy, endorsed by the American college of obstetricians and gynecologists (1997), is 42 completed weeks (294 days) or more from the first day of the last menstrual period. A variety of maternal demographic features such as parity, prior post term birth, socioeconomic class, and age have been suggested as predisposing risk factors to post term pregnancy, and some authors suggested that some prolonged pregnancies are biologically determined [3].

Although the post term pregnancy in this hypothyroid patient with myopathy could be just a coincidence, we think that the association in this particular case is more than incidental for many reasons, including:
1- Animal studies demonstrate that thyroid hormone is necessary for expression of the genes for fast myofibrillar proteins. Both an increase in the concentration of slow myofibrillar proteins and alterations in the myosin composition of myofibrils have been found in hypothyroid rats [4]. This may contribute to the weakness associated with hypothyroidism.
2- It has been shown that hypothyroidism significantly reduces the amplitude and frequency of spontaneous rhythmic contractions of rats’ myometrium [8].
3- The parathyroid hormone (PTH) is raised in hypothyroidism [1], and PTH may act on
myometrial smooth muscles to facilitate the maintenance of uterine tranquility [9].

4- Prostaglandins including (PGE2) are among multiple mediators involved in the onset of human labor [9], it has been shown that there is a decreased PGE2 production in the kidneys of hypothyroid rats [10].

5- Endothelins are very powerful inducers of myometrial contraction while nitric oxide causes myometrial relaxation [9], hypothyroidism causes both an increase in nitric oxide levels and reduction in endothelin levels [11].

6- Platelet-activating factor (PAF) promotes uterine contraction and it is inactivated enzymatically by PAF-acetylhydrolase [9]. Patients with hypothyroidism exhibit an increased activity of PAF-acetylhydrolase, hence more PAF inactivation [12].

7- Angiotensin-II is another uterotonin that promotes increased myometrial cell [ca++] thus promoting uterine contraction [9]. The plasma level of angiotensin-II is reduced by 81% in hypothyroid rats [13].

8- Human chorionic gonadotropin (HCG) acts to activate adenylcylase via a plasma receptor-G alpha S-linked system and this causes a decrease in the frequency and force of uterine contraction [9], in view of the fact that there is a close structural relationship between TSH and HCG and their receptors [14], and since it was demonstrated that HCG can stimulate TSH receptors [15] and increase thyroid hormone secretion, it would be possible that TSH (particularly in high levels as in primary hypothyroidism) also can stimulate HCG receptors and reduce the uterine contractions in the same manner.

From all the previous evidence that clearly demonstrates the reduction in mechanisms that facilitate uterine contraction and augmentation of mechanisms that promote uterine quiescence in hypothyroid state, it may be concluded that primary hypothyroidism during pregnancy might be complicated by a prolonged gestation, a complication that had never been described before with hypothyroidism. However most of the previous findings are derived from animal studies and the stated changes in hypothyroidism should also be proved in human studies both in laboratory and clinical situations.

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