

# Large thyroid cyst in a patient with congenital hypothyroidism

*Grande cisto tireoideano em paciente com hipotireoidismo congênito*

Mahmoud Ali Kaykhaei<sup>1</sup>, Zahra Heidari<sup>1</sup>, Ahmad Mehrazin<sup>2</sup>

## SUMMARY

Thyroid hormone biosynthetic defects are rare causes of congenital hypothyroidism. Although, initial presentations are usually diffuse goiter and hypothyroidism, subsequently they may develop thyroid nodules and or thyroid cancer. We describe a case of hypothyroidism due to dysmorphogenesis whose one of the previously solid nodules degenerates into a large cyst. A 22-year-old male was referred to our clinic for evaluation of enlarging thyroid nodule. Hypothyroidism was diagnosed in infancy, however due to poor compliance to treatment TSH values were elevated most of the times. When he was fifteen the first nodule was detected which was a solid cold nodule. Fine needle aspiration was in favor of benign follicular nodule. Seven years later we found a large multi nodular thyroid with a predominant large cyst corresponding to the previously detected solid nodule. 21<sup>cc</sup> straw colored fluid was aspirated. Cytology was reported as benign cystic nodule. The patient underwent thyroidectomy and pathology confirmed a benign thyroid cyst. Although underreported thyroid dysmorphogenesis may progress to cystic degeneration. Taking into account the risk of malignancy and eventually cyst formation, we recommend more frequent evaluation in the face of nodule formation in these patients. *Arq Bras Endocrinol Metab.* 2014;58(9):958-61

## SUMÁRIO

Os defeitos de biossíntese do hormônio tireoideano são causas raras de hipotireoidismo congênito. Embora as apresentações iniciais sejam geralmente bócio difuso e hipotireoidismo, nódulos tireoideanos ou câncer de tireoide podem se desenvolver subsequentemente. Descrevemos aqui um caso de hipotireoidismo causado por disormonogênese e no qual um dos nódulos sólidos degenerou em um grande cisto. Um homem de 22 anos de idade foi encaminhado para nossa clínica para avaliação do aumento de um nódulo tireoideano. O hipotireoidismo foi diagnosticado na infância. Entretanto, em razão da baixa conformidade ao tratamento, os valores de TSH estavam elevados na maior parte do tempo. Quando o paciente tinha 15 anos de idade, um primeiro nódulo sólido e frio foi detectado. A aspiração por agulha fina mostrou um nódulo folicular benigno. Sete anos depois encontramos múltiplos nódulos na tireoide e um grande cisto predominante que correspondia ao nódulo sólido anteriormente detectado. Foram aspirados 21<sup>cc</sup> de fluido cor de palha. A citologia mostrou um nódulo cístico benigno. O paciente foi submetido à tireoidectomia e o exame histopatológico confirmou um cisto tireoideano benigno. Embora não seja comumente relatada, a disormonogênese da tireoide pode progredir para a degeneração cística. Ao serem considerados o risco de malignidade e a eventual formação de cistos, recomendamos uma avaliação mais frequente da formação de nódulos nesses pacientes. *Arq Bras Endocrinol Metab.* 2014;58(9):958-61

<sup>1</sup> Department of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran

<sup>2</sup> Department of Nuclear Medicine, Zahedan University of Medical Sciences, Zahedan, Iran

### Correspondence to:

Mahmoud Ali Kaykhaei  
Department of Medicine,  
Zahedan University of Medical  
Sciences, Zahedan, Iran  
mazyar44@gmail.com

Received on Feb/15/2014  
Accepted on May/9/2014

DOI: 10.1590/0004-2730000003287

## INTRODUCTION

Thyroid hormone biosynthetic defects are unusual causes of permanent congenital hypothyroidism account for about 10-15% of cases (1). The vast majority of cases are due to mutations in one of the genes encoding Na/I symporter (2), thyroid peroxidase (TPO)

(3), pendrin (4), thyroglobulin (5) or dehalogenases (6). Although the patient typically presents with hypothyroidism and goiter, natural course of disease is poorly defined. In some patients despite adequate treatment, the goiter may worsen and even may become nodular years thereafter (7-10). However to date there is no

firm document considering cystic degeneration of these nodules. We present a case of congenital hypothyroidism that developed a large cyst in one of the previously detected solid thyroid nodules.

## CASE REPORT

A 22 year old young man (JR) presented to our clinic due to slowly enlarging thyroid gland. He was diagnosed of congenital hypothyroidism in infancy; after that, underwent replacement therapy with levothyroxine (LT4). Review of his medical records revealed poor adherence to medication, with TSH values between 0.04 and 72 mU/L (Mean 11.2) over twenty years.

The patient was referred to endocrinology clinic on May 2005 for assessment of goiter, when sonography of thyroid gland disclosed a solid 20 × 19 mm solid nodule in right lobe and a small 10 × 7 mm solid nodule in left lobe. A thyroid scan using <sup>99</sup>Tc one month after discontinuation of LT4 showed a cold nodule in right lobe and increased absorption of radiotracer in other parts of thyroid. Levothyroxine reinstated after fine needle aspiration of cold nodule was reported as benign nodular goiter (July 2005).

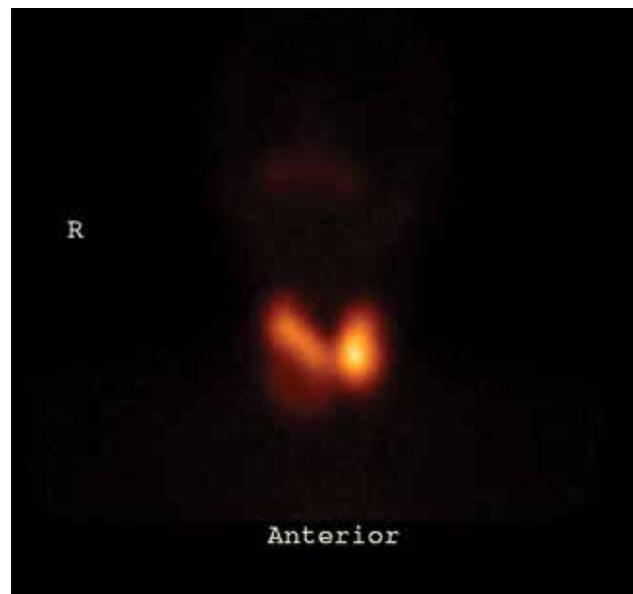
He was referred to our clinic on June 2012 due to further enlargement of thyroid nodules. There was no history of radiation therapy or other coexistent diseases and family history was negative for thyroid diseases. On physical examination a well-developed young man with asymmetrically enlarged nodular thyroid and a 4.0 × 3.0 cm dominant nodule in right lobe without cervical adenopathy was noticed. TSH while receiving 175 µg LT4 daily was 5.5 mU/L (0.4 - 4.2). At the same time, thyroid sonography showed four iso-echo solid nodules of varying sizes, the largest measured 22 × 15 mm, in the left lobe and a cystic 44 × 31 mm nodule in the right lobe. In a search to determine the cause of hypothyroidism LT4 discontinued for four weeks then, serum TSH, thyroglobulin, antithyroglobulin antibody (Anti-Tg), antithyroid peroxidase antibody (Anti-TPO), anti-tissue transglutaminase (Anti-tTG) antibody and serum IgA were measured and a thyroid scan with <sup>99</sup>Tc was obtained. While serum TSH was 37 mU/L, thyroglobulin was 30 ng/mL (20-50) and Anti-Tg, Anti-TPO and Anti-tTG were negative. Thyroid scan indicated a large cold nodule in right lobe and severe increased radiotracer uptake in other regions of both lobes including left nodules (Figure 1). Fine needle aspiration of

right cyst yielded 21<sup>cc</sup> straw colored fluid and cytological smears was reported as benign cystic goiter nodule.

In spite of recommendation for total thyroidectomy, the patient underwent right lobectomy and tissue examination confirmed diagnosis of simple thyroid cyst.

The patient advised to consume his medication regularly. Two months after surgery while taking 150 µg LT4 daily, he was euthyroid with a TSH of 1.4 mU/L.

The patient was discussed about the aims of this report and informed consent was provided.



**Figure 1.** Large cold nodule in the right lobe along with high radioisotope uptake in other regions of thyroid.

## DISCUSSION

Here, we describe a young man with goitrous congenital hypothyroidism that one of his nodules undergone cystic degeneration. According to inappropriately normal thyroglobulin in the presence of large goiter, high TSH with negative antithyroglobulin antibody, high uptake of radiotracer by thyroid, and no evidence of other defect, the most probable underlying abnormality is thyroglobulin synthesis defect. Typically, thyroglobulin synthesis abnormalities manifest with low thyroglobulin levels in the presence of high TSH (quantitative defect), however, in another subgroup thyroglobulin may be within normal values (qualitative defect) (11). Apart from the original abnormality, goiter with subsequent nodule formation has been reported in all types of thyroid dysmorphogenesis (7-10). Thyroid nodules were first detected in this patient when he was fifteen, however the size and number of nodules were increased progressively. Seven years later

when we visited him, there were multiple nodules of varying sizes and a large cyst corresponding to one of the previously discovered solid nodules.

Two main points should be considered according to findings in this patient; the first is an old question; what is the goal of treatment in these cases? While TSH has recognized as the major regulatory component of thyrocytes growth and differentiation, it is not surprising that higher TSH values may be accompanied by larger goiters and nodularity (11,12). Furthermore, as was shown by Chiesa and cols. the underlying mutation per se may play a synergistic role in goiter and nodule formation (7). Taken together it was suggested that TSH should be kept lower or even suppressed in this setting (9,10).

Second, since a great number of thyroid cysts are products of degeneration of solid nodules (13), it is conceivable why this patient developed a large cyst corresponding to his previously solid one. However it is largely unknown whether there is any association between changes in serum TSH and progression of nodular goiter to the cystic one, as in this case. To our knowledge this is the first case of goitrous congenital hypothyroidism whose solid nodule transformed into a large cyst. Therefore the natural course of thyroid biosynthetic defects usually begins with hypothyroidism and diffuse goiter, continues into nodule formation and eventually may terminate in cystic degeneration.

Another aspect of nodular disease in these patients is probable higher risk of malignancy. Again, not only elevated TSH levels (15,16) but also primary genetic abnormality including TPO (17-19) and thyroglobulin gene mutations may further prone these patients to thyroid cancer particularly in those with thyroglobulin gene mutations (20,21). In this regard, polymorphisms in the exon 10-12 cluster (22), biallelic p.R2223H mutation (19), activating mutation of V599E or K600E (20), g.IVS5 + 1G-- >A (23) and R-allele of Tg Q2511R (24) have been associated with higher risk of malignant transformation. Even non goitrous glands in patients with thyroid hormone biosynthetic defects may undergo malignant transformation (25). Owing to multiplicity of these nodules which causes the FNA difficult, higher risk of cancer, retrosternal extension, side effects of thyroid suppression and probable cystic degeneration which further complicates management; one should consider regular assessment and if indicated removing the "useless" thyroid particularly in the face of nodule formation.

In conclusion, thyroid nodules in the setting of dys-hormonogenesis may further progress to cyst formation. To prevent more complications, we recommend more frequent follow ups and a lower threshold for thyroidectomy in these patients.

Acknowledgements: the authors wish to thank Miss A. Kaykhaei for her cooperation in English language editing of the manuscript.

Disclosure: no potential conflict of interest relevant to this article was reported.

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