Parathyroid adenoma in a patient with congenital hypothyroidism

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Abstract

Thyroid dysgenesis, the most common cause of congenital hypothyroidism, includes hypoplasia, ectopia, and agenesis. Agenesis may present as hemiagenesis, bilobar agenesis, or isthmic agenesis. A small ectopic thyroid tissue may sometimes be detected on the embryonal migration pathway of suspected bilobar agenesis cases. Comorbidity of hyperparathyroidism and thyroid dysgenesis has been a topic of interest. The case presented here is a pioneer in medical literature with a comorbidity of parathyroidism and ectopic thyroid tissue.

Keywords: Thyroid dysgenesis, Parathyroid adenoma, Ectopic thyroid.

Introduction

Thyroid dysgenesis is an endocrinal disorder that is the most common cause of congenital hypothyroidism and is relatively more prevalent among newborns. Its prevalence among live births is 1/3000-4000. Thyroid dysgenesis is an organogenetic disorder of the thyroid gland. Hypoplasia, ectopia, and thyroid agenesis may develop as a result.[1] Thyroid dysgenesis with hyperparathyroidism are rarely seen.[2,3] The case we presented here is that of a parathyroid adenoma developed in a congenital hypothyroidism patient. The ectopic thyroid tissue with submental localization has not been sufficient to prevent development of clinical hypothyroidism. This led to the presentation of this case.

Case Report

A 38-year old male patient complained about arm and leg pain at his routine follow-up visit to the outpatient clinics due to hypothyroidism. In laboratory tests were found hypercalcemia and PTH elevation (Table-1). The patient was hospitalized to explain the cause of primer hyperparathyroidism and evaluate the possible side effects. Hypothyroidism was identified when he was admitted with ileus diagnosis for an operation 5 years ago. Thyroid hormone replacement was continued after the ileus operation. The patient had history of congenital mental retardation. There was no family history of thyroid and parathyroid diseases.

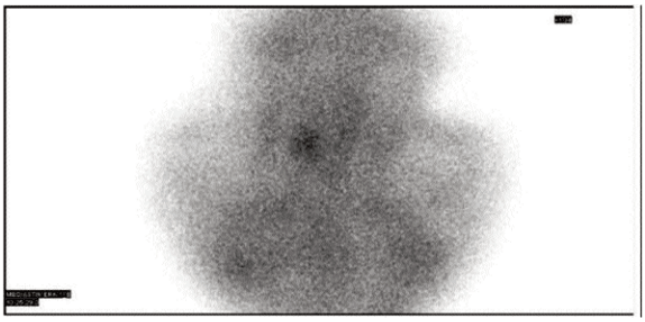

Figure-1: Parathyroid scintigraphy. Tc-99m MIBI uptake was detected in upper right parathyroid region.

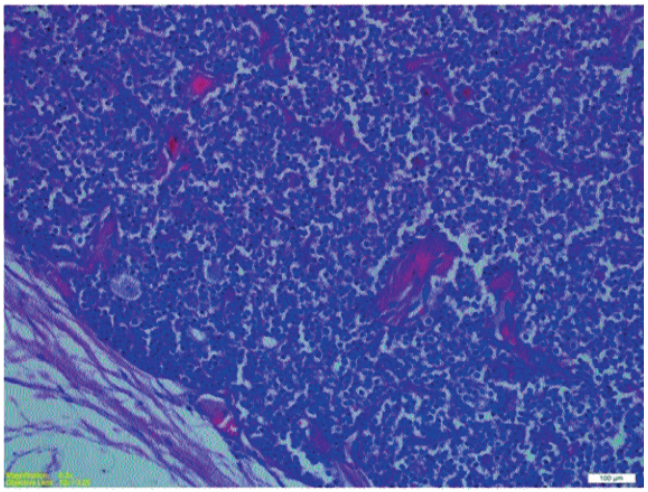

Figure-2: (H&E staining, 100x): Thin capsule of adenoma was observed without capsular invasion. There is no vascular and/or adjacent tissue invasion.

He was taking 100 mcg levothyroxine daily. He did not have a history of renal stone. Distal radial bone mineral density (BMD) examination revealed a bone mass less than expected of the chronological age with a Z-score of -3.1 SD. Hypoechoic nodular lesion (parathyroid adenoma?) of 9x10 mm was identified in the right thyroid lobe in the neck ultrasonography (USG). Upon parathyroid scintigraphy, focal involvement (parathyroid adenoma?) was observed in the upper right parathyroid gland localization (Figure-1). The case who had

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Table-1: Pre- and post-operative values of our patient.

	Initial value	Post operatif first month value	Normal range	Unit
Albümin	3.1	4.1	3.5-5	(g/dl)
Calcium (serum)	12.1	9.7	8.4-10.2	(mg/dl)
Phosphorus (serum)	3.08	3.63	2.3-4.7	(mg/dl)
Parathormone	111	33.9	15-65	(pg/ml)
25(OH) Vitamin D	21.39	25.81	>30	(ng/ml)
Alkaline phosphotase	166		40-150	(IU/L)
Magnesium	1.23		1.6-2.6	(mg/dl)
Calcium excretion (daily)	359		100-300	(mg/daily)
Creatinine (serum)	0.34	0.42	0.6-1.3	(mg/dl)
BUN	7		7-25	(mg/dl)
Glucose	81	90	88	(mg/dl)
Sodium (serum)	142		136-145	(mEq/L)
Potassium (serum)	3.8		3.5-5.1	(mEq/L)
Free T3(serum)	3.26	4.4	2-4.4	(pg/ml)
Free T4 (serum)	1,53	1.31	0.93-1,7	(ng/dL)
TSH	0,46	4.03	0.27-4.2	(IU/ml)
Anti TPO	14,66		0-34	(IU/ml)
Anti Thyroglobulin	30,56		0-115	(IU/ml)
ECG	Shortening of the QT interval	Normal		

Table-2.[1] Transcription factor gene mutations resulting in thyroid dysgenesis and associated clinical findings.

Mutated Gene	Associated Clinical Findings
Thyroid transcription factor 2 (TTF2)	Thyroid dysgenesis, choanalatresia, cleft palate and spikyhair
NKX2.1	Congenital hypothyroidism, respiratory distress ataxia and benign chorea
NKX2.5	Congenital hypothyroidism and cardiac malformations
PAX-8	Thyroid dysgenesis, kidney and ureteral malformations

congenital mental retardation was assumed to have thyroid agenesis as the primary cause of hypothyroidism. Blood thyroglobulin level was 1.23 ng/ml (normal range=1.4-78). Thyroid scintigraphy was performed to find out any thyroid tissue localization; and ectopic thyroid tissue was detected in the submental midline that was also confirmed by USG. A minimally invasive right parathyroid adenomectomy operation targeting the parathyroid adenoma was performed. Intra-operative PTH could not be tested. Histopathological evaluation was compatible with parathyroid adenoma (Figure-2). Postoperative blood calcium, phosphorus, and parathyroid hormone levels values were within normal limits (Table-1). No abnormalities were observed during his routine follow-ups.

Discussion

Thyroid dysgenesis is the most common cause of congenital hypothyroidism. Among these congenital anomalies, ectopic thyroid tissue is the most commonly encountered one.

After detection of primary hyperparathyroidism, a localization intervention was performed on the patient via parathyroid scintigraphy. An involvement in the upper right parathyroid gland was observed in the scintigraphy. In addition to an image of a parathyroid adenoma with a diameter of 10 mm, neck ultrasonography has also detected an image likely to be compatible with ectopic thyroid tissue in the submental area. Thyroid scintigraphy revealed accumulation in the midline of submental area. Based on these findings, ectopic thyroid tissue and parathyroid adenoma were considered.

Thyroid gland is developed via intussusception from the endoderm of the primitive pharynx between the 1st and the 2nd pharyngeal pouches. This canal reaches the state of intussusception on days 16-17 of gestation. Though the canal rapidly proliferates and widens towards the ventral at the distal end, it remains attached to the pharyngeal surface with a stem. Towards the end of month 2, it widens towards the lateral and transforms into the characteristic bilobar form.[4] Environmental and genetic factors can impact the formation of the bilobar structure and may lead to thyroid dysgenesis. Publications on familial thyroid ectopia and hemiagenesis cases support

genetic predisposition.[5-7]

Benign thyroid adenoma, thyroiditis, multinodular goiter and papillary thyroid carcinoma may develop due to thyroid dysgenesis. Ultrasonography plays an important role in diagnoses of these diseases as a noninvasive imaging technique.

Thyroid dysgenesis is usually sporadic. However, few cases are hereditary. Transcription gene mutations proven to be associated with thyroid dysgenesis are PAX8, TTF-2, NKX2.1, and NXK2.5.[3] The clinical findings observed on these mutations are summarized in (Table-2). None of these findings were observed in the case presented here. Therefore, our case can be considered sporadic.

The main regulatory gene in development of parathyroid gland is GCMB. Therefore, this gene must be fully expressed for differentiation of parathyroid cells.[8,9] GCMB gene expression is observed to be up-regulated in presence of hyperparathyroidism, and down-regulated in presence of hypocalcaemia. It has been hypothesized that GCMB transcription factor may mediate the hormone secretion of the calcium parathyroid cells.[9]

While no ectopic thyroid tissue along with parathyroid adenoma is described in medical literature, there are reports of comorbidity of hyperparathyroidism and thyroid hemiagenesis. Parathyroid hyperplasia, solitary and double adenomas were detected in hyperparathyroidism cases.

Our case had congenital hypothyroidism. Ectopic thyroid tissue was incapable of providing the thyroid hormone needs. Parathyroid adenoma had developed in years. The number of cases with thyroid dysgenesis and hyperparathyroidism comorbidity is increasing continuously. A genetic explanation is needed for this comorbidity.

Ruchala's study aimed to evaluate the calcium-phosphate balance in thyroid hemiagenesis. Ruchala reported observation of slight C-cell hyperplasia among the cases with thyroid hemiagenesis compared to the control group. They attempted to associate this condition with compensatory proliferation. However, calcium phosphate levels appear to be unaffected in this condition.[10]

The aim of this case report is to draw attention to hyperparathyroidism development possibility in follow-up of congenital hypothyroidism cases. With help of this case, we attempted to discuss the etiology and genetics of thyroid dysgenesis and hyperparathyroidism comorbidity.

This patient was seen at Hatay Antakya State Hospital on April 2014. An informed consent form was obtained.

Disclaimer: None to declare.

Declaration of Interest: The authors report no conflicts of interest

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