CASE REPORT

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The first case of papillary thyroid carcinoma in an adolescent with congenital dyshormonogenetic hypothyroidism in Serbia

Prvi slučaj papilarnog karcinoma štitaste žlezde kod devojčice sa kongenitalnim hipotiroidizmom u Srbiji

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Abstract

Introduction. Differentiated thyroid carcinoma (DTC) is a rare childhood malignancy, as it represents 0.3–0.4% of pediatric malignancies. Papillary carcinoma is the most common type of pediatric DTC and it represents about 90% of all DTC patients. Although rare, DTC arising from dyshormonogenetic goiter is the most serious complication of congenital hypothyroidism. **Case report.** We presented the development of thyroid papillary carcinoma in a 15-year-old girl diagnosed with congenital dyshormonogenetic hypothyroidism at neonatal age. Considering the early initiation and proper dosage of hormonal substitution, normal levels of thyreotropin and thyroid hormones were achieved quickly and maintained through a follow-up period. The girl remained euthyroid and asymptomatic until 13.8 years of age, when she presented with a large multinodular goiter. The patient underwent total thyroidectomy. Pathological examination revealed intrathyroid microcarcinoma in the right lobe. **Conclusion.** Although differentiated thyroid carcinoma is a rare pediatric malignancy, it is of great importance to have a certain degree of clinical caution and provide a multidisciplinary approach during the follow-up of patients with dyshormonogenetic hypothyroidism.

Key words:
congenital hypothyroidism; thyroid neoplasms; carcinoma, papillary; thiroidectomy; child; treatment outcome; serbia.

Apstrakt

Uvod. Diferentovani karcinom štitaste žlezde (DKŠŽ) je redak malignitet u detinjstvu i predstavlja 0,3–0,4% pedijatrijskih maligniteta. Najčešća forma DKŠŽ je papilarni karcinom pošto se javlja u približno 90% slučajeva. Iako redak, DKŠŽ koji se javlja kod dishormonogenetske strume predstavlja najozbiljniju komplikaciju kongenitalne hipotireoze. **Prikaz bolesnika.** U radu je prikazan papilarni karcinom štitaste žlezde kod petnaestogodišnje devojčice koja je lečena zbog kongenitalne hipotireoze od neonatalnog uzrasta. S obzirom na rano započinjanje i adekvatnu supstitucionu hormonsku terapiju, normalni nivoi tireotropina i tiroidnih hormona brzo su postignuti i devojčica je bila eutiroidna i bez simptoma do uzrasta od 13 godina i 8 meseci, kada je došlo do razvoja velike multinodularne strume. Konsultovan je onkološki hirurg i učinjena je totalna tiroidektomija. Patohistološkim pregledom otkriven je intratiroidni papilarni karcinom desnog režnja. **Zaključak.** Iako je diferentovani karcinom štitaste žlezde redak pedijatrijski malignitet, od izuzetnog je značaja imati određeni stepen kliničke sumnje i multidisciplinarni pristup tokom kliničkog praćenja bolesnika sa dishormonogenetskim hipotiroidizmom.

Ključne reči:
hipotireoidizam, kongenitalni; tireoidna žlezda, neoplazme; karcinom, papilarni; tireoidektomija; deca; lečenje, ishod; srbija.

Introduction

Differentiated carcinoma of the thyroid (DTC) is a rare childhood malignancy, as it represents 0.4–3% of all pediatric malignancies. More than 70% of these appear in patients aged between 11 and 17 and are usually related to radiation exposure. Papillary carcinoma is the most common type of pediatric DTC as it represents about 90% of all DTC cases [1–6]. Compared to adults, children tend to have more aggressive clinical course of this malignant disease, with up to 80% cases presenting with regional lymph node metastasis, and pulmonary metastasis in 10–20% [1, 2, 4, 7, 8]. Although rare, DTC araising from dyshormonogenetic goiter is the most serious complication of congenital hypothyroidism.

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In this case report, we present the developement of thyroid papillary carcinoma in a 15-year-old girl diagnosed with congenital dyshormonogenetic hypothyroidism at neonatal age.

Case report

This 15.2-year-old girl was diagnosed with congenital hypothyroidism as a newborn. The diagnosis of hypothyroidism was made by neonatal screening and the child underwent further examination which confirmed the diagnosis of primary dyshormonogenetic hypothyroidism. The patient started substitutional levothyroxine therapy, that she continued to take regularly. Considering the early initiation and proper dosage of hormonal substitution, normal levels of thyreotropin (TSH) and thyroid hormones were achieved quickly and were present all through the follow-up. Regular physical examinatitions showed no signs of goitre, and the girl was euthyroid and without any simptoms until 13.8 years of age.

At that time, the girl experienced loss of brother who was killed in a traffic accident. Almost immediately after the tragedy, her mother noticed the development of a large goitre and the girl came for an unscheduled appointment. Physical examination discovered a large multinodular goitre. Laboratory tests showed the following results: TSH 0.015 μIU/mL (normal range 0.27 to 4.2 μIU/mL), fT4 12.34 pmol/L (12.0 to 22.0 pmol/L), TPO antibodies over 600 IJ/mL (normal range less than 34 IJ/mL), Tg antibodies 140.4 IJ/mL (normal range ≤ 115 IJ/mL). Ultrasonography revealed a diffuse enlargement of the thyroid as well as the compression of the tracheal cartilage rings and hypoechodensity. Both of the lobi and the isthmus contained confluent nodular masses of 15–20 mm in diameter. These laboratory and ultrasonographic findings were consistent with autoimmune thyroiditis. There was no enlargement of the regional lymph nodes.

At the age of 10, the girl was also diagnosed with hypercholesterolemia, and the family history showed that the girl's mother and mather's father also suffered from this disorder. Also, the girl's grandfather had hyperthyroidism, and underwent thyroidectomy at the age of 63.

The patient was reffered to the surgeon, who recommended surgical treatment (thyroidectomy), with a complete preoperative work-up. Chest X-ray and abdominal ultrasound were normal. Laboratory tests, including parathyroid hormone and calcium levels were within allowed range. The patient was reffered to total thyroidectomy with *ex tempore* biopsy.

Pathological examination revealed the presence of intrathyroid papillary microcarcinoma 2.5 mm in diameter in the right lobe. The girl had two attacks of hypocalcemic tetany, so she was advised to take calcium and vitamine D, as well as substitutional levothyroxine therapy.

Currently, the girl is doing well and is euthyroid.

Data in this case report were presented with the written consent of the patient's parents.

Discussion

The developement of differentiated thyroid carcinoma in patients with dyshormonogenetic goiter is very unexpected, especially when it comes to pediatric patients. The case we presented was the first one the in western Serbia in the last 30 years, since the application of the neonatal screening program.

Most studies report a male predominance in children under the age of 10, that shifts to a female predominance in adolescents [3, 8–12]. As mentioned before, papillary thyroid carcinoma is the most common form of pediatric DTC.

Although the etiology of papillary carcinoma in patients with dishormonogenetic hypothyroidism remains unclear, certain risk factors have been recognised. Radiation exposure is known to be one of the major risk factors [5, 6, 3–15]. Another important element in the development of thyroid carcinoma is genetic factor [9, 16]. It has also been suggested that prolonged TSH stimulation, as well as inadequate substitutional therapy and intermitent TSH elevation can be associated with the development of DTC [17, 18].

Our patient's gender and age were consistent with the previous reports on DTC in children. On the other hand, in the presented patient there was no radiation exposure, pre- or postnatal, accidental or medical. Also, there were no data on thyroid carcinoma in the patient's family history, although her grandfather had suffered from hyperthyroidism and underwent total thyroidectomy. Levothyroxine treatment was initiated in neonatal age, the doses were adequate all the time and the consequent TSH levels were within normal range during the follow-up, so thyreotropin stimulation as a risk factor can be excluded.

In pediatric population, DTC has a great 20-year survival rate, that has been reported to vary between 90 and 95%. On the other hand, it is considered to be more agressive cancer in children, compared to adults [1, 2, 4, 7–9].

Conclusion

Differentiated thyroid carcinoma is a rare pediatric malignant tumor and the presented patient is the only reported case in Serbia. Although it has a more aggressive clinical course in children than in adults, the 20-year survival rate is excellent. Some risk factors are recognised, and should be kept in mind when assessing patients with congenital hypothyroidism. On the other hand, the presented patient did not have any of these risks in her history, so this case can serve as a remainder that it is of great importance to have a multidisciplinary approach and a certain degree of clinical suspicion even in cases with no apparent risks in patients medical history.

R E F E R E N C E S

1. *Brink JS, van Heerden JA, McIver B, Salomao DR, Farley DR, Grant CS*, et al. Papillary thyroid cancer with pulmonary metastases in children: long-term prognosis. Surgery 2000; 128(6): 881−7.
2. *Alkan S, Seven H, Sakalli E, Dadaş B.* Papillary thyroid carcinoma in a 3-year-old child: case report. Int J Pediatr Otorhinolaryngol 2008; 72(2): 275−7.
3. *Shapiro NL, Bhattacharyya N.* Population-based outcomes for pediatric thyroid carcinoma. Laryngoscope 2005; 115(2): 337−40.
4. *Srikumar S, Agada FO, Picton SV Squire R, Knight LC.* Papillary carcinoma of the thyroid in a 2-year-old: case report with review of the literature. Int J Pediatr Otorhinolaryngol 2006; 1(4): 274−8.
5. *Fagin JA.* Familial nonmedullary thyroid carcinoma: The case for genetic susceptibility. J Clin Endocrinol Metab 1997; 82(2): 342−4.
6. *Kikuchi S, Perrier ND, Ituarte P, Siperstein AE, Duh Q, Clark OH.* Latency period of thyroid neoplasia after radiation exposure. Ann Surg 2004; 239(4): 536−43.
7. *Millman B, Pellitteri PK.* Thyroid carcinomain children and adolescents. Arch Otolaryngol Head Neck Sur 1995; 121(11): 1261−4.
8. *Klopper JP, McDermott MT.* Palpable pediatric thyroid abnormalities-diagnostic pitfalls necessitate a high index of clinical suspicion: a case report. J Med Case Reports 2007; 1: 29.
9. *Leboulleux S, Baudin E, Hartl DW, Travagli J, Schlumberger M.* Follicular cell-derived thyroid cancer in children. Horm Res 2005; 63(3): 145−51.
10. *Segal K, Shvero J, Stern Y, Mechlis S, Feinmesser R.* Surgery of thyroid cancer in children and adolescents. Head Neck 1998; 20(4): 293−7.
11. *Grigsby PW, Galor A, Michalski JM, Doherty GM.* Childhood and adolescent thyroid carcinoma. Cancer 2002; 95(4): 724−9.
12. *Kumar A, Bal CS.* Differentiated thyroid cancer. Indian J Pediatr 2003; 70(9): 707−13.
13. *Poddar S, Basu S, Majumder A.* Papillary carcinoma of thyroid in a 11 months old child. Indian J Med Paediatr Oncol 2008; 29(2): 33−5.
14. *La Quaglia MP, Black T, Holcomb GW 3rd, Sklar C, Azizkhan RG, Haase GM,* et al. Differentiated thyroid cancer: clinical characteristics, treatment, and outcome in patients under the 21 years of age who presented with distant metastases. A report from the surgical Committee of Children's Cancer Group. J Ped Surg 2000; 35(6): 955−9, discussion 960.
15. *Spinelli C, Bertocchini A, Antonelli A, Miccoli P.* Surgical therapy of the thyroid papillary carcinoma in children: experience with 56 patients < or =16 years old. J Pediatr Surg 2004; 39(10): 1500−5.
16. *Kebebew E.* Hereditary non-medullary thyroid cancer. World J Surg 2008; 32(5): 678−82.
17. *Medeiros-Neto G, Stanbury JB.* Thyroid malignancy and dyshormonogenetic goiter. In: *Medeiros-Neto G, Stanbury JB*, editors. Inherited disorders of the thyroid system. Boca Raton, FL: CRC Press; 1994. p. 207−18.
18. *Cooper DS, Axelrod L, DeGroot LJ, Vickery AL, Maloof F.* Congenital goiter and the development of metastatic follicular carcinoma with evidence for a leak of nonhormonal iodide: clinical, pathological, kinetic, and biochemical studies and a review of the literature. J Clin Endocrinol Metab 1981; 52(2): 294−306.

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