# Prophylactic Thyroidectomy in Multiple Endocrine Neoplasia Type 2 Syndrome

## Multipl Endokrin Neoplazi Tip 2 Sendromunda Profilaktik Tiroidektomi

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**ABSTRACT**

Multiple endocrine neoplasia(MEN) 2 syndrome is a rare familial cancer syndrome that is usually associated with cancer of the thyroid gland, adrenal gland, and parathyroid gland. Mutation in the RET protooncogene associated with the MEN 2 syndrome is seen in more than 90% of familial thyroid cancer cases. We report a female 7 years and 9 months old and a male 6 years and 8 months male pediatric patients. RET mutation was detected in both patients during family screening due to the diagnosis of MEN 2 syndrome in their families. We evaluated the patients who had no symtomps and we operated with an indication for prophylactic thyroidectomy. Transient bilateral recurrent laryngeal nerve (RLN) injury was developed in the first case, and hypocalcemia was developed in the second case. Families of patients diagnosed with MEN syndrome should be screened for RET mutation by genetic tests, and children with mutations should be scheduled for total thyroidectomy according to the risk of the mutation.

**Keywords:** prophylactic thyroidectomy; MEN 2; Children

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**ÖZET**

Multipl endokrin neoplazi(MEN) 2 sendromu, genellikle tiroid bezi, adrenal bez ve paratiroid bezi kanseri ile ilişkili, nadir görülen bir ailesel kanser sendromudur. MEN 2 sendromu ile ilişkili RET protoonkogenindeki mutasyon, ailesel tiroid kanseri vakalarının %90'ından fazlasında görülür. 7 yaş 9 aylık kız ve 6 yaş 8 aylık erkek çocuk hastaları sunuyoruz. Her iki hastada da ailelerinde MEN 2 sendromu tanısı olması nedeniyle yapılan aile taramasında RET mutasyonu tespit edildi. Semptomları olmayan hastaları değerlendirdik ve profilaktik tiroidektomi endikasyonu ile ameliyat ettik. Birinci olguda geçici bilateral rekürren laringeal sinir (RLN) yaralanması, ikinci olguda hipokalsemi gelişti. MEN sendromu tanısı alan hastaların aileleri genetik testler ile RET mutasyonu açısından taranmalı ve mutasyonu olan çocuklara mutasyon riskine göre total tiroidektomi planlanmalıdır.

**Anahtar Sözcükler:** Profilaktik tiroidektomi; MEN 2; Çocuk

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## INTRODUCTION

The 10% of thyroid malignancies are seen in pediatric patients, approximately 5% of these are medullary thyroid carcinoma (1). Multiple endocrine neoplasia type 2 (MEN 2) is an autosomal dominant inherited syndrome and has three defined subtypes. In MEN 2A, medullary thyroid carcinoma, pheochromocytoma and hyperparathyroidism are seen. In MEN 2B, medullary thyroid carcinoma, pheochromocytoma and characteristic stigmata are seen. The third subgroup is familial medullary thyroid carcinoma and occurs only with medullary thyroid carcinoma (2).

In a study, it was stated that Prophylactic surgery is generally recommended for MEN 2A/FMTC gene carriers at the age of 4-6 years and for MEN 2B syndrome gene carriers by the age of 1 year (3).

In another study, it was stated that the operation time should be adjusted according to the RET mutation genotype. With this study, it was suggested that children with high risk mutations should be operated in the first year of life, those with medium risk until the age of 5, and those with low risk until the age of 10 (4).

With this case report, we wanted to present our prophylactic thyroidectomy experience in two pediatric patients.

## CASE REPORT

*Case 1*

A female patient aged 7 years and 9 months without any complaints was referred to us with the recommendation of prophylactic thyroidectomy upon detection of RET mutation by the medical genetics department. The patient's father, grandfather, and aunt had a history of thyroidectomy, in addition a diagnosis of MEN 2 syndrome in her aunt. Preoperative hemogram, biochemistry and hormone examinations were found within normal limits. The patient, who underwent prophylactic total thyroidectomy, was re-intubated when stridor and desaturation developed during extubation, and was followed-up in pediatric intensive care unit. The patient, who could not tolerate extubation on the postoperative second day, was followed up with suspicion of vocal cord paralysis. The patient, who was given dexamethasone and levothyroxine treatment, started to be followed up in the service when she tolerated the postoperative 4th day extubation. Dexamethasone treatment was reduced and discontinued in the patient who did not experience any additional pathology in the follow-up and the patient was discharged with levothyroxine treatment. In the laryngoscopy performed on the postoperative 3rd month of the patient, it was observed that the vocal cords were bilaterally normal and the patient was evaluated as transient bilateral recurrent laryngeal nerve (RLN) injury. In the pathology report, it was stated that areas of parafollicular C cell hyperplasia were detected in the thyroid parenchyma.

*Case 2*

Asymptomatic RET mutation (heterozygous carriage) was found during family screening in a 6 years and 8 months male patient after his mother was diagnosed with MEN syndrome. Prophylactic total thyroidectomy was performed on the patient. Parathyroid hormone - 2.3 pg / mL, Calcium - 8.65 mg / dL was detected on postoperative first day. Cholecalciferol, calcitriol and vitamin D3 treatment was initiated. Calcium - 6.74 mg / dl was found in biochemistry test performed on post-operative 3rd day. IV calcium treatment was started. He was discharged on the fifth postoperative day with oral calcium and levothyroxine. The pathology report of the patient's thyroidectomy material, total thyroidectomy material without specific pathology, and one parathyroid tissue were evaluated.

It was learned that both patients did not have any problems during their 2-year follow-up.

## DISCUSSION

Medullary thyroid carcinoma is a rare neuroendocrine malignancy and constitutes 5% of thyroid cancers. Early diagnosis is very important in the prognosis of the disease. Genetic testing has enabled early diagnosis in asymptomatic carriers and high risk patients, and early or prophylactic surgery is therapeutic for most patients. All RET mutation carriers should be evaluated and surgically treated for MTC prophylaxis (5). Thyroidectomies performed in childhood may have a higher frequency of complications, especially endocrine complications, compared to thyroidectomies applied to adults (The frequency of endocrine complications is 9.1% in children, 6.3% in adults; the frequency of all complications is 11.6% in children and 10.7% in adults). Also, the frequency of complications increases as the age of the patient gets smaller in thyroid surgery (0-6 age 22%, 7-12 age 15%, 13-17 age 11%) (6). In addition to the lack of experience of pediatric surgeons, the smallness and sensitivity of children's organs and anatomical structures also play a role in this (7). Since prophylactic total thyroidectomies are mostly performed in early childhood, the frequency of prophylactic total thyroidectomy complications may be higher.

In a retrospective study of 44 patients who underwent prophylactic thyroidectomy in children by Kluijfhout and colleagues; Transient hypocalcemia developed in 12 patients and persistent hypocalcemia in 9 patients. Parothyroid gland excision was observed in the pathology reports of 9 patients. Stridor developed in 1 patient due to temporary unilateral RLN injury. One patient could not tolerate extubation, received dexamethasone treatment, and unilateral permanent nerve damage was demonstrated by laryngoscopy performed in the 8th postoperative month (8).

Transient bilateral RLN injury seen in our patient undergoing prophylactic thyroidectomy was connected to dissection and instruments used for bleeding control. Although controversial in the literature, it is recommended to use neuromonitorization in pediatric cases if appropriate intubation tubes are available to reduce RLN damage (9).

Families of patients diagnosed with MEN syndrome should be screened for RET mutation by genetic tests, and children with mutations should be scheduled for total thyroidectomy in experienced centers according to the risk of the mutation. Considering the relatively older age of our patient, who had areas of parafollicular C cell hyperplasia in the thyroid parenchyma in her pathology, surgery at an early age becomes important.

**Conflict of interest**

No conflict of interest was declared by the authors.

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