

# Metastatic Medullary Thyroid Carcinoma as a Presenting Feature of Multiple Endocrine Neoplasia 2B: A Case Report and Literature Review



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## ABSTRACT

**Background:** Multiple Endocrine Neoplasia type 2B (MEN2B) is an autosomal dominant disorder characterized by Medullary Thyroid Carcinoma (MTC) and pheochromocytoma. MTC occurs in almost all MEN2B patients. The tumor develops at an earlier age and is aggressive. Surgery is often not curative for this condition. Death from MTC occurred in 50% of patients with MEN2B. Thus, early diagnosis and prevention are crucial in this regard. Thyroidectomy, as early as the neonatal period, may be indicated in patients with MEN2B identified by genetic screening.

**Case Presentation:** We reported a 24-year-old male presented to the emergency department with dyspnea for the past 3 months. There was a nodule 3\*3 cm in the Right Lower Lobe (RLL) of the thyroid gland. Non-contrast Computer Tomography (CT) scan of the lung revealed multiple nodular lesions compatible with metastasis. The Fine Needle Aspiration (FNA) cytology of the thyroid nodule indicated that the features of medullary thyroid carcinoma were positive stains in Immunohistochemistry (IHC) for calcitonin. A diagnosis of pulmonary metastatic medullary thyroid carcinoma, as a presenting feature of MEN2B, was made. The patient was treated with Vandetanib.

**Conclusion:** In the reported MEN2B patient, MTC occurred in the early stages of life and was multifocal. Thus, it is crucial to diagnose medullary thyroid cancer at the early stages of the disease.

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## Introduction

**M**ultiple Endocrine Neoplasia type 2B (MEN2B) is a rare autosomal dominant syndrome with high penetrance and various phenotypic expression due to the germline mutations of RET proto-oncogene [1]. This disorder is characterized by Medullary Thyroid Carcinoma (MTC), pheochromocytoma, marfanoid habitus, mucosal/intestinal ganglioneuromatosis, and multiple musculoskeletal abnormalities such as kyphosis, scoliosis, lordosis, increased joint laxity, and the weakness of the proximal muscles of the extremities [2]. The age at the diagnosis of MEN 2B varies from 2 days to 52 years in patients [2]. MEN2B should be suspected in any patient with MTC or pheochromocytoma, especially when the tumors occur at a young age, with multifocal status, or when one or more family member is affected [2]. Furthermore, the associated pheochromocytoma could be asymptomatic [3, 4].

In this article, we reported a case of MEN2B with respiratory manifestations induced by the metastasis of the MTC to the lung.

## Case presentation

A 24-year-old referred to our emergency department with dyspnea for the past 3 months. There was no history of fever, cough, or orthopnea. There were no paroxysms of headache, sweating, or palpitation. He did not report diarrhea, constipation, or other gastrointestinal symptoms. His family history and substance use history was negative. On examination, the vital sign was stable, and he had no stridor. There was a palpable nodule of 3\*3 cm in the Right Lower Lobe (RLL) of the thyroid gland. He had a long thin face with marfanoid features

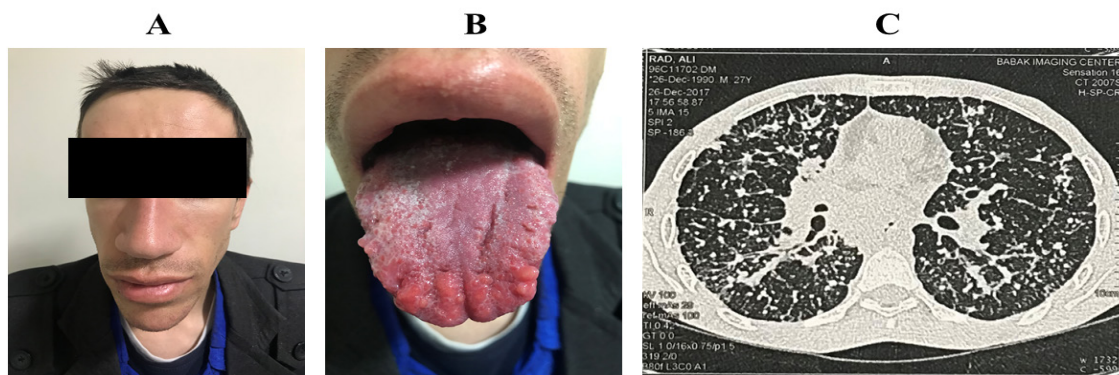
(Figure 1A); high-arched palate, and high arm span to height ratio. Further evaluations indicated multiple mucosal neuromas (Figure 1B). The patient demonstrated no evidence of pectus excavatum and kyphoscoliosis. Other aspects of the physical examination were unremarkable.

An emergency non-contrast chest Computer Tomography (CT) scan of the patient's lung revealed multiple nodular lesions compatible with metastatic lesions in both lungs (Figure 1C). The CBC was normal; the liver and kidney function test data were within the normal range. Serum parathormone was also within the normal range; serum calcitonin levels were extremely high (3600pg/mL).

Thyroid sonography revealed a 3×3 cm nodule in the RLL of the thyroid. The FNA cytology of the thyroid nodule suggested cellular specimens with round, ovoid, plasmacytoid, or spindle cells singly or in a small cluster; cells had abundant cytoplasm and eccentric nuclei, and chromatin had salt and pepper appearance. Features suggestive of medullary carcinoma of the thyroid were positive stains in Immunohistochemistry (IHC) for calcitonin, but negative for thyroglobulin. In abdominal CT scan results, there was no evidence of the liver metastasis. The whole-body bone scan for metastasis and spinal Magnetic Resonance Imaging (MRI) data were negative.

The result of the ophthalmology examination was normal. Pheochromocytoma was excluded based on the laboratory test results, including urinary Vanillylmandelic Acid (VMA), metanephrine, and normetanephrine, i.e., within the normal range.

A diagnosis of pulmonary metastatic MTC as a presenting feature of MEN2B was made. He was treated



**Figure 1.** Clinical and radiologic manifestations of MEN2B

A: Long thin face with marfanoid features; B: multiple mucosal neuromas; C: multiple nodular lesions compatible with metastatic lesions in both lungs

with vandetanib as systemic chemotherapy. This case highlights an unusual presentation of a rare disease. The patient was further planned for the analysis of RET proto-oncogene. The investigation of his family was also undertaken. Eventually, the patient was referred to a hematologist-oncologist specialist at his town, and it was impossible to follow-up the case.

## Discussion

MEN2B is an autosomal dominant syndrome identified by MTC, pheochromocytoma, marfanoid habitus, and mucocutaneous neuromas [5]. The prevalence of MEN2 is estimated to be 1/30000, and MEN2B includes <10% of MEN2 syndromes with a higher mortality rate [6]. All MEN2 variants are induced by a germline mutation in the RET Proto-oncogene, and MEN2B is the most aggressive form of them [5]. All individuals with the RET gene mutation require prophylactic thyroidectomy [6].

MTC occurs in almost all patients, in this regard [5]. MTC in MEN2B syndrome occurs in the early stages of life and is multi-centric [6]. There is a high risk of early metastasis, and the disease is aggressive and life-threatening; thus, early detection of this disease is crucial [6].

MEN2B syndrome is not only associated with the mentioned symptoms but also manifests additional conditions, such as swollen lips, the mucosal neuroma of the oral cavity, nasal cavity, as well as colon and skeletal deformities in >75% of cases [6].

Visual disorders associated with MEN2B syndrome include photophobia, ptosis, and neuromas of the conjunctivae, dry eye, increased intraocular pressure, and eminent corneal nerves. These presentations are observed in >80% of patients at the time of diagnosing [6].

Gastrointestinal symptoms, such as failure to thrive, abdominal pain, dysphagia, projectile vomiting, megacolon, and pseudo-obstruction, are probable presentations of this syndrome [7].

Finally, MEN2B is the least commonly occurring condition in <5% of cases of MEN. It is also the earliest to present and has the worst prognosis with an average life expectancy of 30 years [7].

## Conclusion

In patients with MEN2B, MTC can occur in the early stages of life and is multifocal, thus, it is essential to diagnose it as soon as possible.

## Ethical Considerations

### Compliance with ethical guidelines

All ethical principles were considered in this article.

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### Conflict of interest

The authors declared no conflict of interest.

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