



Medullary Carcinoma Thyroid surgery associated with Multiple Endocrine Neoplasia Type 2B (MEN 2B): a case report

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MEN2B syndrome is a syndrome associated with systemic malignancies such as carcinoma of the thyroid and pheochromocytoma. An 18-year-old male patient with a neck mass was admitted to the Besat hospital in Sanandaj in 2015. In the clinical examination we found a long and delicate face, multiple lesions in the tongue, cheek and lips, atrophy of the temporal mandibular, and mandible protrusibility in the x-ray. It was remarkable that a positive family history was not found and there were no signs and symptoms of pheochromocytoma. According to the pathology, MEN2B syndrome and final diagnosis of medullary thyroid carcinoma was confirmed and total thyroidectomy surgery and left incomplete thymectomy was conducted. With detection of non-endocrine symptoms of MEN2B and prophylactic thyroid surgery, we may expect a better prognosis. Most cases of medullary thyroid carcinoma associated with the syndrome occur in the age of 20 years. And there is a more possibility of invasion to the surrounding tissues. This condition was introduced in accordance with the patient's condition.

INTRODUCTION

Multiple endocrine neoplasia syndrome is a set of genetic disorders which are mostly inherited in the form of autosomal dominant (Walls, 2014). However, in some cases, they are sporadic (Mathiesen et al., 2017). In some endocrine glands, MEN syndrome is extensive, malignant or benign (Racine et al., 2018). The syndrome is classified in two classes (Taieb et al., 2014). The first type is the Wermer syndrome associates with a set of disorders such as pituitary adenoma, hyperparathyroidism, pancreatic islet cell hyperplasia or adenoma (Taieb et al., 2014). The second type includes two types of MEN2B and MEN2A. MEN2A is also called Sipple Syndrome and may be associated with hyperparathyroidism, medullary carcinoma and pheochromocytoma (Walls, 2014). MEN2B, formerly known as MEN3B, in addition to medullary carcinoma and pheochromocytoma, non-endocrine disorders such as neuroma or multiple Ganglioglioma and Marfanoid view can be seen (Walls, 2014). In marfanoid view, there is a decrease in upper parts compared with lower parts of the body and legs are stretched and long; also, face is delicate and pulled (Thakker, 2014).

One of the differences between MEN2B and MEN2A is that hyperparathyroidism is not seen in MEN2B type (Castinetti et al., 2018). MEN2B is less common than MEN2A and is about 10 percent less than the first type (July et al., 2018). It is more aggressive than the first type and the prognosis is not good. In half of the cases, MEN2B are presented as new mutations and it is not possible to find genetic origins, while in MEN2A, eighty percent of the cases have a hereditary origin. Thyroid carcinoma is found in ninety to one hundred percent and pheochromocytoma is found in more than half of patients with MEN2B (Marx, 2011). Medullary thyroid cancer comprises 5 to 10% of the Thyroid cancers. These cancers begin with C cells and the control of cancer is easier before spreading to other parts of the body (Thosani et al., 2013). Medullary thyroid cancer is made after a change or displacement in the RET gene. Altered RET gene, is passed from parents to children. Almost all people with the altered RET gene are affected with medullary thyroid cancer. Altered RET gene can be identified using a blood test. If there is an abnormal gene in patients with medullary thyroid cancer, other family members of the patients should be tested as well (Thosani et al., 2013). If these patients have an altered RET gene, numerous laboratory test or surgical removal of the thyroid is recommended to prevent cancer (Raue et al., 2018). In the case of thyroid cancer in a family, it is called "familial medullary cancer" or "multiple endocrine neoplasia syndromes (MEN)". In patients with MEN syndrome, there is also the risk of other types of cancer (Owens et al., 2015). In this case report we present a case of medullary thyroid cancer in MEN 2B syndrome.

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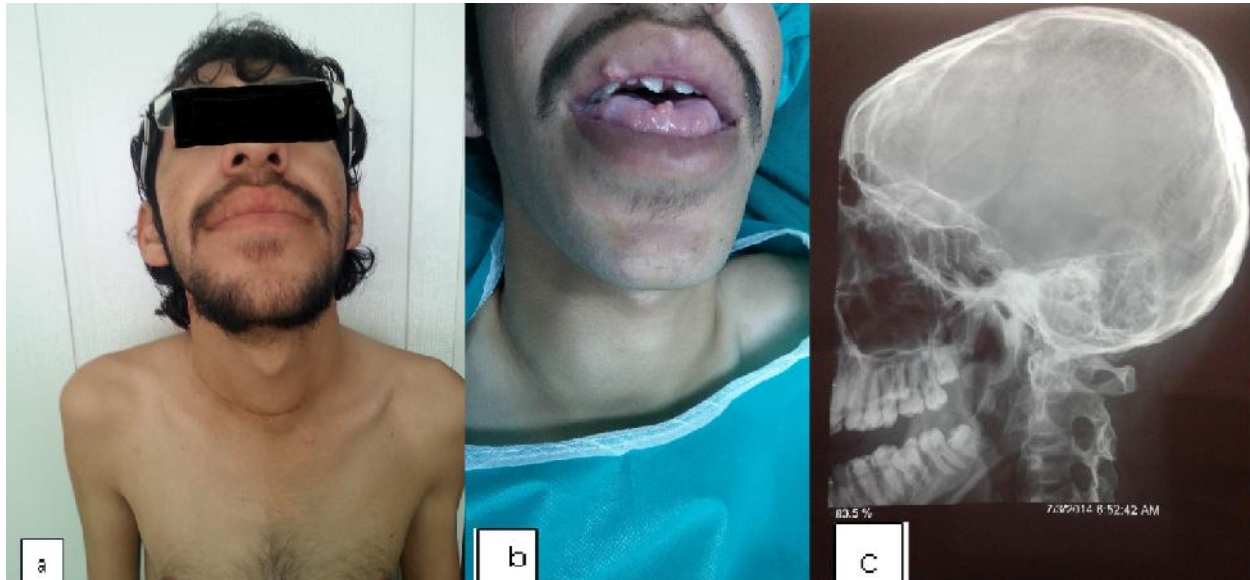


Figure 1 (a) a lump in the neck region. (b) the multiple lesions on tongue, cheeks and lips. (c) Atrophy of the the temporo mandibular joint (TMJ) and forward bulge of the lower jaw

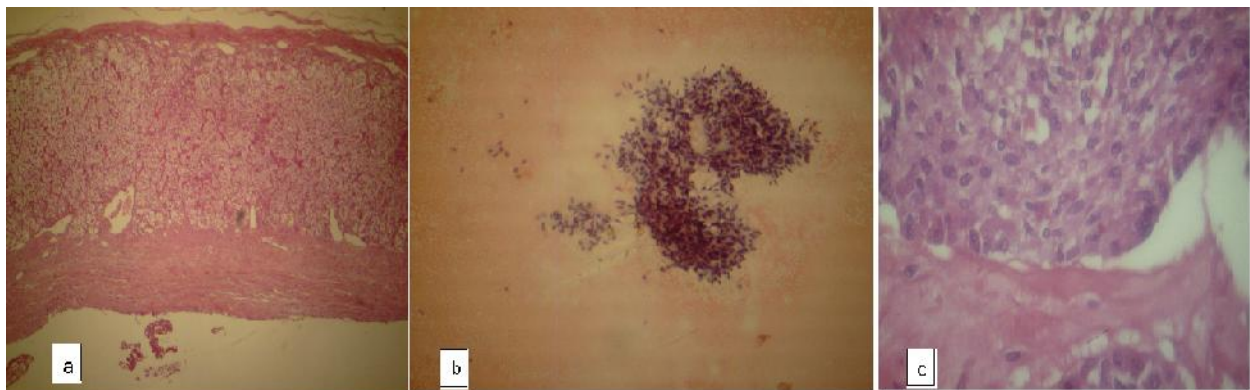


Figure 2 (a) Adrenal cyst, endothelial type. Fibrous wall lined by spindle endothelial type cells (H&E×4). (b) medullary carcinoma, Spindle shaped tumor cells (papanicolausstain×10). (c) Medullary Carcinoma, composed of sheet of spindle cells in vicinity of stromal amyloid (H&E×40)

CASE PRESENTATION

The patient was an 18-year-old man living in a village in Divandarreh, Kurdistan, Iran, complaining of a lump in the neck region (Figure 1.a). Four months ago, he was referred to the Besat specialized Clinic in Sanandaj, Iran in 2015. In the first look, the patient's face was drawn and delicate. Physical examination of the tongue, cheeks and lips showed multiple lesions (Figure 1.b). Atrophy of the temporomandibular joint (TMJ) and forward bulge of the lower jaw was evident in the X-ray (Figure 1.c). However, in the Physical examination, there were no signs of eye symptoms including dry eyes, drooping eyelids, outwards return of the eyelid, nodules on the eyelids, and thickened eyelids. There were no reports of colicky pain, diarrhea, and constipation in the patient's records. On skeletal, physical examination, there was no evidence of skeletal disorders such as kyphosis and scoliosis. No family history of endocrine disorders, including thyroid, pituitary, and other symptoms were found in the patient's history. The patient's family members were tested for RET gene, which was negative. There were no signs or symptoms of pheochromocytoma in the patient. In the biopsy of adrenal gland cystic fibrosis lesions with walls coated with endothelial fusiform cells were observed in the vicinity of adrenal tissue (Figure 2.a).

According to the mucosal lesions in the mouth and tongue and symptoms in the face, the MEN2 B syndrome was diagnosed in the patient. Also, the patient was evaluated for endocrine disorders. On examination, the thyroid gland was enlarged, but there were no pain and shortness of breath and a thyroid mass was found on the right. MRI imaging method, pituitary, and hypothalamus showed no abnormality. In the ultrasonic image, left thyroid lobe was small with a typical hard mass. Interior small echogenic mass presented a filter calcification of about 8 mm in the left lobe of the thyroid; besides, the right lobe of the thyroid was prominent. A large firm mass with small interior calcifications with a cyst in the right lobe of the thyroid was evident. Due to the risk of papillary cell, FNA was performed, resulting in the diagnosis of medullary carcinoma (Figure 2.b).

After definitive diagnosis of medullary carcinoma the patient was prepared for surgery. Before surgery, all the tests, including coagulation and blood serum were performed which had normal results. Chest X-ray and ECG was normal before surgery. In laboratory tests before surgery, calcitonin was abnormally higher than 2000 pg/ml. All blood tests in connection with the pituitary and thyroid hormone levels were normal. For the prevention and control of hypocalcemia, as one of the complications of the disease, serum calcium was lower than its normal

value (8.3 mg/dl), the patient was checked for hypocalcemia before, during and after the surgery and there were no signs of Cheyne Stokes and Trousseau's.

After clinical and para-clinical examination, the patient was diagnosed with medullary carcinoma of the thyroid gland and went under total thyroidectomy surgery and left incomplete thymectomy. During surgery, general anesthesia was used and the patient recovered completely after gaining consciousness in the intensive care unit. Due to the postoperative complications such as thyroid storm and spasm, and airway obstruction, the tracheostomy and CPR set were on the patients table. After stabilizing the vital signs, the patient was transferred to the men's surgical ward. The results of the pathology of the sample from the thyroid and surrounding tissues revealed medullary thyroid carcinoma; Right lobe of the thyroid tumor was 5×3×2 cm. The tumor was metaplasiated into cardiovascular, lymphatic and perineural areas (Figure 2.c). The patient was under supervision for recurrence and the occurrence of clinical symptoms after discharge.

ETHICAL CONSIDERATIONS

The study license was taken from the Ethics Committee of the Kurdistan University of Medical Sciences with the code of ethics 14/5612/4120. Then, the written consent was obtained from the patient to collect data and present the results of the study. In order to obtain consent, the patient was formally invited by the doctor to provide his documentation for publication of the scientific report and The patient signed the written consent. The patient is assured that the personal details will remain confidential.

DISCUSSION

MEN 2 is a syndrome with a prevalence of one in every 30,000 (Brewer, 2015) and MEN 2B subtype makes up approximately 5 % of the MEN 2 (Kreps et al., 2018). Therefore, the prevalence is rare and there are only a few reports (Amir Chaghmaghi et al. 2006, Kudo et al. 2014, Kim et al. 2018, and Kurozumi et al. 2013). Amir Chaghmaghi et al. (2006) reported an 8-year-old referred to the dental clinic with multiple papules on the tongue, lip and lower eyelid the diagnosis of the MEN 2B syndrome was made. Finally, the results of pathology were indicative of medullary thyroid cancer. After complete removal of the thyroid histology, the results showed medullary thyroid carcinoma. The difference between that study and the current study was the age of the patient who referred to the center. In the study of Amir Chaghmaghi et al. (2006) the patient referred at the right age and the final diagnosis was medullary thyroid cancer. The earlier diagnosis is the better the prognosis, because the patient was residing in a rural area with no access to the specialist and notwithstanding his age (18 yrs.), the patient referred to the doctor too late. The patient's symptoms were exactly the same as the 8-year-old child in the Amir Chaghmaghi study (Amir Chaghmaghi et al., 2006), and the only difference was the age-difference. In our study the patient had no family history of the disease. To confirm the findings, literature review showed that all MEN 2 subtypes were inherited in an autosomal dominant manner. In the case of the son of the patient with MEN 2, it was inherited in an autosomal dominant manner. In the son of the patient with MEN 2, the risk of inheriting the mutation MEN 2 was 50%.

More than 95% of patients with MEN 2A and more than 98% of those with MEN 2B have an identifiable mutation in the RET proto-oncogene (Shalmo et al., 2011). In other words, they carry a new mutated gene, which did not appear in their old generations. These children do not have parents, which have been affected by the mutation.

One of the highlights of the recent clinical study was late attendance of the patients to the medical centers and late-onset diagnosis of the disease. The patient underwent surgery at the age of 18 with the diagnosis of medullary thyroid cancer, which had a high risk for metastasis and recurrence of the disease. If the child was diagnosed by screening according to the non-endocrine symptoms such as marfanoid appearance, the prognosis was better which did not occur in the case of this patient. Another very important finding was the absence of pheochromocytoma, given the age of the patient, which was normal; which is frequent in 50% of the cases. Its prevalence is around 28 years.

CONCLUSION

Based on the results of this study, apart from family history and endocrine symptoms, the patient was monitored after surgery due to non-endocrine symptoms like Marfanoid appearance, mouth and facial lesions, etc. These can help with early diagnosis and prophylactic removal of the thyroid gland before creating a malignancy and subsequent metastasis.

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Authors' Contributions

Loghman Ghaderi performed the clinical data collection. Shahnaz Ghafoori and Fazel Dehvan performed the literature review, and drafting the manuscript. Ramesh Rahehagh performed the clinical data collection. All authors read and approved the final manuscript. Jamal Seidi performed the clinical data collection, literature review, and drafting the manuscript.

Implication for health policy makers/practice/research/medical education

This study provides a basis for screening and treating strategies by health policy makers and care-givers in practice. It recommended further studies. It can be integrated into medical curriculum and continuing education programs.

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