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Ectopic Thyroid in Submandibular and Sublingual Region: Report a Case and Review of Literatures

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Abstract: Ectopic thyroid consists of thyroid cells are at sites other than anterior or lateral to the second, third and fourth tracheal rings. Seventy percent of patients with ectopic thyroid, do not have any thyroid tissue at its normal anatomical location. In these patients, ectopic thyroid is prone to functional insufficiency and may come to attention only after compensatory enlargement. If there is no other functioning thyroid tissue, the removal of ectopic thyroid frequently leads to severe hypothyroidism. A patient with a lingual or sublingual thyroid does not require treatment. If patient illustrates hypothyroidism and obstructive symptoms, it is necessary to manage with hormone replacement therapy. If obstructive symptoms can not be decreased, surgical excision is recommended and if the patient does not have eutopic thyroid, the patient will require lifelong hormone replacement therapy. We introduce a 31 year-old female with a firm, nontender mass with smooth surface, mildly mobile mass in both left submandibular and sublingual regions extended to right region. A surgery of the mass of floor of the mouth with salivary gland tumor clinical diagnosis was performed. The histopathologic examination revealed ectopic thyroid. Because of the lack of eutopic thyroid, she is undertaken hormone replacement therapy. Ectopic thyroid should be considered in differential diagnosis of sublingual mass for avoiding from unnecessary treatments.

Key words: Ectopic thyroid, sublingual, submandibular, hypothyroidism

INTRODUCTION

A thyroid gland is the first endocrine gland that appears during embryonic development (Hollander *et al.*, 2004). At the end of the third embryonal week, the thyroid gland is formed as an endodermal diverticulum in the median plane at the base of the pharyngeal gut. The thyroid anlagen is connected with the base of the pharynx by thyroglossal duct. Until the seventh embryonal week the thyroid anlagen continues migration by the hyoid bone and laryngeal cartilages. Then, thyroid anlagen reaches its final location. Normaly, this gland is located in front of the developing trachea at the level of the second and third tracheal cartilages. Thyroid gland consists of two lateral lobes and a small median lobe formed from the remnants of the thyroglossal duct (Feller *et al.*, 2000). The opening of thyroglossal duct

in the tongue is called the foramen cecum (Hollander *et al.*, 2004).

Ectopic thyroid is defined as thyroid cells that are located at sites other than anterior or lateral to the second, third and fourth tracheal rings (Erich *et al.*, 2007). Ectopic thyroid is usually found in the midline sites of the neck, such as lingual, sublingual, prelaryngeal and intralaryngeal thyroid. Although ectopic tissue has also been described in non-midline sites such as eye, intratracheal location, submandibular region, aortic wall, intra thymic site, retropharyngeal region, intracardiac site, in the esophagus, abdomen, adrenal and liver (Soscia *et al.*, 2004; Gungor *et al.*, 2002; Hagiuda *et al.*, 2006; Strohschneider *et al.*, 1993). Anterior midline masses that appear suddenly are most commonly due to thyroglossal duct remnant. Less frequently, such a quickly arising mass are because of an incompletely

migration of thyroid during embryological development (Erich *et al.*, 2007; Zieren *et al.*, 2006). As in 70% of patients with displaced thyroid, there is no other functioning thyroid tissue at its normal location, the removal of ectopic thyroid frequently is followed by severe hypothyroidism (Maurice *et al.*, 1995). Tumors with identical pathological characteristics to those arising in thyroid tissue may be present in ectopic locations, although very few cases of malignant ectopic thyroid tumors reported in the literatures (Falvo *et al.*, 2005).

However, ectopic lingual thyroid tissue is an uncommon congenital anomaly, it must be considered in differential diagnosis of sublingual mass to avoid unnecessary treatments.

We report an ectopic thyroid in submandibular and sublingual region in the patient didn't have any other functional thyroid.

REPORT A CASE

A 31 year-old female patient referred to oral medicine department of Mashhad dentistry school complaining of a gradually enlarging mass in the right submandibular and sublingual region. The sublingual mass had a few years duration and submandibular mass had a 6 months duration (Fig. 1 a, b). She stated a remarkable weigh loss over the recent past weeks. All blood tests were normal including thyroid function, calcitonin and thyroglobulin.

Extraoral examination revealed a firm nontender mass located in sublingual and submandibular region. Intraoral examination revealed a firm, nontender mass with smooth surface, mildly mobile mass in the right sublingual region extended to left sublingual region. It extended from mesial of first left incisor to distal of right second molar. Its color was normal. It appears that mass involved both submandibular and sublingual region. Milking of both submandibular glands was normal.

The patient didn't have any systemic problem. Occlusal grahy and CT scan of patient's oral cavity had been performed. Occlusal grahy was normal. CT scan illustrated a hetrogen mass with calcification of the right floor of the mouth with almost well-defined border, nearly 4 cm diameter, without invasion to the bone. The CT findings were morphologically consistent with an dermoid cyst (Fig. 2). An incision biopsy of the floor of the mouth was performed, which revealed chronic mild sialadenitis. A surgery of the mass of floor of the mouth with salivary gland tumor clinical diagnosis was performed. The swelling of the floor of the mouth declined after second surgery. The histotopathologic examination revealed

follicular structures composed of single layer of cuboidal epithelial cells bounded by a basement membrane (Fig. 3a). The follicules contained an eosinophilic homogenous colloid material (Fig. 3b). The specimen was divided into several segments by extending septae from the surrounding fibrovascular capsule. These finding was consistent with the diagnosis of an ectopic thyroid gland. The postoperative scintigraphy illustrated no evidence of remaining thyroid tissue in normal anatomical site (Fig. 4) corresponding with a decrease of the serum thyroxin and increase of TSH up to $(21.7 \text{ mIU mL}^{-1})$. The patient received a substitution therapy with 1 mg day^{-1} levothyroxin. One month later laboratory tests were rechecked, TSH level was decreased. We followed up her for 1.5 years. Now she takes 2 tablet (2 mg) levothyroxin daily and she doesn't have any problem.

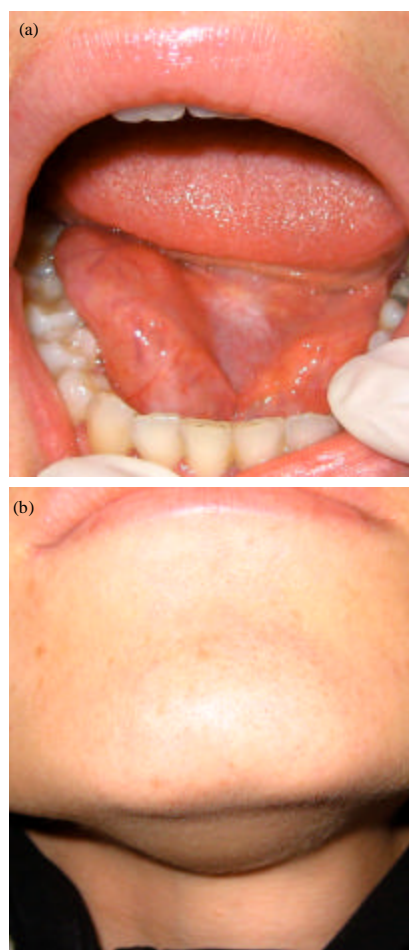


Fig. 1: Swelling in A: floor of the mouth; B: submandibular region

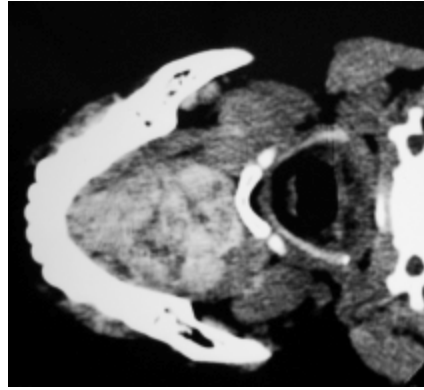


Fig. 2: CT showed a heterogenous mass with calcification in floor of the mouth with well-defined border. CT findings were morphologically consistent with a dermoid cyst

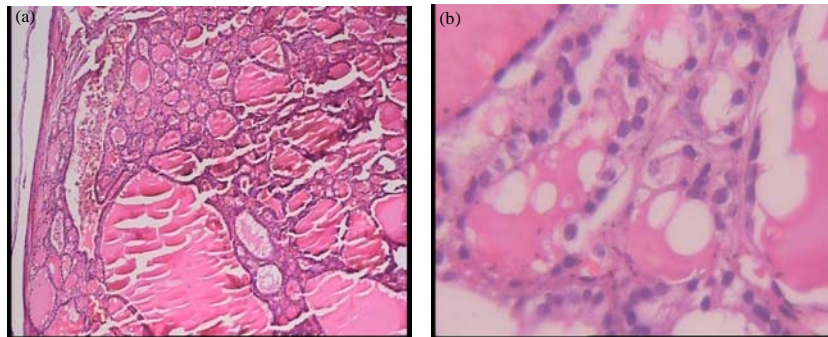


Fig. 3: Histopathologic examination (a): Follicular structures composed of single layer of cuboidal epithelial cells bounded by a basement membrane. They are surrounded by fibrovascular capsule (100 x). (b): Single layer of cuboidal epithelial cell and clear cell were observed (400 x)

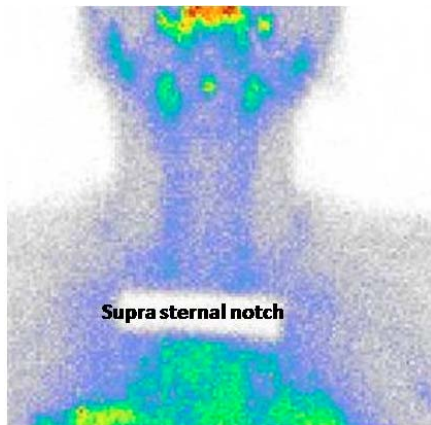


Fig. 4: An image of the Tc99m Pertechnetate scan illustrated the absence of a functioning area in the location of thyroid gland. It revealed absence of normal thyroid gland postoperative scintigraphy illustrating no evidence of remaining thyroid tissue

DISCUSSION

We reported an ectopic thyroid tissue located in submandibular and sublingual region. Ectopic thyroid consists of thyroid cells that are not located anterolaterally to the second to fourth tracheal cartilages (Feller *et al.*, 2000). However, Radkowski *et al.* (1991) and Morgan *et al.* (1995) both proposed that hypoglossal duct cysts can be displaced from the midline because of inflammation, but often, ectopic thyroid tissue is located in the midline, between the foramen caecum and the proper location of the thyroid gland (Radkowski *et al.*, 1991; Morgan *et al.*, 1995). Often it is found at the base of the tongue which so-called lingual thyroid that can rarely induce upper airway obstruction, dysphagia or hypothyroidism symptoms (Hollander *et al.*, 2004; Huang and Chen, 2007; Maurice *et al.*, 1995). Ectopic thyroid can be located in other rare sites such as the mediastinum, lung, porta hepatis, duodenum, esophagus, heart, breast, intratrachea, adrenal, pancreas and liver

(Soscia *et al.*, 2004; Gungor *et al.*, 2002; Strohschneider *et al.*, 1993). Extralingual thyroid tissue in the neck presenting as a mass in anterior cervical area, must be differentiated from thyroglossal duct cyst (Damiano *et al.*, 1996). Ectopic thyroid in the submandibular space is with a coexisting normally located; functioning thyroid gland is extremely rare (Feller *et al.*, 2000). However, cells of ultimobranchial bodies can differentiate toward thyroid follicular cells but the function of these thyroid follicular cells is not normal (Huang and Chen, 2007), so in the most patients with thyroid tissue, such as our patient, the ectopic thyroid tissue is the only functioning thyroid.

The incidence of ectopic thyroid is unknown. Post-mortem studies suggest that asymptomatic thyroid tissue may be found along the path of the thyroglossal duct in as many as 7-10% of adults (Sauk, 1970). But, some cases ectopic thyroid can lead to some complications. In 1896, Hickman first described the lingual thyroid in a newborn who was suffocated 16 hours after birth because of the mass causing upper airway obstruction (Huang and Chen, 2007). Ectopic thyroid such as sublingual deposits in other sites is much less frequent (Feller *et al.*, 2000).

Zieren in a review of the literatures reported 18 cases of an ectopic submandibular thyroid gland (Zieren *et al.*, 2006).

Ectopic thyroid tissue may coexist with a eutopic thyroid, or may be the only functioning tissue. A study of 230 patients with a clinical diagnosis of thyroglossal

duct cyst, revealed that 4 cases of ectopic thyroid tissue had simultaneously eutopic thyroid and 3 cases were without an eutopic thyroid. They suggested that the two may be equal in incidence (Radkowski *et al.*, 1991). Table 1 illustrates, a summary of studies and cases reporting ectopic thyroid in submandibular and sublingual region in the English literature cited.

The simultaneous identification of dual ectopic thyroid tissue is very unusual. In review of literature, Sood *et al.* (2008) reported 27 cases of dual ectopic thyroid gland that the mean age was 15 years. In these patients ectopic thyroid tissue was seen at the lingual region of 19 and sublingual site of 8 patients. The second ectopic thyroid gland was located at the subhyoid area in 15 cases, the suprahyoid in 8, the sublingual in 2, porta hepatis in 1 and in the submandibular area in 1 patient.

Kumar reported dual ectopic thyroid in sublingual and subhyoid regions (Kumar *et al.*, 2000a).

Ectopic thyroid was in sublingual and submandibular region in our patient but she didn't have eutopic thyroid.

The coexisting of dual ectopic thyroid tissue and a normally located functioning thyroid gland is extremely rare. Kuehn *et al.* (1966) reported one case of dual thyroid ectopy with a normal pretracheal thyroid gland.

If the patients do not have eutopic thyroid, hypothyroidism is common because ectopic tissue is hypofunctioning (McCoul and de Vries, 2009; Batsakis *et al.*, 1996).

Table 1: Summary of studies and cases reporting ectopic thyroid in submandibular and sublingual region in the English literature cited

Author(s)	Years	Age	Eutopic	Site	Gender	Country
Babazade <i>et al.</i> (2009)	2009	29	?	Sub mandible	f	Iran
Piantanida <i>et al.</i> (2009)	2009		+	Sub mandible	f	Italy
Paksoy (2007)	2007	27	?	Sub mandible	f	Turkey
Huang and Chen (2007)	2007	71	+	Sub mandible	f	Taiwan
Omur <i>et al.</i> (2007)	2007	31	+	Sub mandible	f	Turkey
Zieren <i>et al.</i> (2006)	2006	81	?	Sub mandible	f	Germany
Kanaya <i>et al.</i> (2005)	2005	53	-	Sub mandible	f	Japanese
Paresi and Shah (2005)	2005	39	-	Sub mandible	f	USA
Emlik <i>et al.</i> (2003)	2003	43	-	Sub mandible	f	Turkey
Kumar <i>et al.</i> (2001)	2001	12	-	Sub mandible	m	India
Feller <i>et al.</i> (2000)	2000	75	+	Sub mandible	f	Germany
Kumar <i>et al.</i> (2000a)	2000	42	-	Sub mandible	f	India
Kumar <i>et al.</i> (2000b)	2000	14	+	sublingual	m	India
Tucci and Rulli (1999)	1999	?	-	Sub mandible		Italy
Akoz <i>et al.</i> (1998)	1998	66	+	Sub mandible	m	Turkey.
Temmel <i>et al.</i> (1998)	1998	18	?	Sub mandible	f	Austria
Di Benedetto (1997)	1997	4	?	Sub mandible	m	Italy
Sironi <i>et al.</i> (1996)	1996	45	-	Sub mandible	f	Italy
Hansen and Christensen (1996)	1996	?	?	Sub mandible		Danish
Sambola-Cabrera <i>et al.</i> (1996)	1996	34	+	Sub mandible	f	Spain
Morgan <i>et al.</i> (1995)	1995	50	-	Sub mandible	f	Wales
Aguire <i>et al.</i> (1991)	1991	47	-	Sub mandible	f	USA
Alsop <i>et al.</i> (1986)	1986	61	-	Sub mandible	m	Canada
Helidonis <i>et al.</i> (1980)	1980	30	-	Sub mandible	f	Greece

F (female), M (male), - (negative), + (positive), ? (undetectable)

In our patient the thyroid function tests-calcitonin and thyroglobulin-were normal before the exision of the ectopic tissue. It suggests that probably the ectopic thyroid gland was functional in this patient.

Thyroid ectopy, may associate with familial and hereditary background. In sporadic and familial cases of thyroid hypoplasia or ectopy, heterozygous mutations in PAX8 and expression of the Thyroid-Per Oxidase. (TPO) and Thyro Globulin (TG) genes, have been documented (Macchia *et al.*, 1998; Congdon *et al.*, 2001). The same PAX8 mutation can lead to different biochemical and morphological phenotypes among patients (Congdon *et al.*, 2001). Some defects in other transacting proteins have not been discovered, yet (Kopp, 2002). This patient was a sporadic case that did not have any familial history about ectopic thyroid.

Pathological changes such as thyrotoxicosis and benign or malignant tumors can occur in ectopic thyroid tissue as same as eutopic thyroid gland.

Malignant transformation of ectopic thyroid tissue is rare. The estimated incidence for carcinoma arising in a lingual thyroid is only 1% (Massine *et al.*, 2001).

See *et al.* (1998) revealed the incidence of malignancy, among the 125 cases of intralaryngotracheal thyroid, was very low (1.6%).

Carcinoma arising in a congenital thyroglossal cyst is rare, these tumours arise from ectopic tissue within the cyst. Prognosis is good and metastasis is uncommon (Kum *et al.*, 1993).

Carcinoma arising in a lingual thyroid is more unusual (Massine *et al.*, 2001). However, if thyroid tissue is found in the lateral cervical lymph nodes, a metastasis of a malignant thyroid tumor should be excluded (Kousta *et al.*, 2005).

Kumar *et al.* (2000b) reported a case with symptoms of thyrotoxicosis and an expanding submandibular swelling without eutopic thyroid tissue. But our patient didn't have any symptom and sign of thyrotoxicosis or malignancy.

Differential diagnosis of sublingual mass includes dermoid cyst, salivary gland tumors, mesenchymal tumors, lymphoid tissue, metastatic tumors. The most common sites of dermoid cyst in head and neck is floor of the mouth in midline or laterally. They usually present as soft to firm, nontender mass and may be slow growing or sudden onset (Burger *et al.*, 2006; Zapater *et al.*, 2005). Because Ectopic thyroid tissue in the submandibular region cannot be clinically distinguished from a salivary gland tumors, mesenchymal tumors and lymphoid tissue, ectopic thyroid tissue should be considered in the differential diagnosis of swellings involving the submandibular area (Aguirre *et al.*, 1991).

Also, ectopic thyroid tissue should be considered in the diagnosis of a sublingual mass even in the presence of a eutopic thyroid gland.

Thyroid tissue can pose difficult diagnostic and management problems. The diagnosis is usually ascertained by fine needle aspiration cytology.

Because our patient complained of the enlarging of the mass, we considered dermoid cyst or salivary gland tumors as initial clinical diagnosis.

The three diagnostic tools in evaluating sublingual mass are radionuclide thyroid scanning, ultrasound and Computed Tomographic (CT) scanning (Erich *et al.*, 2007). Several reports in the literatures suggest an ultrasound scan will determine whether an eutopic thyroid gland is present. For identification of activity of thyroid tissue, technetium 99 m is preferred to iodine-131 because of lower dose of radiation (De Jong *et al.*, 1993). However, on CT imaging ectopic thyroid will present as high-density or hyper dense soft tissue mass, but this diagnostic medium is usually avoided because of cost and the provision of similar results by ultrasound and radionuclide scanning (Erich *et al.*, 2007; De Jong *et al.*, 1993).

On MRI, an ectopic thyroid will appear as a hyper intense mass and demonstrate considerable homogeneous enhancement on T1 and T2 weighted images (De Jong *et al.*, 1993). The importance of these diagnostic tools is to ascertain the presence of functioning thyroid before surgical excision of the ectopic mass (Mosier, 2008).

No treatment is required for a patient with a lingual, sublingual thyroid or parathyroid gland. But, if a patient presents hypothyroidism and obstructive symptoms is best managed with hormone replacement therapy, which induces the decreasing in the size of the gland. If obstructive symptoms cannot be relieved, then excision is required. If it is the only thyroid tissue, the patient will require lifelong hormone replacement therapy (Erich *et al.*, 2007). The present patient was prescribed levothyroxin after the gland excision.

Techniques of thyroid transplant that have become more promising include autotransplantation of the thyroid tissue to the lateral pharyngeal wall involving a vascular pedicle (Erich *et al.*, 2007). In one study, 131I RAID has been used successfully to demonstrate the function of partially implanted large sublingual thyroid in the left iliac fossa that kept its functional activity up to 105 days after implantation. But in that patient large sublingual thyroid had to be partially removed because of dysphagia. (Giannoulis *et al.*, 1968).

Briefly, it is very important to consider ectopic thyroid gland in differential diagnosis of submandibular

and sublingual masses. It is necessary to identify the presence of eutopic thyroid gland before the excision because if the ectopic tissue is the only functional thyroid, the hormone replacement therapy may be prescribed.

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