Review Article

Dual thyroid ectopia: A pictorial case series and review of literature

ABSTRACT

Ectopic thyroid (ET) is a developmental anomaly of the thyroid gland with the presence of thyroid tissue at sites other than the normal cervical location anterior to second and third tracheal ring due to abnormal migration of the gland. It may be found along the path of descent of the developing thyroid primordium from the foramen caecum to the isthmus of the thyroid and up to the base of the diaphragm. Dual thyroid ectopia, where ET tissue is simultaneously present at two different abnormal locations, is a very rare developmental defect. Only a few cases have been reported worldwide. ET is predominantly seen in females and during puberty when the hormonal demand is high. Patients with ET may remain asymptomatic or present with swelling in the neck, symptoms such as dysphagia, dysphonia, dyspnea, and features of hypothyroidism. The diagnosis is usually made on clinical examination, laboratory tests, imaging studies, and cytology. Careful clinical evaluation is essential as ET may be the only functioning thyroid tissue. Thyroid scintigraphy is an important imaging tool and the gold standard for the diagnosis of ET tissue, as it has high sensitivity and specificity. Early and accurate diagnosis of ET is essential to start hormone replacement and avoid unnecessary surgery. The authors report here a series of four patients with dual ET tissue, diagnosed on thyroid scintigraphy.

Keywords: Dual ectopic thyroid, dual thyroid ectopia, ectopic thyroid tissue, ^{99m}Tc-pertechnetate scintigraphy

INTRODUCTION

Ectopic thyroid (ET) is a rare developmental defect of the thyroid gland with an incidence of 16 per 100,000 births, predominantly seen in females with a male–to-female ratio of 1:2.6.[1] Having two ectopic foci of thyroid tissue is very rare and only a few cases have been reported in the literature so far.[2] The exact incidence of dual thyroid ectopia is not known. In a recent study Meng *et al*. have reported the incidence of dual ETT in the patients who underwent thyroid scintigraphy as 0.05%.[3] Another study by Wildi-Runge *et al*. and Tucker *et al*. reported an incidence of 2.5/100,000 live births for dual thyroid ectopia with a male-to-female ratio of 1:3.2[1,4] However, it is largely underestimated, as only a few individual cases are reported and not many large studies have been documented. Second, patients with dual ETT, are usually euthyroid or have less severe hypothyroidism[3] and thus might not be investigated.

The thyroid gland is normally located at the anterolateral aspect of the second and third tracheal ring,[5] but it can be found anywhere along the line of descent of thyroglossal duct (TGD) from the foramen cecum of the tongue to the base of the diaphragm.[6] They are commonly found at the base of tongue in 90% of the reported cases[6,7] In the majority of such cases (70%) orthotopic thyroid gland is absent in the pretracheal region.[5] Up to 10% of ET tissue is found in additional locations, including the sublingual space, along TGD, in the mediastinum, heart, and

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esophagus. We report here a series of four cases where ET tissue was present at two different locations simultaneously with the absence of functioning orthotopic thyroid gland on ^{99m}Tc-pertechnetate thyroid scintigraphy.

CASE REPORTS

Case 1

A 13-year-old male presented with a midline neck swelling since birth with growth retardation and hypothyroidism, he required L-thyroxine (L-T4) replacement for 5 months. ^{99m}Tc-pertechnetate thyroid scintigraphy revealed features suggestive of dual ET tissue, one in the prehyoid region, and another small focus in the lingual region with the absence of orthotopic thyroid gland [Figure 1].

Case 2

A 17-year-old male presented with a midline suprathyroid neck swelling of 2 years duration with hypothyroidism, requiring thyroxine replacement. ^{99m}Tc-pertechnetate thyroid scintigraphy was done following the withdrawal of L-thyroxine for 3 weeks, which showed the presence of dual thyroid ectopia with an ovoid focus in the neck in the subhyoid region in the midline and another small focus in the lingual region [Figure 2]. The orthotopic thyroid gland was not seen.

Case 3

An 8-year-old female child presented with midline neck swelling of 4 months duration. She had hypothyroidism and was on L-T4 replacement. Ultrasonography (USG) neck showed an oval mass in the pretracheal region with the absence of an orthotopic thyroid gland. Thyroid scintigraphy revealed a large ovoid focus seen in the suprahyoid region of the neck with an additional small focus of thyroid tissue in the lingual region, suggestive of dual thyroid ectopia [Figure 3]. Following scintigraphy, the patient was examined and a pea size swelling with a smooth surface was seen at the posterior third of the tongue.

Case 4

A 7-year-old male child presented with midline neck swelling since birth with euthyroid status. USG neck revealed the absence of an orthotopic thyroid gland, but a 2.0 cm × 2.2 cm × 0.8 cm size, nodular swelling was seen in the subcutaneous plane, suprathyroid, midline neck region, having echotexture, and vascularity similar to thyroid tissue with suspicion of the thyroglossal cyst (TGC). ^{99m}Tc-pertechnetate thyroid scintigraphy showed features suggestive of dual ET tissue, larger one in midline neck suprathyroid region, and another small focus in the lingual region with the absence of orthotopic thyroid gland [Figure 4].

DISCUSSION

ET was first described by Hickman in 1869 in a newborn who suffered airway obstruction due to lingual thyroid.[8] Only 76 cases have been reported so far with dual ET worldwide on PUBMED search as on 21 January 2020, which makes it a rare developmental anomaly. Patients may initially present with a palpable neck swelling, oral mass, or foreign-body sensation in the throat. These patients may either be asymptomatic or present with enlargement of the ectopic tissue when there is high hormonal demand during adolescence or pregnancy. The incidence of clinical hypothyroidism with ET tissue varies from 24 to 60%.[7] Majority of the reported cases had a mean age of 15 years,[2] with a male–to-female ratio 1:2.6.[1] Our patients were also young with neck swellings and hypothyroidism as presentation.

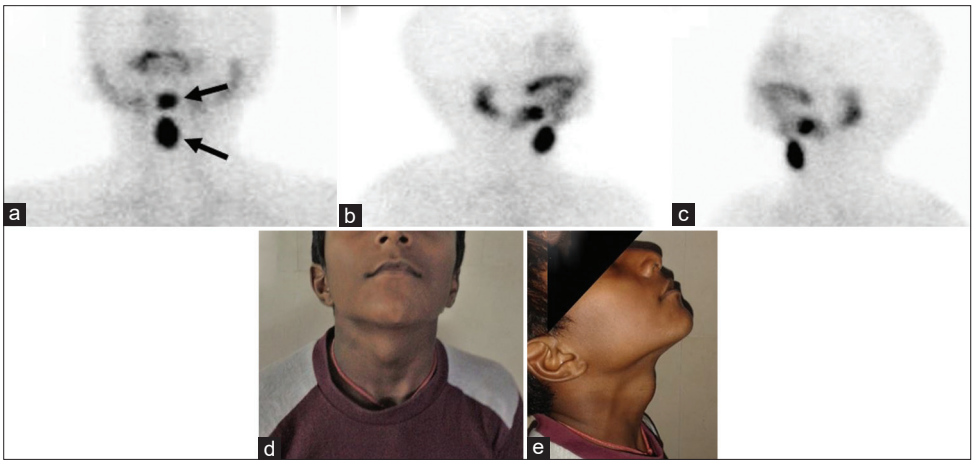

Figure 1: ^{99m}Tc-pertechnetate thyroid scintigraphy. (a) Anterior, (b) right, and (c) left anterior oblique static images. (d and e) Clinical images. A 13-year-old male child presented with midline suprathyroid neck swelling since birth with hypothyroidism, he was on LT-4 replacement. Tc-99m sodium pertechnetate thyroid scintigraphy revealed features suggestive of dual ectopic thyroid tissue one in prehyoid region (Marker 1) and another small focus in the lingual region (Marker 2)

The thyroid is the first endocrine gland to develop in humans and is the largest endocrine gland. Development occurs between the third and ninth week of gestation. It appears as an epithelial proliferation at the floor of the pharynx indicated by the foramen cecum. Thyroid descends in front of the pharyngeal gut and remains connected to the tongue by the TGD. It reaches the final position by the seventh week and starts functioning by three months of gestation.[9-11]

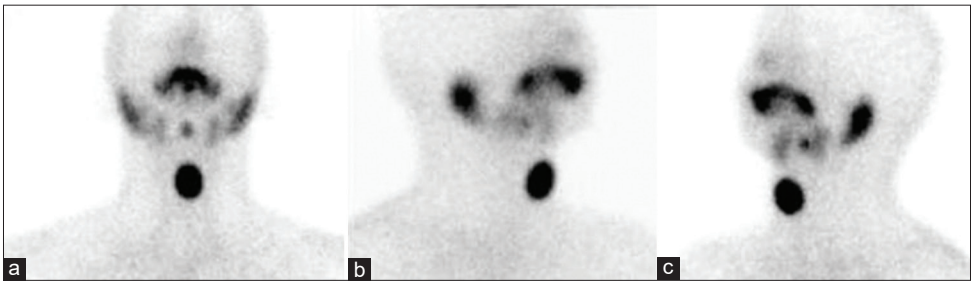

Figure 2: Tc-99m sodium pertechnetate thyroid scintigraphy. (a) Anterior, (b) right, and (c) left anterior oblique static images. A 17-year-old male presented with midline suprathyroid neck swelling of 2 years duration with hypothyroidism. Tc-99m sodium pertechnetate thyroid scan showed the presence of dual thyroid ectopia with an ovoid focus in the neck prehyoid region (Marker 1) in midline neck and another small focus in the lingual region (Marker 2) There is no tracer uptake seen in the thyroid bed

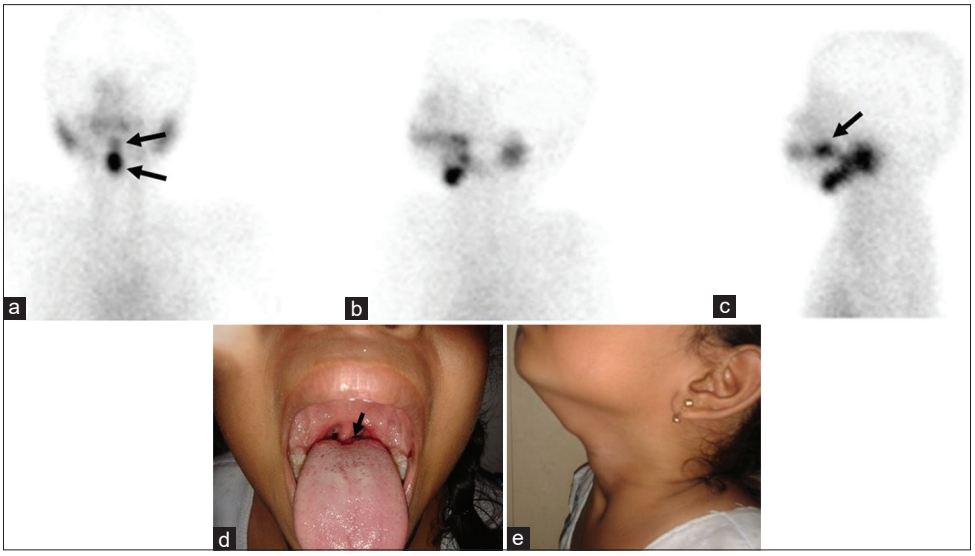

Figure 3: Tc-99m sodium pertechnetate thyroid scintigraphy. (a) Anterior, (b) right, and (c) left anterior oblique static images. (d and e) Clinical images. An 8-year-old female child presented with midline neck swelling of 4 months duration with hypothyroidism, was on LT-4 replacement. USG neck showed an oval mass in the paratracheal region with the absence of an orthotopic thyroid gland. Thyroid scintigraphy revealed a large ovoid focus seen in the suprahyoid region of the neck (Marker 1) and an additional small focus of thyroid tissue in the lingual region, posterior one-third of the tongue (Marker 2) suggestive of dual thyroid ectopia. On local examination, a pea-size swelling with a smooth surface was seen at the posterior 3rd of the tongue (marker 3)

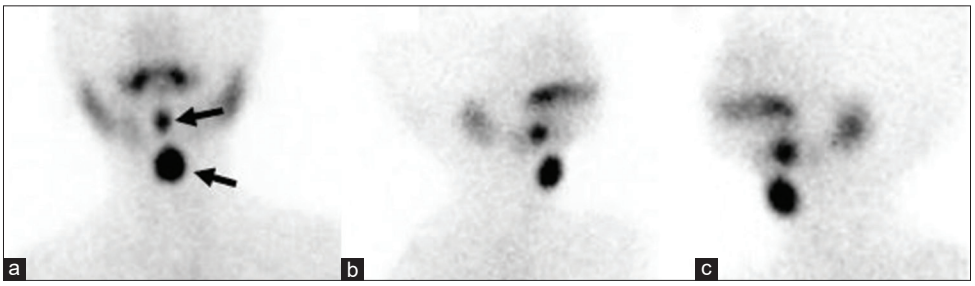

Figure 4: Tc-99m sodium pertechnetate thyroid scintigraphy. (a) Anterior, (b) right and (c) left anterior oblique static images. A 7-year-old male child presented with midline neck swelling since birth with euthyroid status. Tc-99m sodium pertechnetate scan revealed features suggestive of dual ectopia thyroid in midline neck suprathyroid region (Marker1) and another small focus in the lingual region (Marker 2). Orthotopic thyroid gland was not visualized in the normal location

Migration defects in the form of incomplete migration or displacement of cells are the most common cause of ET. Migration of thyroid anlage is attributed both due to an active process, by a mechanism not yet identified, and to mechanical traction due to its close association with primitive heart mesoderm.[12]

Exact molecular mechanism leading to abnormal thyroid migration is not well understood, mouse models suggest thyroid transcription factor 2-FOXE-1 is necessary for thyroid migration and mutation of TTF-1, TTF-2, and PAX-8 transcript factor have also been suggested. In humans, no exact genes have been identified. It has been postulated that dual ectopia thyroid can occur either due to insufficient signal gradients, which may lead to two migration pathways and due to polyclonal or oligoclonal primordial thyroid cells which do not reach the normal location.[3,11,12]

The locations in which they are commonly present are along the pathway of TGD that is lingual, sublingual, and prelaryngeal. Intrathoracic locations are reported in the mediastinum, trachea, esophagus, and pericardiac regions but can be found anywhere from the base of the tongue till diaphragm [Figure 5]. The presence of thyroid tissue away from the neck and thorax, for example., dermoid cyst, ovarian cyst is not considered ET but are considered to be development anomaly of the fetus.[6]

^{99m}Tc-pertechnetate scintigraphy, ultrasound neck, computed tomography, and magnetic resonance imaging are modalities used to diagnose ET tissue.[2] Radionuclide scintigraphy has been reported to have high sensitivity and specificity for the demonstration of functional tissue. The sensitivity of USG and scintigraphy was 10% versus 92%, respectively for the diagnosis of ET tissue, whereas the specificity was 100% versus 97.1%, respectively, to diagnose athyreosis the sensitivity of USG and scintigraphy was 90.5% versus 96.2%, respectively, and specificity of 47.8% versus 100%, and to diagnose hypoplasia of thyroid, the sensitivity of USG and scintigraphy was 100% for both modality and specificity of 80.4% versus 96%, respectively.[13] Scintigraphy with 99 mTc-Pertechnetate is considered the gold standard for the diagnosis of ET tissue as it confirms both the location and extension of the ET tissue and also the presence or absence of the thyroid gland in its normal anatomic location.[14] About 1%–3% of patients with ET tissue have been reported to undergo malignant transformation. In TGD tumors 80% of them were of papillary carcinomas; thus, fine-needle aspiration cytology may be required in certain cases wherever clinically indicated.[8,15]

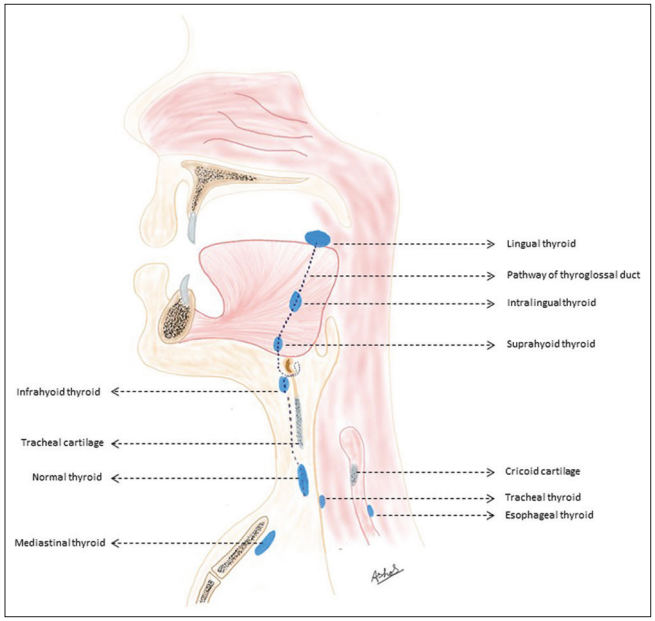

Figure 5: Diagrammatic representation of the different positions of the ectopic thyroid gland

In patients who are biochemically hypothyroid, treatment is hormonal (levothyroxine) replacement, which also reduces the goiter size. The surgery is not recommended in the absence of the orthotopic thyroid gland, as it may be the only functioning thyroid tissue. The surgery is advised only when there is proven malignancy in ET tissue.[7]

Scintigraphy allows to differentiate ET from other causes of midline neck masses such as TGD cyst, enlarged lymph node, epidermoid cyst, lipoma, vascular malformation, and malignancies. TGC is seen in 7% of the population and also presents as a midline neck mass. TGD cyst is often due to the failure of TGD to involute and atrophy. Most of the TGCs are located in the infrahyoid region (25%–65%) but may be suprahyoid (15%–50%), hyoid (20%–25%), or intralingual (3%).[6] They usually present with a midline cervical swelling that moves with deglutition and elevates on protrusion of tongue, while ET moves only with deglutition. TGD cyst is removed usually by the Sistrunk operation, which involves removal of the cyst along with the tract, body of the hyoid bone, and core tissue up to foramen cecum.[16]

In our series of four cases, dual thyroid ectopia was diagnosed only on thyroid scintigraphy. We also found that patients with dual ET tissue present with mild or less severe hypothyroidism. In all cases reported here, functioning orthotopic thyroid tissue was absent. In most of the patients, the larger ET focus is usually seen in hyoid or subhyoid locations, whereas a second smaller ET tissue was seen in lingual or sublingual location. As the size of lingual ET tissue was very small in most of the cases, thyroid tissue was not

identified on routine clinical examination. Our findings in these cases are consistent with previously published data that most common sites of dual ET tissue are hyoid, subhyoid, and lingual locations.

To conclude, dual thyroid ectopia is a rare developmental thyroid anomaly. Considering published literature, our series of cases also emphasizes the significance of thyroid scintigraphy in the diagnosis of ETT that can be missed on conventional imaging such as USG. Young individuals presenting with midline neck swelling with hypothyroid symptoms should be evaluated with ^{99m}Tc-pertechnetate scintigraphy, in addition to the detailed clinical examination and routine investigations. As early and accurate diagnosis of ET tissue enables early intervention in form of hormone replacement therapy, that not only improves the quality of life, helps in the growth and development of the young population but also sidesteps unnecessary thyroid surgeries.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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