A case report and literature review of an intrathyroid epidermoid cyst

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A case report and literature review of an intrathyroid epidermoid cyst

Abstract
Epidermoid cysts are the most common cutaneous cysts, and infrequently develop within mucosal or glandular tissue. Rarely, epidermoid cysts have been described as arising within the thyroid gland in the form of a nodule. In this paper, we describe a case of a 72-year-old female with a suspicious-appearing thyroid nodule on ultrasound, which was eventually found to be an epidermoid cyst. To our knowledge, this is the first surgical biopsy-proven case that demonstrates an intrathyroid epidermoid cyst in multiple radiographic modalities including ultrasound, nuclear medicine I-123 thyroid scan, and MRI. In addition, we present a concise review of previously described cases of intrathyroid epidermoid cysts, including patient clinical manifestations, initial sonographic appearance, and management of lesions. This case reinforces the importance of considering rare diagnoses in the workup of a thyroid nodule based on its sonographic appearance.

Keywords
epidermoid cyst, epidermoid inclusion cyst, epidermal cyst, intrathyroid epidermoid cyst

Conflict of Interest Statement
Authors have no conflict of interest

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Introduction:
Epidermoid cysts, also known as epidermal cysts, epidermal inclusion cysts, infundibular cysts, and keratin cysts, are the most common benign lesions of the skin, ovaries, and testicles. They represent approximately 85% to 90% of all excised cysts. Epidermoid cysts are derived from ectoderm and consist of an epithelial-lined wall that may be partly keratinized; this contrasts with dermoid cysts, which contain mesodermal tissue. Epidermoid cysts seldom occur in mucosal or glandular tissue, especially in the thyroid gland. These can present as solid thyroid nodules on ultrasound (US) and can be misinterpreted as aggressive nodules. In this case, a benign epidermoid cyst initially presented as a highly suspicious nodule classified as TI-RADS 5 (based on the White Paper of ACR TI-RADS committee), underwent pathological analysis and was subsequently surgically removed.1

Case presentation:
A 72-year-old female presents with complaint of a palpable midline neck lesion. The patient was found to have subclinical hyperthyroidism with a low TSH of 0.26 (normal range: 0.55-4.78) and a normal T3 of 133 (normal range: 60-181) and normal free T4 of 1.3 (normal range: 0.9-1.8). The patient denied any symptoms of hyper or hypothyroidism.

On ultrasound, the right thyroid lobe measured 4.3 x 2.2 x 1.7 cm and the left thyroid lobe measured 4.1 x 1.6 x 1.4 cm. A well-circumscribed, unilocular, avascular, homogeneous, hypoechoic mass measuring 3.0 x 2.1 x 1.3 cm was found in the right mid-inferior thyroid lobe extending into the isthmus (Fig 1a and 1b). Within this mass, there were scattered hyperechoic foci, some of which exhibited posterior acoustic enhancement. These hyperechoic foci were similar in appearance to calcifications and are highly suspicious for cancer. These types of suspicious calcification typically exhibit posterior acoustic shadowing instead of enhancement. Based on its characteristics, the nodule was classified as TI-RADS 5 for solid composition (2 points), hypoechogenicity (2 points), and punctate echogenic foci (3 points).1 For the sake of comprehensiveness, another smaller nodule that measured 1.0 x 0.9 x 0.6 cm³ was identified incidentally in the left lobe, biopsied, and found to be a benign nodule.

On nuclear medicine I-123 thyroid scan, the right thyroid gland was enlarged with mildly elevated 24-hour radioactive iodine uptake. There was photopenia in the right inferior thyroid lobe in the region of the US nodule. The above radiographic findings, along with the size of the nodule, warranted an US-guided biopsy based on the suggested diagnostic and treatment approach for thyroid nodules and TI-RADS criteria (Fig 1C)1,2. US-guided fine needle aspiration (FNA) biopsy was performed, which demonstrated nucleated and anucleated squamous cells with few interspersed keratinized squamous cells without evidence of colloid or other thyroid cellular elements (Fig 2A and 2B). At this point the differential diagnosis was epidermoid cyst, dermoid cyst, and metastatic squamous cell carcinoma. A repeat FNA biopsy was performed to decrease the chances of missing any underlying and under-sampled squamous cell carcinoma especially in older adults such as in this case. The results were unchanged when compared to the first FNA. Given the rarity of this nodule in the thyroid, MRI with contrast was performed to further characterize lesion and for surgical planning. On MRI, the nodule exhibited high T1 intensity, low to intermediate T2 intensity with no significant fat suppression or contrast enhancement (Fig 3). High T1, suggests that cyst contents are mostly proteinaceous and is likely due to keratin given the FNA results showed keratinized squamous cells in Fig 3B.
The decision to perform a right hemithyroidectomy was made based on the nodule’s suspicious appearance and high TI-RADS score for thyroid cancer. On gross pathology after resection, the cyst contained thick, dark brown fluid with a smooth and tan-pink cyst lining. The surrounding parenchyma was rubbery and dark-red, suggestive of a fibrous layer (Fig 4A). The final diagnosis of epidermoid inclusion cyst was made based on histology. The cyst contained abundant keratin and the cyst-wall lining was composed of stratified squamous epithelium with a granular layer which are characteristic features of an epidermoid cyst. No papillary areas, columnar cells, cuboid cells, cilia, glands, or hair follicles were found within the cyst wall (Fig 4B and 4C). Initially, the possibility of an intrathyroid thyroglossal duct cyst was entertained. However, due to the absence of columnar or cuboid epithelium and glands in the cyst wall, as well as the presence of keratinizing squamous epithelium, this diagnosis was unlikely.

Discussion:
The pathophysiology of intrathyroid epidermoid cysts is not well understood. Classified as congenital or acquired, many theories have been proposed regarding their pathophysiology in the neck. Congenital cysts can arise from reactivation of the ectodermic elements entrapped during the midline fusion of the first and second branchial arches. Acquired cysts are theorized to be derived from traumatic or iatrogenic inclusion of epithelial cells.

Squamous cells and keratin are principal components of epidermoid cysts. Histologically, epidermoid cysts are unilocular, well circumscribed, and lined with mature superficial squamous cells with intact nuclei, anucleate squames, and clusters of neutrophils, lymphocytes, and macrophages in a background of amorphous debris. Keratin debris is usually found within the cyst.

A brief review of 18 cases from literature search along with this case report is presented in Table 1. Based on a review of these 19 case studies describing intrathyroid epidermoid cysts, the typical age of presentation ranged from 4 to 78 years of age with a bimodal age distribution of 20’s and 50’s with a mean age of 39.9 years. (Table 1) A majority of these are unilocular and well-circumscribed with a maximum lesion size ranging from 2.0 - 6.5 cm. There is no definite predilection for sex or location of the lesion within the thyroid gland. (Table 1)

The most common presenting symptom is a painless, non-tender thyroid nodule (11 out of 19). Of the 19 cases, 12 are biochemically euthyroid given the benign nature of this lesion. Pain is reported in only 4 cases. Other presenting symptoms are neck mass, globus pharyngeus, dysphonia, dysphagia, and left recurrent nerve palsy. In our case, patient presented with a swelling in the neck with no other associated symptoms even though biochemically patient was subclinically hyperthyroid. The pathogenesis of this nodule associated with subclinical hyperthyroidism is anomalous given that this epidermoid nodule was cold on the nuclear medicine thyroid scan. Likely, this patient’s subclinical hyperthyroidism is an incidental discovery. There are no surrounding inflammatory signs to suggest leakage of thyroid hormone like thyroiditis based on radiographic imaging, gross pathology, and histology.

On sonographic imaging, an epidermoid cyst typically appears as a unilocular, well-circumscribed, and hypoechoic which is similar to our case. Hypoechogenicity is due to the densely packed proteinaceous/keratinaceous material in the cyst. Cysts can present with
hyperechoic foci as the result of highly compact deposits of cholesterol or fat as was observed in our case which are similar in appearance to microcalcifications and hence can be considered highly suspicious (Fig 1). In contrast to the typical US characteristics, one case from literature describes internal content of the cyst as isoechoic, which likely is due to variable ratio of proteinaceous to fat content. Another distinct epidermoid cyst consists of a superficial hyperechoic wall with heavy posterior acoustic shadowing. Due to this shadowing artifact, internal contents are not visualized.\(^4\) This is likely due to a partially calcified epidermal cyst with active surrounding inflammation, which has been reported in epidermal cysts in other regions.\(^5\)

Based on sonographic imaging and FNA in our case, besides thyroid parenchymal neoplasms, differential diagnoses which should be considered include dermoid/epidermoid, laryngocele, thymic cyst, lymphatic malformation, intrathyroid thyroglossal duct cyst and intrathyroid branchial cleft cyst.\(^6\) Although the risk of malignant transformation is rare, squamous cells within the thyroid gland can present as metaplastic or dysplastic cells. Benign squamous metaplasia can occur in goiter, myxedema, and thyroiditis.\(^7\) Squamous dysplasia can be seen in papillary carcinoma, squamous carcinoma, mucocellular carcinoma, adenosquamous carcinoma, and teratomas.

In the majority of the cases, including in our case, the lesions are primarily treated with hemithyroidectomy and among 19 cases, only 2 reported simple excision. A decision to perform a hemithyroidectomy was made based on the high TI-RADS criteria. None of the case reports mention any recurrence. Interestingly, one case reports drainage of the cyst with close ultrasound follow-up for a 15-year-old patient.\(^8\) The initial size of the lesion measured 2.0 x 2.8 x 3.4 cm, which was followed by drainage and reduction in the size of the lesion to 1.1 x 0.5 x 2.5 cm on follow-up with no recurrence. Drainage is a possible alternative, especially if patients would like to avoid surgery due to the potential postoperative morbidity, including recurrent laryngeal nerve injury, bleeding, and infection. However, long-term follow-up of these patients is needed, to ascertain if this is a reliable alternative to simple excision or hemithyroidectomy.
Figure 1. (A) Sagittal view of right thyroid lobe. Hypoechoic lesion with multiple punctate hyperechogenic foci (white arrowheads) which exhibit posterior acoustic enhancement. (B) Transverse view of the right thyroid lobe with hyperechogenic foci (white arrowheads). Same lesion from Figure 1A shown extending from the right lobe into the isthmus. (C) I-123 thyroid of the thyroid gland shows enlarged right thyroid lobe with mildly elevated 24-hour uptake (26.5%; normal 8%-25%) of radioactive iodine. There is a photopenic region (white arrowhead) in the inferior right thyroid lobe on anterior (ANT), left anterior oblique (LAO) and right anterior oblique (RAO).
Figure 2. Fine needle aspiration biopsy of the intra-thyroid lesion. (A) Anucleated (black arrowheads) and nucleated (white arrowheads) squamous cells seen (10x cytospin prep PAP stain). (B) Keratinizing squamous cells (pink colored squamous cells) interspersed with anucleated and nucleated squamous cells (10x PAP stain).
Figure 3. MRI of the neck. (A) Axial T1 sequence shows a high T1 intensity nodule in the right thyroid lobe (white arrows), (B) Axial T1 fat saturation sequence shows no significant fat suppression of the contents (white arrows), (C) Axial T1 fat saturation sequence with intravenous ProHance contrast shows no significant enhancement, (D) Axial T2 sequence shows a low to intermediate signal.
Figure 4. (A) Right hemithyroidectomy gross pathology showing right lobe of thyroid measuring 5.0 x 4.0 x 2.5 cm with a nodule (*) measuring 3.5 x 3.0 x 1.5 cm. (B) Histology of the surgical specimen shows the lining of the intrathyroid cyst with stratified squamous epithelium with granular layer; note the surrounding thyroid follicles and the lack of columnar cells, cuboidal cells, sebaceous glands, or eccrine glands within the wall; the cyst (Cy) contents are composed of some keratin flakes shown by arrows (10x H&E stain). (C) Abundant keratin flakes (black arrows) within the cyst (4x H&E stain).
<table>
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<th>Case</th>
<th>Age</th>
<th>Gender</th>
<th>Location</th>
<th>Size</th>
<th>US</th>
<th>Symptoms, Physical exam</th>
<th>Biochemical</th>
<th>Treatment</th>
<th>Reference</th>
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<td>1</td>
<td>28</td>
<td>M</td>
<td>Right</td>
<td>6.5 x 6.0 cm</td>
<td>Cystic, hypoechoic with punctate echogenic foci, and smooth margins</td>
<td>Painless, firm, swelling for 10 years</td>
<td>Euthyroid</td>
<td>Hemithyroidectomy</td>
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<td>2</td>
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<td>3.1 x 1.8 x 3.2 cm</td>
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<td>Surgical excision</td>
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<td>Left</td>
<td>2.0 x 2.8 x 3.2 cm</td>
<td>Solid and homogeneous hypoechoic lesion macrocalcifications</td>
<td>Smooth, painful, palpable lump for 3 weeks with globus pharyngeus and pain with swallowing</td>
<td>Euthyroid</td>
<td>Drainage with close followup</td>
<td>Ref 8</td>
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<td>54</td>
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<td>Right</td>
<td>3.2 x 3.0 x 2.6 cm</td>
<td>Hypoechoic mass</td>
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<td>Euthyroid</td>
<td>Hemithyroidectomy</td>
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<td>6</td>
<td>46</td>
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<td>Right</td>
<td>2 x 3 cm</td>
<td>Characteristics of a colloid goiter (iso-hypoechoic with possible multiple echogenic foci)</td>
<td>Painless neck swelling for 6 months.</td>
<td>Euthyroid</td>
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<td>7</td>
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<td>Left</td>
<td>4 x 3.5 x 2.0 cm</td>
<td>Homogenous, isoechoic to thyroid parenchyma with a clear margin</td>
<td>Painless neck swelling for 10 years</td>
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<td>Ref 14</td>
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<td>2 x 2 cm</td>
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<td>Painless, firm mass for 6 months</td>
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<td>Procedure</td>
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<td>9</td>
<td>26</td>
<td>F</td>
<td>Right</td>
<td>-</td>
<td>Pain with swallowing and neck swelling for 6-7 months</td>
<td>Euthyroid</td>
<td>Hemithyroidectomy</td>
<td>Ref 16</td>
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<td>10</td>
<td>38</td>
<td>F</td>
<td>Left</td>
<td>1.2 x 3.0 x 1.0 cm</td>
<td>Hypoechoic lesion</td>
<td>Nonpalpable</td>
<td>Euthyroid</td>
<td>Hemithyroidectomy</td>
<td>Ref 3</td>
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<tr>
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<td>27</td>
<td>M</td>
<td>Left</td>
<td>3.2 x 1.5 cm</td>
<td>Crescentic, slightly hyperechoic anterior surface with deep posterior acoustic attenuation, making it impossible to evaluate the internal structure</td>
<td>Palpable lesion slowly growing for 10 years.</td>
<td>Euthyroid</td>
<td>Hemithyroidectomy</td>
<td>Ref 4</td>
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<td>12</td>
<td>60</td>
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<td>3.0 x 3.0 cm</td>
<td>Hypoechoic mass</td>
<td>Dysphonia, and left recurrent laryngeal nerve palsy</td>
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<td>Hemithyroidectomy</td>
<td>Ref 17</td>
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<td>13</td>
<td>50</td>
<td>F</td>
<td>Right</td>
<td>4.4 cm</td>
<td>Hypoechoic mass with multiple echogenic foci</td>
<td>Nontender, palpable mass in neck with discomfort on swallowing</td>
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<td>Hemithyroidectomy</td>
<td>Ref 18</td>
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<td>Left</td>
<td>3.0 x 2.0 cm</td>
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<td>-</td>
<td>-</td>
<td>Surgical excision</td>
<td>Ref 19</td>
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<td>M</td>
<td>Left</td>
<td>2.0 cm</td>
<td>-</td>
<td>Tender nodule and discomfort with swallowing</td>
<td>-</td>
<td>Hemithyroidectomy and isthmusectomy</td>
<td>Ref 20</td>
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<td>58</td>
<td>M</td>
<td>Right</td>
<td>1.1 cm</td>
<td>Hypoechoic</td>
<td>Asymptomatic, incidentally found</td>
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<td>Hemithyroidectomy and isthmusectomy</td>
<td>Ref 20</td>
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<td>17</td>
<td>26</td>
<td>F</td>
<td>Left</td>
<td>-</td>
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<td>Tender, palpable, mobile</td>
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<td>Simple excision</td>
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<tr>
<td>18</td>
<td>M</td>
<td>Right</td>
<td>Painful palpable neck swelling for 6 weeks followed by sore throat and progressive neck swelling for 2 weeks</td>
<td>Mixed echogenic multiloculated solid-cystic lesion</td>
<td>Subclinical hypothyroidism with low TSH and normal T3 and T4</td>
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<td>Ref 22</td>
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<td>19</td>
<td>F</td>
<td>Right</td>
<td>Asymptomatic painless neck swelling</td>
<td>Hypoechoic mass with scattered hyperechoic foci</td>
<td>Subclinical hypothyroidism with normal T3 and T4</td>
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Conflict of interest:
The authors have no conflict of interest to declare. All co-authors have seen and agree with the contents of the mauscript and there is no financial interest to report.
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