

Ultrasound Diagnosis of Primary Squamous Cell Carcinoma of Thyroid Gland: Case Report and Review

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Abstract: Primary squamous cell carcinoma (PSCC) arising from the thyroid gland is an unusual entity with a lower incidence among all thyroid malignancies. It has an extremely aggressive phase and an overall poor prognosis. PSCC of the thyroid is commonly treated with surgical excision, followed by additional resection for tumor recurrence. We describe here a rare case report of a male patient who had complained of neck swelling and dysphagia for 6 months. Conventional ultrasonography showed a huge suspicious mass characterized as being heterogeneous hypoechoic, microlobulating, and solid with blurred margins and microcalcifications and with a seemingly defective thyroid capsule; color Doppler flow imaging showed the patient had little blood at the margins, and power Doppler examination was noted with patterns II of blood flow. Real-time ultrasound elasticity was performed to improve accuracy in predicting the malignancy of the mass, and ultimately, the carcinoma was definitely diagnosed as PSCC with the ultrasound-guided core needle biopsy. When pathologist conducted a comprehensive review of the specimens, immunohistochemistry showed nests of tumor cells showing positive immune-reactivity for P63, CK19 (+), and CK5/6 (+) and negative for TTF-1 and thyroglobulin. Herein, we report the findings of conventional ultrasonography and real-time ultrasound elastography of a rare case of PSCC.

Key words: Thyroid gland; Squamous cell carcinoma; Ultrasonography; Elastography

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Primary squamous cell carcinoma of the thyroid gland (PSCCT) is an unusual entity with an incidence of less than 1% of all thyroid malignant diseases [1]. Diagnosis is difficult at an early stage due to the rarity and the lack of typical radiological findings [2, 3]. Furthermore, PSCCT is highly aggressive with a very poor prognosis. Complete surgical excision is recommended as an optimal therapy for a longer survival, however, the cancer has a high chance of recurrence and local invasion or infiltration after its surgical excision [2]. PSCCT responds poorly to chemotherapy and is relatively resistant to radiotherapy, and the outcome and benefit of postoperative adjuvant therapy is controversial [4]. In the present study, ultrasound was used to make the

diagnosis and surgical excision was used as a primary choice of the treatment based on available evidence. Only a few sporadic cases of ultrasound used in PSCCT have been published in the literature. This study aims to investigate the multi-mode ultrasonic features of PSCCT in order to identify whether multi-mode ultrasound is beneficial to improve the efficiency of diagnosis.

Case Report

A 75-year-old male patient presented with complaints of tenderness and enlargement on the right lobe of the thyroid, dyspnea with exertion, and hoarseness of voice within the past 6 months. He had smoked and consumed

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tobacco or the past 50 years He had no medical history of diabetes mellitus and hypertension, but reported recent weight loss of about 5 kg.

Physical examination detected a hard and immobile neck mass 4×4 cm in size and palpable in the right neck. Examination of the chest, heart and abdomen with all vital signs was normal. Laboratory findings showed that the thyroid hormone profile was in the normal range; anti TG antibody and anti TPO antibody assays were negative; and there was no leukocytosis or hypercalcemia.

The result of computed tomography scan of the neck and upper thorax revealed an enhancing soft tissue mass in the right lobe of the thyroid lesion, extending up to the retrosternal area, which compressed the trachea and the carotid region. Ultrasonography findings showed a huge tissue mass, $4.6 \times 3.6 \times 4.9$ cm in size, that was heterogeneously hypoechoic, microlobulating, and solid in the right thyroid lobe with blurred margin and micro-calcifications, and a seemingly defective thyroid capsule (Fig. 1A). Color Doppler flow imaging showed the patient had little blood at the margin (Fig. 1B). Power Doppler examination showed patterns II of blood flow (Fig. 1C). Several lymph nodes were

revealed with suspicious hypoechoic features in the right neck and bilateral supraclavicular area (Fig. 1D). Since strain elastography can be affected by the degree of compression and experience of the sonographers, examinations were performed, that revealed 4-scale scoring systems and a strain ratio value of 299.3 (Fig. 2A). Ultrasound-guided core needle biopsy (CNB) was performed to collect specimens for histological examination of the tumor growth in the thyroid gland immediately after ultrasonography, Color Doppler examination, and strain elastography. Hematoxylin-eosin (HE) staining shows nest-like squamous cells with hyperchromatic nuclei, obvious atypia, and keratinizing components (Fig. 2B). Immunohistochemistry showed nests of tumor cells that were positive for P63, CK19 (+), and CK5/6 (+) and negative for TTF-1 and thyroglobulin. The histopathology diagnosis confirmed the mass was squamous cell carcinoma (SCC). Additional examinations, including bronchoscopy, oesophagoscopy, chest radiography, echocardiography, a bone scan, and PET-CT, had ruled out all of the primary lesions and secondary SCC of any other origins. However, the patient refused to undergo thyroidectomy, chemotherapy, or radiotherapy, and did not return for follow-up.

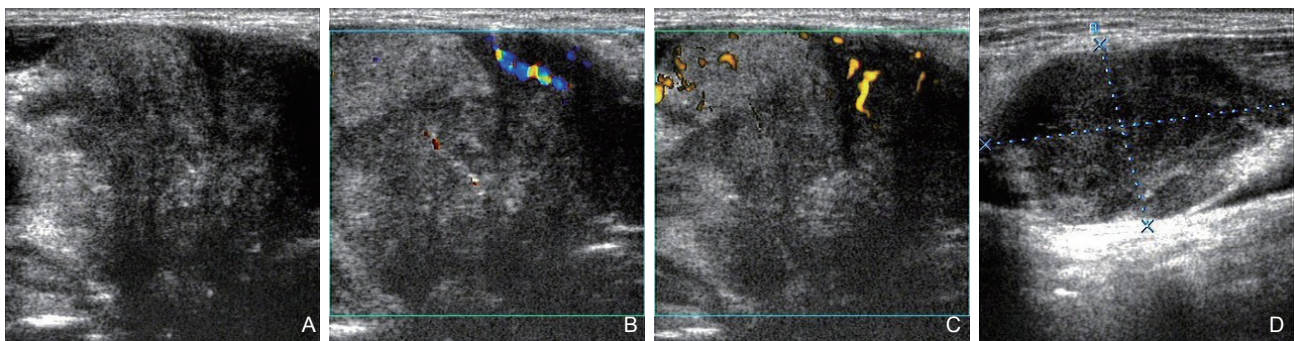


Figure 1 Conventional ultrasonography of the right lobe of thyroid gland showed a huge heterogeneous hypoechoic, microlobulating, solid mass, with blurred margin and microcalcifications and an apparently defective thyroid capsule (A). Color Doppler flow imaging showed the mass had little blood at the edge (B) and power Doppler examination showed patterns II of blood flow (C). Grayscale ultrasound scan showed several lymph nodes with suspicious hypoechoic features in the right neck (D).

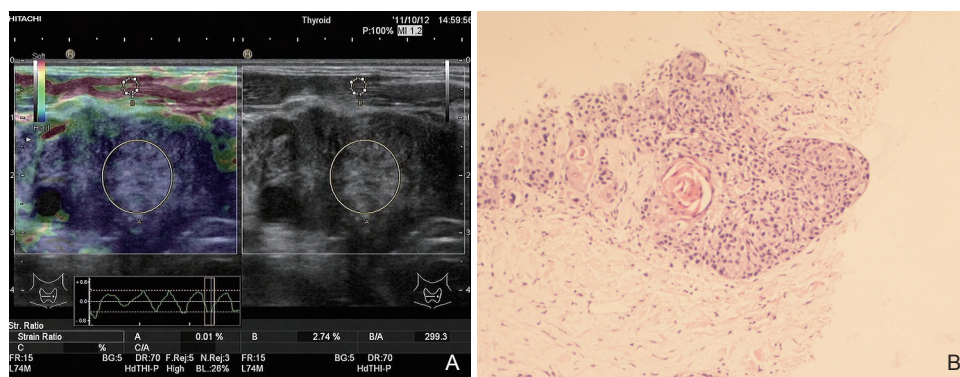


Figure 2 Real-time elastography showed the mass with a score of 4. (A) Elastographic map indicated that strain ratio was 299.3, one circle on the infrahyoid muscle and one on PSCCT. (B) Hematoxylin-eosin (HE) staining showing nest-like squamous cells with hyperchromatic nuclei, obvious atypia, and keratinizing components ($\times 100$).

Discussion

Primary squamous cell carcinoma of the thyroid gland (PSCCT) is extremely rare, constituting less than 1% of all thyroid carcinomas, and characterized by an aggressive, highly fatal clinical course. Typical clinical features of PSCCT are a rapidly enlarging neck mass and obstructive symptoms [8]. The main cause of death is respiratory interference from airway infiltration or compression of the upper respiratory tract. Median survival is reported as less than six months [5]. PSCCT usually occurs in adults 60–70 years of age, but it can be seen at any age [6]. Complete surgical excision of the carcinoma and adjuvant radiotherapy of adjacent organs could prolong life. However, this uncommon malignancy has a poor response to chemotherapy and is relatively resistant to radiotherapy [4, 7].

As the normal thyroid gland lacks squamous cell epithelium, the exact etiology of primary SCC is uncertain. Several hypotheses have been put forward to explain PSCCT, including the “embryonic rest theory” and the “metaplasia theory”, and in recent years, the metaplasia theory has gained more recognition [4].

Ultrasonography and ultrasound elastography findings of PSCCT have seldom been published. PSCCT has been described previously as a tumor with eggshell calcification [5]. Another report revealed the ultrasound and CT findings of local recurrence of PSCCT, including a huge sized, lobulating, heterogeneously hypoechoic mass with diffuse micro-calcifications. Contrast-enhanced CT showed a well-defined heterogeneously enhancing soft tissue mass with a central nonenhancing portion and peripheral heterogeneously enhancing portion. The US and contrast-enhanced CT showed a capsule that seemed to be defective [9]; in our case report, CT findings of PSCCT were similar. Conventional US findings showed the neoplasm presented as a relatively huge, isolated, heterogeneously hypoechoic soft tissue mass with blurred margins and a micro-lobulated shape. Moreover, the US findings revealed that the solid mass had diffuse micro-calcifications, a defective capsule, and several lymph nodes with suspicious features. The primary SCC was large, which may reveal the nature of neoplasm by its rapid growth. The speculated margins and micro-calcifications were suspicious features of malignant cancer of the thyroid, which disclosed a better specificity and sensitivity. The nature of tumor mass with hypoechoic and lobulation also indicated thyroid tumor [10]. Even though all US findings of the primary squamous cell carcinoma were consistent with thyroid malignancy, we could not confidently confirm it as malignancy, based on US findings alone.

Power Doppler examination, a noninvasive sonographic technique that can be used to evaluate

thyroid nodules [11]. Blood flow on power Doppler is classified into five patterns. The feature of pattern I indicates the absence of blood flow. Pattern II is defined as exclusively perinodular blood flow. If both perinodular and comparatively intense central blood flow were identified, the pattern is defined as III. Pattern IV indicates perinodular and comparatively central blood flow. Pattern V denotes exclusively central blood flow. The features of pattern IV and V are central blood flow predominating over perinodular blood flow and exclusively central blood flow respectively [12]. In this case, power Doppler US of the soft tissue mass showed pattern II, which was identified exclusively as perinodular blood flow in malignancy of the thyroid gland. However, power Doppler patterns III and IV of blood flow were considered to be features of thyroid cancer [13]. One reason for Pattern II may be the massive amount of proliferating fibrous tissue in the interstitial area while another reason may be the invasion of blood vessels, which can lead to the formation of blood clots that can block blood vessels

Ultrasound elastography is another adjuvant tool that plays a vital role in differentiating benign and malignant nodules and in diagnosing the progression of growth through assessment of tissue hardness and strain ratio value [13]. Strain elastography requires the operator to exert an endogenous stress with the probe, resulting in an axial displacement of the tissue, whose stiffness will display a series of colors from red to blue or calculate strain ratio through the machine [11]. As the strain ratio increases, the likelihood of thyroid carcinoma also increases [14]. In our case, the elastographic point scores of soft tissue were 4 with Asteria scores. The strain elastography indicated the elastic strain ratio value at 299.3. Nodules with Asteria scores ≤ 2 were defined as benign nodules.

Immunohistochemistry is necessary for the diagnosis of PSCCT, histological features of intercellular bridges, and keratin are the classic triad of features of PSCCT [15]. Chavan et al. [16] reported that all PSCCTs were positive for CK5/6 (+), CK19, P63 and negative for TTF-1 and thyroglobulin. Six of eight primary thyroid SCCS reported by Booya et al. [17] were negative for TTF-1, and Chen et al. [5] reported the staining was negative for TTF-1 and positive for P63. In our case, immunohistochemistry showed nests of tumor cells showing positive immune-reactivity for P63, CK19 (+) and CK5/6 (+), the tumor was negative for TTF-1 and thyroglobulin, similar to previous reports.

Conclusion

PSCCT is an extremely rare malignancy with a poor

prognosis and difficult diagnosis. PSCCT presents on ultrasound as a large solid mass with heterogeneous hypoechoic tissue, blurred margins and a microlobulated shape, along with a higher strain ratio than benign nodules. The ultrasound elastography score was 4. Earlier detection and accurate diagnosis should be considered to achieve surgical resection and a better prognosis. Grasping ultrasound manifestations of PSCCT combined with elastography are beneficial to improve the efficiency of diagnosis. Therefore, the importance to the diagnostic value of multi-mode ultrasound in uncertain thyroid nodules should be accorded.

Conflict of Interest

The authors have no conflict of interest to declare.

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