Primary squamous thyroid cancer: A case report

SHUCHANG DONG[1], XUEWEN WANG[2], ZIWEN ZHOU[1], LINGJUN FENG[2] and QINGLIANG XU[2]

[1]School of Clinical Medicine, Shandong Second Medical University, Weifang, Shandong 261000, P.R. China;
[2]Department of Thyroid and Breast Surgery, Affiliated Hospital of Shandong Second Medical University, School of Clinical Medicine, Shandong Second Medical University, Weifang, Shandong 261000, P.R. China

Received January 15, 2025; Accepted August 27, 2025

DOI: 10.3892/ol.2025.15301

Abstract. Primary squamous cell carcinoma of the thyroid (PSCCT) is a rare malignancy characterized by low incidence, high aggressiveness and poor prognosis, with no established standardized treatment guidelines. The present case involves a 66-year-old female who presented with a painless left neck mass discovered incidentally in July 2023. The mass progressed over two months, accompanied by dyspnea. In September 2023, surgical intervention confirmed a poorly differentiated thyroid carcinoma (6.0x5.0 cm, invading the anterior cervical muscles; Ki-67 ≈60%, mutant-type p53) in the left lobe and nodular goiter in the right lobe. The patient underwent left radical thyroidectomy and right lobectomy (no lymph node metastasis detected in 9 central compartment nodes). Postoperative PD-L1 testing revealed high expression (CPS=50). From November 2023 to February 2024, the patient completed 6 cycles of chemotherapy (albumin-bound paclitaxel + carboplatin) combined with immunotherapy (tislelizumab). Partial radiotherapy (16/25 fractions) was initiated in March 2024 but discontinued due to radiation-induced mucositis and leukopenia. Follow-up in June 2024 demonstrated complete response (CR) with no evidence of recurrence. This case achieved complete response (CR) through multidisciplinary integrated therapy, providing clinical evidence for PSCCT treatment optimization. Given the rarity and therapeutic uncertainty of PSCCT, our study highlights: The critical value of immunohistochemistry (CK19+, CK5/6+, TTF-1-, TG-) in differential diagnosis; Potential benefits of immunotherapy in PD-L1-high expressors; The necessity of combining surgery with systemic therapies and demand for individualized strategies.

Correspondence to: Professor Lingjun Feng or Professor Qingliang Xu, Department of Thyroid and Breast Surgery, Affiliated Hospital of Shandong Second Medical University, School of Clinical Medicine, Shandong Second Medical University, 2428 Yuhe Road, Kuiwen, Weifang, Shandong 261000, P.R. China
E-mail: wfyxyfsyyflj@163.com
E-mail: qingliang1230@163.com

Abbreviations: PSCCT, primary squamous cell carcinoma of the thyroid; CK, cytokeratin; TG, thyroglobulin; MRI, magnetic resonance imaging; LDH, lactate dehydrogenase

Key words: squamous thyroid cancer, primary, surgery, radiation oncology, chemotherapy

Introduction

Primary squamous cell carcinoma of the thyroid (PSCCT) is a rare and aggressive malignancy comprising <1% of all thyroid cancer cases (1) and is attributed to the normal absence of squamous epithelium in the thyroid gland under physiological conditions (2,3). Immunohistochemistry is pivotal for a definitive diagnosis, helping to distinguish PSCCT from metastatic tumors of other primary origins (4). Immunohistochemical results of PSCCT tumor cells showed diffuse positivity for cytokeratin 5/6 (CK5/6), cytokeratin 19 (CK19), epithelial membrane antigen (EMA), p53, and p63, while being negative for thyroid transcription factor-1 (TTF-1), galectin-3, and thyroglobulin (TG) (5). Clinically, PSCCT typically manifests as a rapidly enlarging mass in the anterior neck region. Surgical resection remains the primary treatment modality; however, no standardized therapeutic guidelines exist owing to its rarity (6). Consequently, the efficacy of adjuvant chemotherapy, radiotherapy, and targeted therapy remains unclear.

The study of SCCT is important in modern medical research; however, it poses considerable challenges. The low incidence of PSCCT, coupled with its aggressive nature and therapeutic challenges, have attracted extensive research interest (3,4,7,8). Investigations primarily focus on etiology, pathology and treatment (7,8). Etiologically, the underlying pathogenic mechanisms remain unclear, with only a few hypotheses having been proposed. It may originate from the thyroid follicular epithelium or develop through squamous metaplasia (9), whereas other studies propose a potential association with the thyroglossal duct epithelium (10-12). Pathologically, further detailed analyses are required regarding the tumor cell microstructure, molecular markers and tissue relationships. Therapeutically, surgical resection is the mainstay; nevertheless, standardized protocols are absent owing to the rarity of the disease. Consequently, the evaluation and optimization of chemotherapy, radiotherapy and targeted therapies remain exploratory and contentious (13). Targeted therapy, for example, faces challenges such as drug resistance, limited efficacy and individual variability (14). Furthermore, cytokines play a dual role in tumor therapy and inflammatory regulation, potentially enhancing antitumor immunity and influencing the

tumor-associated microenvironment (15). In summary, regardless of research progress, a comprehensive diagnostic and therapeutic framework for PSCCT remains elusive. Therefore, the present study aims to provide an in-depth investigation into the pathological and therapeutic challenges of PSCCT, with a particular focus on its molecular biological characteristics and treatment responses. This objective was accomplished through a detailed analysis of a representative case report combined with a comprehensive review of relevant literature. The case report forms the core of our research, offering concrete clinical and molecular insights that complement the existing body of knowledge. In the discussion section, we integrate these observational findings with current evidence to elucidate the pathogenesis of PSCCT, highlight novel treatment approaches, and identify potential strategies for improving patient survival rates and quality of life. The present study aimed to lay a solid theoretical foundation for the development of more scientific and rational clinical guidelines.

Case report

In July 2023, a 66-year-old female patient discovered a swelling in the left anterior neck, which was approximately the size of a walnut, without accompanying pain, compressive symptoms or hyperthyroidism. The patient had a history of psoriasis, which remained untreated, with no other notable medical conditions. Thyroid ultrasound examination using the Resona 8S system (Mindray) equipped with an L14-5WU transducer (Fig. 1) revealed multiple bilateral thyroid nodules (Chinese Thyroid Imaging Reporting and Data System-3) (16) upon referral to Affiliated Hospital of Shandong Second Medical University (Shandong, China). A fine-needle aspiration biopsy was recommended for a definitive diagnosis; however, the patient declined the procedure.

After 2 months, the patient returned with marked enlargement of the mass, accompanied by increased neck swelling and dyspnea. The patient was readmitted with a provisional diagnosis of 'thyroid mass (nature to be determined)'. The patient underwent a surgical intervention under general anesthesia in September 2023. Preoperative blood routine tests showed no significant abnormalities; preoperative thyroid function tests indicated anti-thyroglobulin (TG) antibody level at 320 IU/ml (reference range, ≤115 IU/ml), with all other parameters normal. Postoperative re-examination of six thyroid function items yielded the following results: Free triiodothyronine, 4.26 pmol/l (reference range, 3.1-6.8 pmol/l); thyrotropin receptor antibody <0.8 IU/l (reference range, ≤1.75 IU/l); free thyroxine, 15.60 pmol/l (reference range, 11.97-21.88 pmol/l); anti-TG antibody, 87.60 IU/ml (reference range, ≤115 IU/ml); thyroid-stimulating hormone, 3.93 μIU/ml (reference range, 0.27-4.2 μIU/ml); and anti-thyroid peroxidase antibody, 19.40 IU/ml (reference range, ≤34 IU/ml). The preoperative cardiac enzyme profile showed the following results: LDH, 239.0 U/l (reference range, 120-250 U/l); creatine kinase, 43.0 U/l (reference range, 40-200 U/l); CK-MB, 14.00 U/l (reference range, <25 U/l); and α-hydroxybutyrate dehydrogenase, 191.0 U/l (reference range, 95-250 U/l), with all the indicators within the normal ranges.

Intraoperative examination showed a firm, 6.0x5.0-cm mass in the left thyroid lobe, with invasion into the anterior cervical muscles. The right lobe contained a well-circumscribed, regularly shaped, firm, 1.5x1.0-cm nodule at its lower pole. Sections were prepared at a freezing temperature of -20°C with a thickness of 5 μm. Hematoxylin and eosin staining was subsequently performed at 26°C for 10 min. The stained sections were examined using an optical microscope at magnifications of 10x and 20x.) (Fig. 2) revealed a poorly differentiated carcinoma in the left thyroid and a nodular goiter with focal papillary hyperplasia of the follicular epithelium and cholesterol crystal deposition in the right thyroid. Consequently, the patient underwent a radical left thyroidectomy for the carcinoma and a right lobectomy for the nodular goiter. No metastatic carcinoma was found in all nine examined central lymph nodes in the postoperative pathology. Immunohistochemical (IHC) analysis yielded the following results: CK19(+); thyroid transcription factor-1(-); TG(-); carcinoembryonic antigen(-); galectin-3(-); cyclin D1(-); p53(mutant type); epithelial membrane antigen(+); CK5/6(+) and Ki-67(+) (~60%). The following primary antibodies were employed: CK19 (OriGene Technologies, Inc.; cat. no. ZM-0074), galectin-3 (ZSGB-BIO, Cat#: ZM-0143), CEA (ZSGB-BIO, Cat#: ZM-0062), EMA (cat. no. ZM-0095), TG (ZSGB-BIO, Cat#: ZM-0241), Ki-67 (ZSGB-BIO, cat. no. ZM-0166), TTF-1 (Gene Tech, Cat#: GT-2180), p53 (Gene Tech, Cat#: GT-2095), CK5/6 (Gene Tech, Cat#: GT-2438), and cyclin D1 (RMA-1125). All antibodies were ready-to-use and required no dilution. Incubation was carried out at 37°C for 30 min. For detection, DAB Titan Super (Fuzhou Maixin Biotech, Cat#: TT-0805) was used as a ready-to-use, high-sensitivity labeled anti-mouse/rabbit IgG polymer. The staining reaction was developed at 25°C for 30 min. Finally, the specimens were examined using optical microscopes at 10x magnification (Fig. 3). Based on the clinical presentation and pathological findings, the diagnosis was confirmed as Primary squamous thyroid cancer. The following recommendations were made, following multidisciplinary consultations involving nuclear medicine, radiation oncology and medical oncology teams: i) Comprehensive systemic evaluation including contrast-enhanced magnetic resonance imaging (MRI) of the brain and cervical spine, along with whole-body MRI, to establish accurate clinical staging, rule out secondary malignancies and provide baseline tumor assessment; ii) molecular profiling, including programmed death-ligand 1 (PD-L1) expression and BRAF/RAS mutation testing; and iii) implementation of combination therapeutic strategies (including potential immunotherapy or chemotherapy) based on comprehensive diagnostic workup. The patient had routinely taken 200 mcg levothyroxine sodium tablets each day in the postoperative period until December 2024.

In October 2023, the patient underwent PD-L1 testing at another hospital. IHC analysis was employed to assess protein expression levels, utilizing the PD-L1 IHC 22C3 pharmDx assay kit (Dako North America Inc.; cat. no. CH5.3 SK006). This kit qualitatively detects PD-L1 protein in neutral buffered formalin-fixed, paraffin-embedded tumor tissue. The test results indicated high PD-L1 expression (combined positive score=50) (17). Radiotherapy combined with immunotherapy was recommended to the patient according to the multidisciplinary team. The patient underwent six cycles of chemotherapy combined with immunotherapy in the Department of

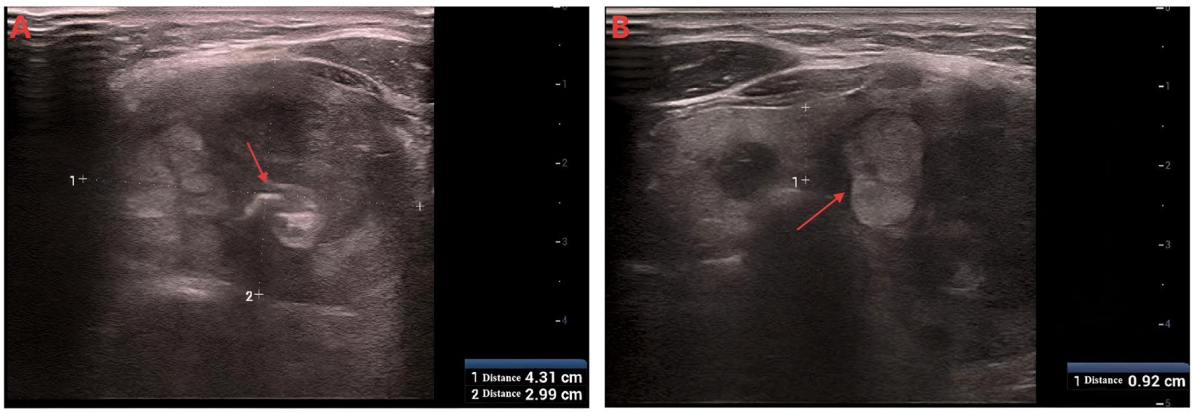

Figure 1. Ultrasound showing multiple bilateral thyroid lobes (Chinese Thyroid Imaging Reporting and Data System grade 3). The ultrasound examination was performed using a Resona 8S system with an L14-5WU transducer. The red arrow indicates the location of the thyroid mass. Multiple cystic-solid nodules in both lobes, demonstrating well-defined borders and regular morphology. A: The largest nodule in the left thyroid lobe measures approximately 4.3x3.0x4.0 cm. B: The largest nodule in the right thyroid lobe measures approximately 1.4x0.9x1.4 cm. CDFI (Color Doppler Flow Imaging): Linear blood flow signals are detected within and around the nodules. The echogenicity of the remaining parenchyma appears relatively uniform.

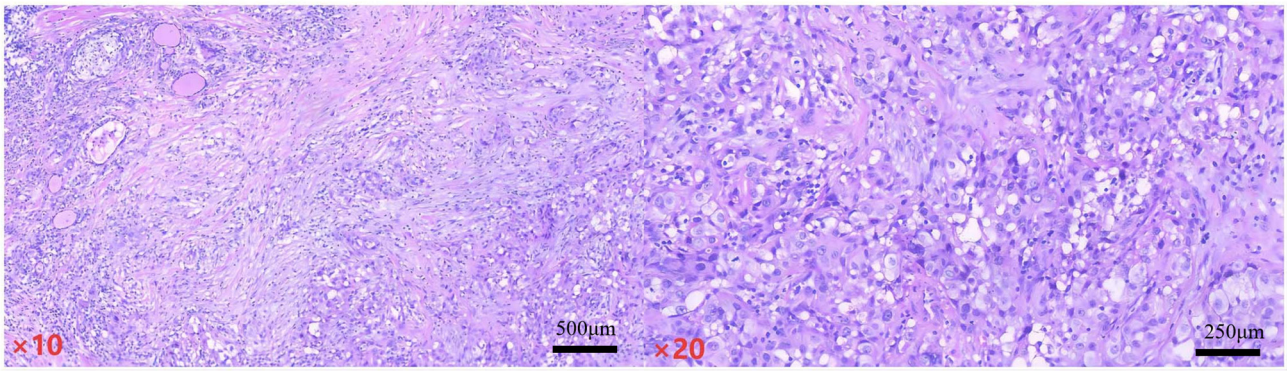

Figure 2. Pathological image of thyroid squamous cell carcinoma with hematoxylin and eosin staining.

Oncology of Affiliated Hospital of Shandong Second Medical University between November 2023 and February 2024. The regimen specifically included 200 mg tislelizumab on day 0 as immunotherapy, and 200 mg albumin-bound paclitaxel on days 1 and 8 + 450 mg carboplatin on day 2 as systemic chemotherapy, supplemented with adjunctive medications including hepatoprotective magnesium isoglycyrrhizinate Injection (200 mg, days 1 and 8, intravenous infusion), and antiemetics Ondansetron Injection (8 mg, days 1 and 8, intravenous) plus Aprepitant Capsules (125 mg, days 1 and 8, orally), which was tolerated well. The patient commenced radiotherapy in March 2024. The prescribed dose to achieve the planning target volume, including the tumor bed and bilateral neck drainage areas, was 50 Gy/2 Gy/25 fractions. Following this, five fractions were administered to the local tumor bed during the treatment period. The patient experienced a sore and dry throat, accompanied by difficulty in eating, consistent with radioactive-induced mucositis. Radiotherapy was temporarily suspended, and parenteral nutrition was provided owing to poor oral intake. A routine blood examination revealed leukopenia, with a white blood cell count of $1.96x10^9$/l (reference range, 3.5-9.5x10^9/l). The condition improved following leukopoietic therapy. Subsequently, the patient refused to continue radiotherapy after completing 16 sessions. The patient returned for monthly follow-up visits, with the last follow-up in June 2024. Postoperative thyroid changes were noted on imaging, while neck CT revealed no signs of recurrence. The tumor response was assessed as complete remission. The patient has reported no discomfort and maintains an excellent mental status. In this case, following radical surgery, the patient was treated with paclitaxel + platinum-based chemotherapy combined with tislelizumab immunotherapy, along with localized radiotherapy. At the last follow-up, the patient exhibited stable vital signs with no recurrence or metastasis.

Discussion

SCCT was previously classified as a separate entity in the World Health Organization Classification of Tumors. However, it is now considered a subtype of interstitial thyroid carcinoma (18). The thyroid gland typically lacks squamous epithelium, and squamous carcinoma accounts for <1% of all thyroid malignancies. The pathogenesis of PSCCT remains controversial and inconclusive, as squamous epithelial cells are absent in the thyroid gland. Currently, more scholars believe that there is a high possibility that the tissue origin of PSCCT is a direct transformation of follicular cells. This is supported by findings such as the detection of BRAF gene

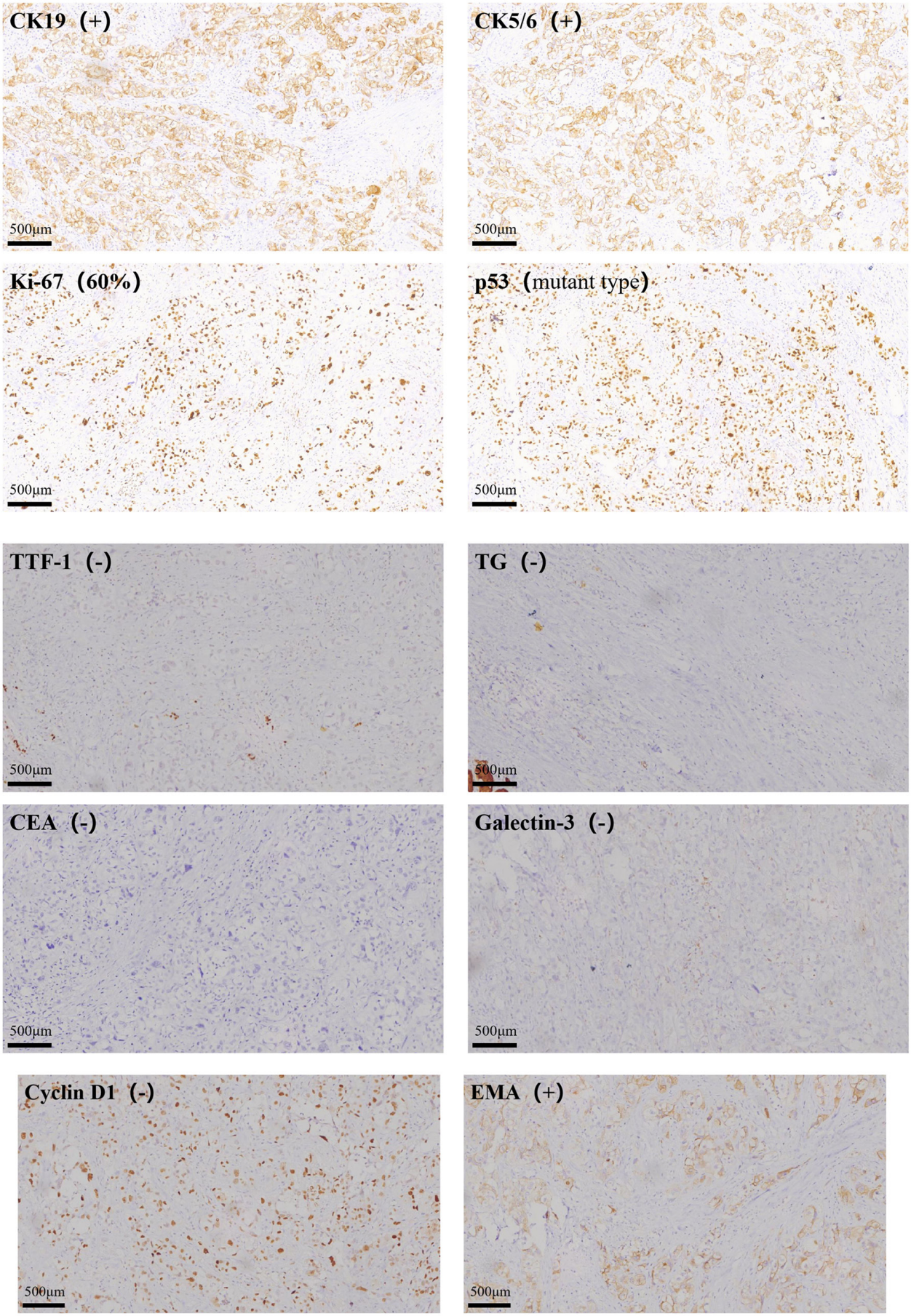

Figure 3. Immunohistochemical analysis of, CK5/6, Ki-67, p53, TTF-1, TG, CEA, Galectin-3, Cyclin D1 and EMA expression in primary squamous cell carcinoma of the thyroid; CK, cytokeratin; TTF, thyroid transcription factor-1; TG, thyroglobulin; CEA, carcinoembryonic antigen; EMA, epithelial membrane antigen.

mutations in PSCCT specimens (5). Additionally, the origin may be derived from remnants of the thyroglossal duct epithelium (19). Secondary SCCT may arise via infiltration and metastasis from neighboring structures such as the larynx, trachea and esophagus. The 'squamous epithelial hyperplasia theory' reveals that SCC develops as a degeneration secondary to squamous epithelial hyperplasia of the thyroid tissue, possibly occurring at the expense of underlying histological abnormalities of the thyroid gland (20). Surgical resection is the primary treatment for PSCCT, with postoperative chemotherapy and radiotherapy serving as adjuvant therapies. However, due to PSCCT poor response to radiotherapy, relative resistance to chemotherapy, and the ineffectiveness of radioactive iodine ablation, more effective treatment strategies are needed to improve patient survival (2,13). Studies (21,22) have found that the multi-receptor tyrosine kinase inhibitor lenvatinib may potentially extend the survival of patients with PSCCT patients, though further research is required to support this finding. Additionally, PD-L1 immunotherapy for PSCCT has garnered attention, with certain studies (23-25) suggesting that anti-PD-L1 immunotherapy could be an effective option for patients affected by the most aggressive forms of thyroid cancer. However, one study reported that in a patient with lung metastases, the primary thyroid lesion gradually enlarged during pembrolizumab treatment, while the lung lesions progressively diminished (26). Lactate dehydrogenase (LDH) is a valuable enzyme biomarker in patients with cancer (27). The present cardiac enzyme profile showed the following results: LDH, 239.0 U/l (reference range, 120-250 U/l); creatine kinase), 43.0 U/l (reference range, 40-200 U/l); CK-MB, 14.00 U/l (reference range, <25 U/l); and α-hydroxybutyrate dehydrogenase, 191.0 U/l (reference range, 95-250 U/l), with all the indicators within the normal ranges. The patient's preoperative thyroid function showed that the anti-TG antibody level was 320 IU/ml, and there was a history of untreated psoriasis, suggesting that autoantibodies and inflammatory stimuli may have led to repeated damage to the thyroid follicular cells. PSCCT involves the lymph nodes in 59% of cases, and distant metastases occur in 26% of cases. The reported median survival time of patients is 8 months (2). There is no systematic treatment for PSCCT; however, radical surgery is the mainstay of treatment. SCCT can easily invade surrounding tissues and organs, as the lesions are not completely removed in numerous cases, when surgery is performed alone. Therefore, adjuvant local radiotherapy post-surgery is an accepted treatment method (28). Studies have shown that surgical treatment can be associated with complications, such as hypoparathyroidism, triggering hypocalcemia, recurrent laryngeal nerve injury, cervical hematoma and wound infection (29-31). Studies have shown that high Ki-67 expression and p53 high expression are associated with a poor patient prognosis and an increased risk of local recurrence post-surgery (32-35). The incidence of TP53 mutations varies between sporadic cancers: it ranges from 38% to 50% in ovarian, esophageal, colorectal, head and neck, laryngeal, and lung cancers, while being only about 5% in primary leukemias, sarcomas, testicular cancers, malignant melanomas, and cervical cancers (36). Due to the high expression of PD-L1, blocking the programmed cell death protein 1/PD-L1 immune checkpoint pathway has become an important therapeutic tool for various tumors by restoring the antitumor activity of T cells. The treatment has been more widely used in non-small cell lung cancer, melanoma, bladder cancer, SCC of the head and neck, triple-negative breast cancer and gastric cancer (37). In the present study, following the patient's IHC and genetic test results, six cycles of tislelizumab immunotherapy were administered combined with chemotherapy and adjuvant radiotherapy, based on the initial radical surgery. However, the patient refused to continue radiotherapy after 16 sessions owing to the severe side effects of radiotherapy, which were found to be intolerable. With a high degree of malignancy, PSCCT has unique clinical, pathological and molecular features. It is important to recognize this unique variant of thyroid cancer, perform possible curative surgical resection and conduct further genomic studies to reveal its molecular pathogenesis. In the 3rd and 4th editions of the World Health Organization (WHO) classification of endocrine tumors, squamous cell carcinoma of the thyroid was categorized as a distinct entity among thyroid neoplasms; however, in the 5th edition of the WHO classification of thyroid tumors, it has been reclassified as a subtype of anaplastic thyroid carcinoma (2,13,38,39). It is characterized by highly aggressive behavior and poor patient prognosis. The diagnosis of SCCT is difficult due to the insufficiency of reported cases nationally and internationally. Conversely, it needs to be differentiated from thyroid carcinoma, undifferentiated thyroid carcinoma and metastatic carcinoma of neighboring upper digestive organs (40). Undifferentiated thyroid cancer has a high rate of distant metastasis; therefore, more patients receive chemotherapy; its regimen includes Adriamycin alone or in combination with cisplatin and 5-fluorouracil. However, it is inefficient, and complete eradication with chemotherapy alone has not been reported. Recently, a number of new chemotherapeutic agents or regimens have been used for the treatment of undifferentiated thyroid cancer, and their efficacy remains under evaluation (41). PSCCT is a highly aggressive malignancy, often detected at advanced stages and associated with a poor prognosis, with a median survival time of 6-9 months and a 1-year survival rate of 33.3% (2,13,40-42). Age >60 years, lymph node metastasis and tumor size >7 cm are risk factors affecting patient survival (43). The patient in this case was diagnosed at 66 years of age, with a maximum tumor diameter of only 6 cm-both of which are significant factors affecting survival rates. However, due to early detection, precise treatment, and the administration of tislelizumab, the patient exhibited neither lymph node metastasis nor distant metastasis. The tumor was completely surgically resected with negative margins, and the patient has now survived for over one year. This outcome stands in stark contrast to the reported one-year survival rate of merely 33.3% in the literature, underscoring how early detection, diagnosis, and treatment can significantly improve patient survival. It also suggests that tislelizumab may contribute to increased survival rates. In conclusion, the present study reported a case of PSCCT, reviewing its surgical and subsequent course of treatment. When discussing its pathogenesis and current therapeutic approaches, PSCCT is shown to be rare and highly malignant, with limited treatment options, all contributing to a poor prognosis. Consequently, early detection is important for radical surgical resection. In addition, more genomic studies are needed to reveal the

molecular pathogenesis and identify novel targeted therapies. This includes immunotherapy, owing to the cancer being refractory to current chemotherapeutic modalities.

Acknowledgements

Not applicable.

Funding

No funding was received.

Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

SD, XW, ZZ, LF and QX confirm the authenticity of all the raw data. SD was responsible for conceptualization, writing the original draft, patient diagnosis and treatment. XW analyzed and interpreted data. ZZ wrote and revised the manuscript and analyzed patient data. LF was responsible for reviewing and editing the manuscript, supervision, patient diagnosis and treatment. QX designed the study design, acquisition of medical images, and reviewed and approved the final version for publication. All authors have read and approved the final manuscript.

Ethics approval and consent to participants

Not applicable.

Patient consent for publication

Written informed consent for the publication of this case report was obtained from the patient.

Competing interests

The authors declare that they have no competing interests.

References

1. Lu Z, Lijun C, Dezhuan D and Hongyi C: Primary squamous cell carcinoma of the thyroid: A systematic review. Asian J Surg 45: 1016-1017, 2022.
2. Lam AKY: Squamous cell carcinoma of thyroid: A unique type of cancer in World Health Organization classification. Endocr Relat Cancer 27: R177-R192, 2020.
3. Chen C, Xu Q, Deng Y, Peng J, He X and Liu L: Ultrasound combined with contrast-enhanced ultrasound in the diagnosis of primary squamous cell carcinoma of the thyroid: A case report and literature review. Oncol Lett 29: 131, 2025.
4. Liu J and Li S: Primary squamous cell carcinoma of the thyroid: A case report and literature review. Asian J Surg 47: 2469-2471, 2024.
5. Ko YS, Hwang TS, Han HS, Lim SD, Kim WS and Oh SY: Primary pure squamous cell carcinoma of the thyroid: Report and histogenic consideration of a case involving a BRAF mutation. Pathol Int 62: 43-48, 2012.
6. Lévay B, Kiss A, Oberna F, Slezák A and Tóth E: Primary squamous cell carcinoma of the thyroid gland. Orv Hetil 164: 1556-1559, 2023 (In Hungarian).
7. Yang S, Li C, Shi X, Ma B, Xu W, Jiang H, Liu W, Ji Q and Wang Y: Primary squamous cell carcinoma in the thyroid gland: A population-based analysis using the SEER database. World J Surg 43: 1249-1255, 2019.
8. Ou D, Ni C, Yao J, Lai M, Chen C, Zhang Y, Jiang T, Qian T, Wang L and Xu D: Clinical analysis of 13 cases of primary squamous-cell thyroid carcinoma. Front Oncol 12: 956289, 2022.
9. Sahoo M, Bal CS and Bhatnagar D: Primary squamous-cell carcinoma of the thyroid gland: New evidence in support of follicular epithelial cell origin. Diagn Cytopathol 27: 227-231, 2002.
10. Hanna E: Squamous cell carcinoma in a thyroglossal duct cyst (TGDC): Clinical presentation, diagnosis, and management. Am J Otolaryngol 17: 353-357, 1996.
11. Goldberg HM and Harvey P: Squamous-cell cysts of the thyroid with special reference to the aetiology of squamous epithelium in the human thyroid. Br J Surg 43: 565-569, 1956.
12. Miyauchi A, Kuma K, Matsuzuka F, Matsubayashi S, Kobayashi A, Tamai H and Katayama S: Intrathyroidal epithelial thymoma: An entity distinct from squamous cell carcinoma of the thyroid. World J Surg 9: 128-135, 1985.
13. Ding W, Gao X and Ran X: Progress in diagnosing and treating thyroid squamous cell carcinoma under the 5th edition of WHO classification. Front Endocrinol (Lausanne) 14: 1273472, 2024.
14. Hamidi S and Maniakas A: Recent advances in anaplastic thyroid cancer management. Curr Opin Endocrinol Diabetes Obes 30: 259-264, 2023.
15. Jurisic V: Multiomic analysis of cytokines in immuno-oncology. Expert Rev Proteomics 17: 663-674, 2020.
16. Zhou J, Yin L, Wei X, Zhang S, Song Y, Luo B, Li J, Qian L, Cui L, Chen W, *et al*: 2020 Chinese guidelines for ultrasound malignancy risk stratification of thyroid nodules: The C-TIRADS. Endocrine 70: 256-279, 2020.
17. Vranic S and Gatalica Z: PD-L1 testing by immunohistochemistry in immuno-oncology. Biomol Biomed 23: 15-25, 2023.
18. Gupta S, Guo R and Erickson LA: Anaplastic thyroid carcinoma, squamous cell carcinoma pattern. Mayo Clin Proc 97: 1584-1585, 2022.
19. Shah S, Kadakia S, Khorsandi A, Andersen A, Iacob C and Shin E: Squamous cell carcinoma in a thyroglossal duct cyst: A case report with review of the literature. Am J Otolaryngol 36: 460-462, 2015.
20. Kallel S, Kallel R, Ayadi S and Ghorbel A: Primary squamous cell carcinoma of the thyroid associated with papillary thyroid carcinoma and Hashimoto's thyroiditis. Eur Ann Otorhinolaryngol Head Neck Dis 135: 291-293, 2018.
21. Yasumatsu R, Sato M, Uchi R, Nakano T, Hashimoto K, Kogo R, Taura M, Matsuo M, Nakashima T and Nakagawa T: The treatment and outcome analysis of primary squamous cell carcinoma of the thyroid. Auris Nasus Larynx 45: 553-557, 2018.
22. Kimura-Tsuchiya R, Sasaki E, Nakamura I, Suzuki S, Kawana S, Okouchi C, Fukushima T, Hashimoto Y, Suzuki S and Saji S: A case of squamous cell carcinoma of unknown primary that responded to the multi-tyrosine kinase inhibitor lenvatinib. Case Rep Oncol 11: 75-80, 2018.
23. Ulisse S, Tuccilli C, Sorrenti S, Antonelli A, Fallahi P, D'Armiento E, Catania A, Tartaglia F, Amabile MI, Giacomelli L, *et al*: PD-1 ligand expression in epithelial thyroid cancers: Potential clinical implications. Int J Mol Sci 20: 1405, 2019.
24. Paolino G, Pantanowitz L, Barresi V, Pagni F, Munari E, Moretta L, Brunelli M, Bariani E, Vigliar E, Pisapia P, *et al*: PD-L1 evaluation in head and neck squamous cell carcinoma: Insights regarding specimens, heterogeneity and therapy. Pathol Res Pract 226: 153605, 2021.
25. Torrez M, Braunberger RC, Yilmaz E and Agarwal S: Primary squamous cell carcinoma of thyroid with a novel BRAF mutation and High PDL-1 expression: A case report with treatment implications and review of literature. Pathol Res Pract 216: 153146, 2020.
26. Hsieh ML, Besch BM, Peterson JEG and Henson C: Primary squamous cell carcinoma of the thyroid treated with concurrent chemoradiation and palliative immunotherapy: A case report. J Med Case Rep 16: 364, 2022.
27. Jurisic V, Radenkovic S and Konjevic G: The actual role of LDH as tumor marker, biochemical and clinical aspects. Adv Exp Med Biol 867: 115-124, 2015.
28. Sniezek JC and Holtel M: Rare tumors of the thyroid gland. Otolaryngol Clin North Am 36: 107-115, 2003.

29. Tolone S, Roberto R, del Genio G, Brusciano L, Parmeggiani D, Amoroso V, Casalino G, Verde I, Bosco A, D'Alessandro A, *et al*: The impact of age and oral calcium and vitamin D supplements on postoperative hypocalcemia after total thyroidectomy. A prospective study. BMC Surg 13 (Suppl 2): S11, 2013.
30. Canu GL, Medas F, Cappellacci F, Giordano ABF, Gurrado A, Gambardella C, Docimo G, Feroci F, Conzo G, Testini M and Calò PG: Risk of complications in patients undergoing completion thyroidectomy after hemithyroidectomy for thyroid nodule with indeterminate cytology: An Italian multicentre retrospective study. Cancers (Basel) 14: 2472, 2022.
31. Gambardella C, Offi C, Romano RM, De Palma M, Ruggiero R, Candela G, Puziello A, Docimo L, Grasso M and Docimo G: Transcutaneous laryngeal ultrasonography: A reliable, non-invasive and inexpensive preoperative method in the evaluation of vocal cords motility-a prospective multicentric analysis on a large series and a literature review. Updates Surg 72: 885-892, 2020.
32. Dobashi Y, Sakamoto A, Sugimura H, Mernyei M, Mori M, Oyama T and Machinami R: Overexpression of p53 as a possible prognostic factor in human thyroid carcinoma. Am J Surg Pathol 17: 375-381, 1993.
33. Nishida T, Nakao K, Hamaji M, Nakahara MA and Tsujimoto M: Overexpression of p53 protein and DNA content are important biologic prognostic factors for thyroid cancer. Surgery 119: 568-575, 1996.
34. Kleer CG, Giordano TJ and Merino MJ: Squamous cell carcinoma of the thyroid: An aggressive tumor associated with tall cell variant of papillary thyroid carcinoma. Mod Pathol 13: 742-746, 2000.
35. Booya F, Sebo TJ, Kasperbauer JL and Fatourechi V: Primary squamous cell carcinoma of the thyroid: Report of ten cases. Thyroid 16: 89-93, 2006.
36. Olivier M, Hollstein M and Hainaut P: TP53 mutations in human cancers: Origins, consequences, and clinical use. Cold Spring Harb Perspect Biol 2: a001008, 2010.
37. Mirjačić Martinović K, Vuletić A, Tišma Miletić N, Matković S, Gavrilović D, Ninković A, Jurišić V and Babović N: Circulating IL-6 is associated with disease progression in BRAFwt metastatic melanoma patients receiving anti-PD-1 therapy. J Clin Pathol 77: 343-351, 2024.
38. Juhlin CC, Mete O and Baloch ZW: The 2022 WHO classification of thyroid tumors: Novel concepts in nomenclature and grading. Endocr Relat Cancer 30: e220293, 2022.
39. Baloch ZW, Asa SL, Barletta JA, Ghossein RA, Juhlin CC, Jung CK, LiVolsi VA, Papotti MG, Sobrinho-Simões M, Tallini G and Mete O: Overview of the 2022 WHO classification of thyroid neoplasms. Endocr Pathol 33: 27-63, 2022.
40. Cho JK, Woo SH, Park J, Kim MJ and Jeong HS: Primary squamous cell carcinomas in the thyroid gland: An individual participant data meta-analysis. Cancer Med 3: 1396-1403, 2014.
41. Wu Y, Sun C, Xi Y, Sun R, Fe J, Li X and Sui J: Treatment and prognosis of squamous cell carcinoma of thyroid. Lin Chuang Er Bi Yan Hou Tou Jing Wai Ke Za Zhi 24: 241-243, 2010 (In Chinese).
42. Yan W, Chen H, Li J, Zhou R and Su J: Primary squamous cell carcinoma of thyroid gland: 11 Case reports and a population-based study. World J Surg Oncol 20: 352, 2022.
43. Kim TY, Kim KW, Jung TS, Kim JM, Kim SW, Chung KW, Kim EY, Gong G, Oh YL, Cho SY, *et al*: Prognostic factors for Korean patients with anaplastic thyroid carcinoma. Head Neck 29: 765-772, 2007.