(30)
邁向甲狀腺癌的個人化醫療

Towards Personalized Medicine in Treatment of Thyroid Cancers

時　　間：113 年 6 月 23 日(星期日) 08:20~12:00
地　　點：臺北榮民總醫院 致德樓第四會議室

08:20-08:30	*Opening Remarks*	胡啟民教授 Chii-Min Hwu
	座長：胡啟民 教授 (Chii-Min Hwu)	
08:30-09:10	甲狀腺癌術前分子診斷 Preoperative Molecular Testing for Thyroid Cancers	郭錦松醫師 Chin-Sung Kuo
09:10-09:50	甲狀腺癌的術前超音波診斷 Preoperative Diagnostic Ultrasound for Thyroid Cancers - Focus on TIRADS	黃君睿醫師 Chun-Jui Huang
09:50-10:30	經口甲狀腺切除術 Transoral Endoscopic Thyroidectomy: A Paradigm Shift in Thyroid Surgery	陳瑞裕醫師 Jui-Yu Chen
10:30-10:40	*Coffee Break*	
	座長：郭錦松 醫師 (Chin-Sung Kuo)	
10:40-11:20	晚期甲狀腺癌的標靶治療 Target Therapy in Advanced Thyroid Cancers	姜和均醫師 He-Jiun Jiang
11:20-12:00	甲狀腺髓質癌的個人化醫療 Personalized Management for Medullary Thyroid Cancer	劉峻宇醫師 Chun-Yu Liu
12:00-12:10	*Closing Remarks*	胡啟民教授 Chii-Min Hwu

Preoperative molecular testing for thyroid cancers

甲狀腺癌術前分子診斷

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Thyroid cancer commonly presents oncogenic genetic alterations, The *BRAF* V600E mutation is the most frequently observed, primarily in papillary thyroid carcinoma (PTC). Molecular genetic testing performed before thyroid nodule surgery has demonstrated effectiveness in improving diagnostic accuracy, thereby contributing to the reduction of unnecessary thyroidectomies.

We introduce a case involving the Bethesda system (TBS) category III thyroid nodule harboring a positive *BRAF* V600E mutation detected via qPCR assay, followed by thyroidectomy and lymph node dissection. Nevertheless, the definitive pathology report yielded an unexpected diagnosis of indolent follicular thyroid carcinoma accompanied by a rare non-V600E *BRAF* mutation, V600_K601insNTV, mutation confirmed by Sanger sequencing. The case presented highlights the critical need to thoroughly evaluate molecular genetic testing results in thyroid nodule FNA cytology, particularly in cases with borderline Ct values detected by qPCR assays.

Furthermore, we share the experience of a TBS VI thyroid nodule with molecular testing. The 31-year-old woman without underlying diseases discovered a thyroid nodule as a solid, hypoechoic, wider-than-tall nodule measuring $11.8 \times 10.2 \times 12.4$ mm in size. Fine-needle aspiration cytology was classified as TBS VI, and the diagnosis was PTC. To screen for common genetic alterations, the analysis did not reveal the presence of mutations such as *BRAF V600E*, *NRAS Q61R*, *NRAS Q61K*, *HRAS Q61R*, or *HRAS Q61K* mutations nor fusions of *CCDC6-RET*, *NCOA4-RET*, *PAX8-PPARG*, *ETV6-NTRK3*, *TPM3-NTRK1*, *IRF2BP2-NTRK1*, or *SQSTM1-NTRK1*. Subsequently, the patient underwent total thyroidectomy and central lymph node dissection to make a pathological diagnosis of cribriform and morular cribriform morular thyroid carcinoma.

Molecular testing performed before thyroid nodule surgery has demonstrated effectiveness in improving diagnostic accuracy.

Preoperative diagnostic ultrasound for thyroid cancers: Focus on TIRADS

甲狀腺癌的術前超音波診斷

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Ultrasound risk stratification systems for evaluation of thyroid nodules are important to estimate the risk of malignancy and determine whether fine needle aspiration (FNA) should be performed. Diagnostic ultrasound is the first step to diagnosis of thyroid cancer.

The American College of Radiology Thyroid Imaging Reporting and Data System (ACR-TIRADS) Committee has proposed a point score system using the sum of points for individual sonographic features to assess incidental thyroid nodule. A sum of point ≥ 7 is indicative for FNA in nodules ≥ 1 cm, whereas a sum of point 3 or 4-6 is indicate for FNA in nodules ≥ 2.5 or ≥ 1.5 cm. The American Thyroid Association (ATA) has also published guidelines for thyroid nodules describing a pattern based atlas without points. The ACR-TIRADS and ATA share commonalities regarding sonographic features for high risk (hypoechogenicity, punctate echogenic foci, irregular margins, taller than wide shape) and very low risk (entirely cystic nodules or spongiform appearance) nodules. For low to intermediate suspicious nodules, the two systems differ in size cutoffs for FNA. The ATA system is more sensitive but less specific due to lower FNA size cutoffs.

The strength of ACR-TIRADS lies in the harmonization of the reporting of nodules and classification of all possible sonographic appearances. In contrast, 7.8% of the nodules are not classifiable by the current ATA system. The ATA is drafting an updated guideline to include new evidences for the literature including the findings of macrocalcification as an independent predictor for high malignancy risk in solid nodules and the significance of marked hypoechogenicity compared to not marked hypoechogenic nodules. A review of sonographic pattern of thyroid nodules shall be presented in this section.

Transoral endoscopic thyroidectomy: A paradigm shift in thyroid surgery

經口甲狀腺切除術

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Transoral endoscopic thyroidectomy, especially the vestibular approach, is a groundbreaking surgical technique that has revolutionized the field of thyroid surgery. Pioneered by Dr. Angkoon Anuwong, this innovative approach represents a significant departure from traditional open thyroidectomy methods. By utilizing endoscopic instruments inserted through small incisions in the oral cavity, transoral endoscopic thyroidectomy offers patients the benefits of scarless surgery and improved cosmetic outcomes.

Indications for transoral endoscopic thyroidectomy encompass a wide range of thyroid pathologies, including benign thyroid nodules, Graves' disease, and select cases of thyroid cancer. It's crucial to note that the procedure's suitability for thyroid cancer is limited to tumors of relatively small sizes, tumor locations and the surgeon's confidence in performing the procedure safely and effectively. Patient selection criteria are carefully evaluated to ensure optimal outcomes, with emphasis placed on appropriate anatomical considerations and pathological characteristics. With advancements in surgical techniques and instrumentation, transoral endoscopic thyroidectomy has become increasingly versatile and applicable to a broader range of thyroid conditions.

The future trend of transoral endoscopic thyroidectomy is characterized by ongoing advancements aimed at further enhancing its safety, efficacy, and applicability. Continued research and development efforts focus on refining surgical techniques, optimizing patient selection criteria, and integrating innovative technologies such as robotic-assisted surgery. Additionally, the evolution of transoral endoscopic thyroidectomy is expected to lead to improved patient outcomes and shorter recovery times, further solidifying its role as a cornerstone of modern thyroid surgery. These advancements also target the reduction of procedure-related complications, such as mitigating the risk of injury to adjacent structures like the mental nerve, alleviating postoperative discomfort, and lowering the incidence of surgical site infections. These strides in enhancing safety and efficacy contribute to heightened patient confidence and satisfaction, positioning transoral endoscopic thyroidectomy as an increasingly preferred choice for thyroid surgery.

In conclusion, transoral endoscopic thyroidectomy represents a paradigm shift in the field of thyroid surgery, offering patients a scarless and cosmetically favorable alternative to traditional open procedures. With its origins rooted in the pioneering work of Dr. Angkoon Anuwong and ongoing advancements in surgical techniques and technology, transoral endoscopic thyroidectomy is redefining the landscape of thyroid surgery and holds great promise for the future of patient care.

Target therapy in advanced thyroid cancers

晚期甲狀腺癌的標靶治療

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Thyroid cancer is the most prevalent endocrine malignancy, with differentiated thyroid cancer (DTC) making up the majority of cases. Standard treatments for DTC typically include surgery, radioactive iodine therapy, and thyroid hormone therapy. However, a subset of patients develops resistance to radioiodine treatment, known as radioiodine-refractory DTC (rrDTC), presenting significant challenges in treatment. Over the past decade, significant advancements in understanding the molecular basis of thyroid cancer have led to the development and clinical adoption of tyrosine kinase inhibitors (TKIs) as a crucial treatment strategy for advanced disease stages. This overview examines the use of TKIs, specifically Lenvatinib, Sorafenib, and Cabozantinib, highlighting their effectiveness in halting cancer progression and managing symptoms. Nonetheless, the successful management of TKIs requires careful attention to their associated side effects, which is critical for maximizing treatment benefits and extending patient survival. Common adverse events (AEs) associated with TKI therapy include hepatic impairment, gastrointestinal issues, hypertension, proteinuria, hand-foot skin reaction, and fatigue, which typically manifest within several weeks of initiating treatment and significantly impact patient adherence to the therapy. Furthermore, the emergence of tumor-agnostic therapies marks a significant advancement in precision medicine, offering a more personalized treatment approach by targeting genetic mutations rather than the cancer's location. By exploring current research and clinical findings, we demonstrate the potential of TKIs to transform the therapeutic landscape for advanced thyroid cancer and offer insights into clinical practice.

Personalized management for medullary thyroid cancer

甲狀腺髓質癌的個人化醫療

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Medullary thyroid cancer (MTC) represents a rare but clinically significant malignancy originating from the parafollicular C cells of the thyroid gland. Unlike other types of thyroid cancer, MTC often presents therapeutic challenges due to its resistance to conventional treatments such as radioiodine therapy. However, recent advancements in personalized medicine have provided new avenues for tailored approaches in managing MTC patients.

This review explores the landscape of personalized treatment strategies for MTC, encompassing molecular profiling, targeted therapies, immunotherapy, and emerging modalities such as peptide receptor radionuclide therapy (PRRT). Through the identification of specific genetic mutations, particularly mutations in the RET proto-oncogene, and the development of novel agents targeting pathways implicated in MTC pathogenesis, personalized treatment regimens offer promising prospects for improved outcomes and enhanced quality of life for patients with MTC. Additionally, the integration of multimodal approaches including surgery, systemic therapy, and precision radiotherapy holds potential for synergistic effects in disease management.

Despite these advancements, challenges remain, including the optimization of treatment sequencing, the management of treatment-related toxicities, and the identification of reliable predictive biomarkers. Future directions in MTC research aim to refine personalized treatment algorithms, enhance therapeutic efficacy, and ultimately transform the management paradigm for this complex malignancy.