



## THYROGLOBULIN ELEVATION AND NEGATIVE IODINE SCINTIGRAPHY (TENIS) SYNDROME: DIAGNOSTIC CHALLENGES, TREATMENT, AND NURSING IMPLICATIONS

### Nursing

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### ABSTRACT

Thyroglobulin Elevation and Negative Iodine Scintigraphy (TENIS) syndrome presents a unique diagnostic and therapeutic challenge in the management of differentiated thyroid cancer (DTC) patients. Thyroglobulin (Tg) is a tumor marker produced by thyroid follicular cells, and its elevated levels in the blood are often used to monitor disease recurrence or metastasis in patients who have undergone total thyroidectomy and radioactive iodine therapy. In TENIS syndrome, patients exhibit persistently elevated serum thyroglobulin levels but have negative iodine-131 whole-body scintigraphy scans. This condition complicates the management of DTC, as iodine scintigraphy, which is typically used to detect recurrent disease, becomes ineffective. This paper explores the diagnostic challenges, treatment strategies, and the nursing implications associated with TENIS syndrome, with the goal of improving patient outcomes through comprehensive care.

### KEYWORDS

TENIS syndrome, TSH, Thyroglobulin, Differentiated thyroid cancer, Thyroid malignancy

### INTRODUCTION

Thyroid cancer is the most common malignancy in adolescents and adults (Chen, Lang, McLeod, Newbold, & Haymart, 2023). The global burden of thyroid cancer is increasing, the relatively low mortality rate and high survival rates highlight the importance of early detection and access to appropriate treatments. Thyroid cancer is broadly categorized into four types papillary, follicular, medullary, and anaplastic. Papillary thyroid cancer accounts to approximately 84% of all thyroid cancers (Boucai, Zafereo & Cabanillas, 2024). Not uncommonly, during the course of thyroid cancer management, a situation arises where there is no radiologically or clinically evident disease, but thyroglobulin (Tg) levels remain detectable or even significantly elevated (Sinha, Conrad & West, 2011).

### DIAGNOSTIC CHALLENGES IN TENIS SYNDROME

**Lack of Detectable Disease:** The primary diagnostic challenge in TENIS syndrome is the discordance between the elevated serum thyroglobulin levels, indicating probable disease recurrence or metastasis, and negative iodine scintigraphy, which fails to detect iodine-avid lesions. As a result, there is an increased risk of delayed diagnosis of recurrent or metastatic disease.

**IMAGING LIMITATIONS:** While iodine scintigraphy remains a cornerstone of DTC monitoring, its sensitivity decreases when cancer cells lose the ability to uptake radioactive iodine. This makes it difficult to detect disease progression.

Diagnosis of TENIS involves a combination of biochemical (high thyroglobulin levels) and imaging methods (negative iodine scintigraphy) PET scans and other non- iodine-based imaging technique such as FDG- PET, are often used to locate Iodine-refractory metastatic disease. Ozdemir et al.(2014) suggest that (18)F-FDG-PET/CT is a valuable tool to predict the occurrence of recurrent disease in patients with DTC, negative WBS and elevated Tg levels.. Basu, Kalshetty & Fargose (2017) states the use of dual imaging technique for patients with elevated thyroglobulin and negative iodine scintigraphy. Lesions may alternatively take up 68Ga- DOTATATE PET -CT or FDG PET / CT, indicating differing biological activity between lesions within the same patients.

Advanced techniques 68Ga-PSMA-11 PET-CT are emerging tools that can identify non-iodine-avid metastases in these patients. TENIS presenting with FAPI- avid metastatic lesion demonstrated the use of 68Ga- fibroblast activation protein inhibitor(FAPI) PET- CT for localizing recurrent or metastatic lesions (Fu, Fu, Huang, Su & Chen, 2021).

**Monitoring Thyroglobulin Levels:** Serial measurements of thyroglobulin levels are vital for monitoring disease status, but interpreting these values is complex. Non-cancerous thyroid tissue remnants, assay variability, and the presence of thyroglobulin antibodies can complicate accurate diagnosis and disease monitoring. Khoo, Fong & Hamzah (2018) stated that Tg  $\geq 15$  ng/ml is indicated preferable for performing 18FDG PET-CT. The increased angiogenesis in the hyperplastic thymus may also contribute to the persistence of elevated Tg level in DTC patients with TENIS

syndrome. (Zhang et al., 2018).

### TREATMENT APPROACHES

**Empirical Radioiodine Therapy:** In some cases, empirical high-dose radioactive iodine therapy promoted beneficial effects and could be recommended for patients with TENIS syndrome, especially those with micro metastasis (Kim, 2024) although the response rates vary. It remains a challenge to justify the use of radioiodine in the absence of identifiable iodine-avid disease on scintigraphy, leading to uncertainty in treatment effectiveness. It is also shown that patients with TENIS syndrome without structural disease can benefit from the empirical RAI therapy in both PFS (progression free survival and Tg ( thyroglobulin) normalization.(Yuan et al., 2023)

**TARGETED RADIONUCLIDE THERAPY:** In patients with TENIS syndrome, receptor-targeted radionuclide therapies are emerging as potential treatment modalities (Sonavane, Salvi, Asopa & Basu, 2024). These therapies offer an alternative for patients whose cancer cells no longer respond to radioactive iodine therapy.

**Systemic Therapy:** For patients with progressive disease that cannot be targeted by radionuclide therapy, systemic treatment options such as tyrosine kinase inhibitors (TKIs) are available (Silbertin, 2011). These drugs inhibit angiogenesis and tumor growth but come with significant side effects requiring close monitoring and supportive care.

**SURGICAL INTERVENTION:** In certain cases where localized disease is suspected or confirmed through other imaging modalities, surgical resection of metastases may be considered. However, surgery in the context of TENIS is complex due to the difficulty in identifying all disease sites. The minimally invasive surgery is suggested option for residual recurrent locoregional disease in post-surgical set up requiring accurate presurgical localization. Intra operative gamma probe using low dose tracer has shown its utility in radio guided surgery (Prashar et al., 2020).

### NURSING IMPLICATIONS

The role of nursing in managing patients with TENIS syndrome extends beyond traditional patient care, encompassing diagnostic support, treatment adherence, education, and emotional support. Key nursing responsibilities include:

### PATIENT EDUCATION AND COUNSELING

Nurses play a critical role in educating patients and families about the nature of TENIS syndrome, diagnostic procedures, and potential treatment options. Understanding the uncertainty associated with the diagnosis can help patients cope with the emotional distress of ongoing monitoring without clear answers.

Education on self-monitoring, such as reporting symptoms of recurrence (e.g., neck pain, difficulty swallowing, unexplained weight loss), is essential.

### SUPPORTING DIAGNOSTIC PROCESSES

Nurses can assist in coordinating the complex diagnostic process,

including scheduling advanced imaging studies (FDG PET/CT, 68Ga-DOTATATE PET-CT) and ensuring timely follow-up on laboratory tests such as thyroglobulin levels and antibody assays.

### SYMPTOM MANAGEMENT

Patients undergoing systemic therapy with TKIs may experience side effects such as hypertension, hand-foot syndrome, and gastrointestinal disturbances. Nurses are instrumental in educating patients about these side effects and implementing strategies to manage them, such as skin care protocols, nutritional support, and blood pressure monitoring.

### PSYCHOSOCIAL SUPPORT

The uncertainty of TENIS syndrome can lead to anxiety and distress among patients. Nurses provide vital psychosocial support, helping patients manage their mental health through counseling, support groups, and referral to mental health professionals when necessary.

### FOLLOW-UP AND MONITORING

Nurses ensure regular follow-up visits and blood work, which are critical in monitoring disease progression. This includes the timely collection of thyroglobulin levels, managing potential adverse effects of treatments, and assessing the patient's overall well-being.

### COORDINATION OF MULTIDISCIPLINARY CARE

TENIS syndrome requires a collaborative approach involving endocrinologists, oncologists, nuclear medicine specialists, radiologists, and surgeons. Nurses act as a bridge between these specialists, ensuring seamless communication and comprehensive care delivery.

### CONCLUSION

TENIS syndrome presents a unique set of challenges in the management of differentiated thyroid cancer patients. The diagnostic limitations of iodine scintigraphy, coupled with elevated thyroglobulin levels, complicate both disease monitoring and treatment decisions. Advanced imaging techniques and targeted radionuclide therapies offer new hope but require careful consideration and multidisciplinary management. Nurses are pivotal in providing education, symptom management, and psychosocial support, ensuring that patients receive comprehensive care throughout their treatment journey.

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