

Case Series Of Local Experience In Differentiated Thyroid Cancer Management In The Department Of Nuclear Medicine And Research In Zambia

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Abstract

Thyroid cancer accounts for about 2% of all malignancies in the world. The incidence has tripled in the USA from 1975 to 2009 and worldwide due to incidental detection of small volume papillary carcinomas on imaging studies. The increase in incidence could be related to increased use of imaging modalities and fine needle aspiration with changes in histologic criteria. This maybe similar to the Zambian scenario which has led to early diagnosis and prompt treatment in patients with differentiated thyroid cancer.

The aim of this study was to evaluate differentiated thyroid cancer management of the first two cases in nuclear medicine department.

This was a case series design. It looked at the first two patients who diagnosed and managed at the Department of Nuclear Medicine and research, the university Teaching Hospital, Lusaka, Zambia. The cases were selected using convenience sampling and included the first two cases.

The participants included two females aged 66 (Case 1) and 48 (Case 2) referred from local clinic and medical admission ward respectively. Case 1 presented with invasive and incompletely excised papillary thyroid carcinoma, classic variant type with no metastases. Case 2 presented with papillary thyroid cancer diffuse variant and no metastases. The treatment plan for both cases included thyroidectomy and I131 ablation with excellent response.

The use of radioactive iodine therapy in management of DTC is well established as it may reduce risk of recurrence, improves patients quality of life and overall survival rate.

Key words: Differentiated thyroid cancer, multiple endocrine neoplasia, multinodular goitre, Thyroid stimulating hormone and radioactive Iodine therapy.

Introduction

Thyroid cancer accounts for about 2% of all malignancies in the world (Cancer Research UK 2013). The incidence tripled in the USA between 1975 and 2009 and worldwide due to incidental detection of small volume papillary carcinomas on imaging studies (Davies & Welch, 2013). The increase in incidence could be related to increased use of imaging modalities and fine needle aspiration with changes in histologic criteria (Hodgson, et al, 2004). This may be similar to the Zambian scenario which has led to early diagnosis and prompt treatment in patients with differentiated thyroid cancer (DTC). According to Cinar and Tas, (2015) cancer in the elderly, 60% of all cases with cancer, and 70% of cancer-related deaths occur in patients aged 65 years and over. The most common subtypes of thyroid cancer are papillary, follicular, medullary and anaplastic. Thyroid follicular cells give rise to two forms of DTC: papillary which accounts for approximately 85% and follicular thyroid cancer which accounts for about 12% (American Thyroid Association, 2015). DTC is defined as carcinoma derived from the follicular epithelium and retain basic biological characteristics of healthy thyroid tissue, which include the capacity to express the sodium iodide symporter (NIS) (Schmidbauer, Menhart, Hellwig & Grosse, 2017). Anaplastic and poorly differentiated thyroid cancers are rarer and aggressive. The American Thyroid Association Medullary Cancer Guidelines (2008), indicate that the medullary thyroid cancer arises from the C-cells and accounts for about 4% of thyroid cancers, and is less often associated with multiple endocrine neoplasia type 2 (MEN2) (Kloos et al., 2008). The survival rate depends on the histological subtype at presentation, patients age and tumour differentiation (Haugen et al., 2015).

Over a number of years, there has been significant advances in diagnosis and therapy of DTC. However, controversies still exist (Haugen et al., 2015). Feasibility and cost implications of the diagnostic and therapeutic options present practical challenges in many low-income countries including Zambia. Traditionally, the treatment of thyroid cancer usually requires surgical removal of the thyroid gland often with compartmental dissection of abnormal lymph nodes followed by radioactive Iodine therapy (RAI) to destroy any remnant benign or malignant thyroid tissue. Following thyroidectomy and ablation therapy, the management protocol includes administering appropriate suppressive thyroid stimulating therapy (TSH) therapy which could improve the outcome especially in high-risk patients (Luster et al, 2008, Haugen et al, 2015). It has been reported that over suppression has no additional value to the management of the patient but causes adverse effects which may include subclinical

thyrotoxicosis, atrial fibrillation, exacerbation of angina and osteoporosis (Sugitani & Fujimoto, 2010). Chemotherapy and radiation therapy treatment options are not used in routine treatment of DTC, but in a few exceptional cases (Cooper et al, 2006).

It is anticipated that results of this study may inform the improvement of clinical practice and patient care management. Zambia currently has no national protocol in the management of DTC. This study may inform the development and adoption of local protocols. Research results may also add to the body of knowledge on clinical practice and patient care management of patients with DTC.

Objective

This study was conducted to evaluate differentiated thyroid cancer (DTC) management in a nuclear medicine department

Design

This study used the case series design.

Population and Sample

The first two participants who were diagnosed and managed were enrolled in the study.

Setting

The study was conducted at the Nuclear Medicine and Research Department at the University Teaching Hospital.

Sampling Technique

The cases were selected using convenience sampling and included the first two cases.

Data Collection

The data was collected via record review. These records included information generated from the health facilities which referred them for further management.

Clinical Cases

There were two cases under the review period, both females aged 66 and 48 years old.

Case 1

A 66 year old female was referred from a local clinic for euthyroid goitre with associated occasional difficulty in swallowing. There were no other presenting symptoms. There was no history of thyroid disease in the family or neck irradiation. She was known to have hypertension which was well controlled by medications. Otolaryngology assessment was none revealing.

Investigation and Findings

The ultrasound of the neck demonstrated a diffusely enlarged thyroid gland, heterogeneous in texture, suggestive of multinodular goitre (MNG). About 2 months from first presentation, the patient underwent right lobectomy in January 2018 for MNG. Intra-op the right lobe was described as enlarged with multinodular lesions. The CT scan of the head and neck done in January 2018, post right thyroidectomy showed some collection with foci of air in the right thyroid fossa and left lobe of thyroid was enlarged in size with multiple ill-defined hypodense areas with foci of calcification in it (Fig 1). There was no evidence of metastases. In February 2018, left lobectomy was done for the purpose of total thyroidectomy. Histologically, the tumour was papillary thyroid carcinoma, classic variant type described as invasive and incompletely excised.

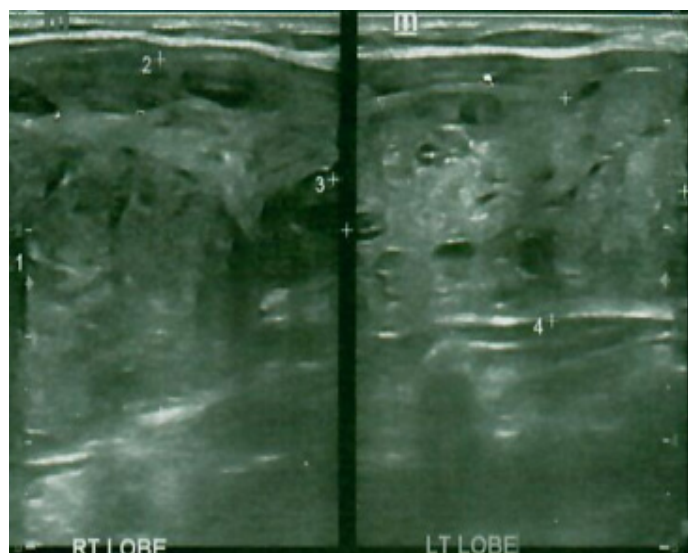


Figure 1 Diffusely enlarged thyroid gland

Lympho-vascular and perineural invasion was not identified. The tumour was positive for margins. Then the patient was referred for radio-active iodine therapy (RAIT). Investigations done prior to ablation included the following: (i) thyroid-stimulating hormone (TSH) was measured at more than 60uIU/ml which was conducive for therapy (ii) the pre-ablation whole body scan (WBS) with I131 showed remnant tissue in the thyroid bed with no loco-regional or distant metastases (Fig 2). About 6 weeks post completion thyroidectomy, the patient was ablated with 2960 MBq of I 131 capsule, according to the stage and risk stratification.

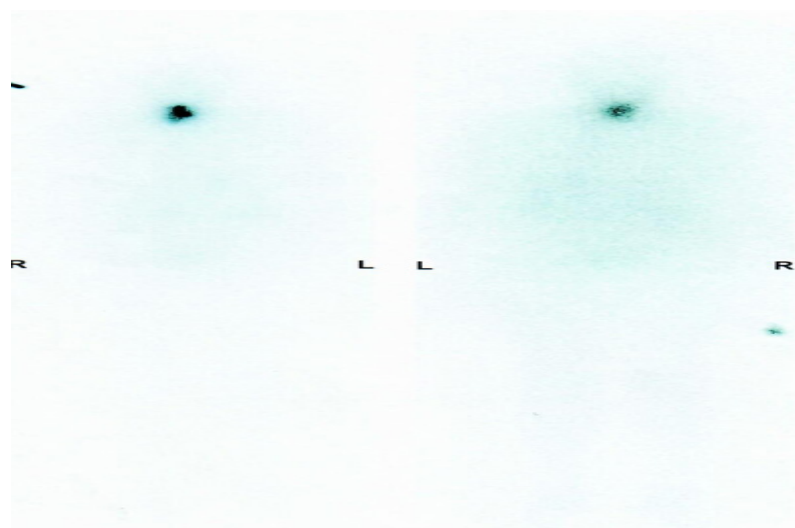


Figure 2 Pretherapy I131 scan showing residual thyroid tissue with no distant metastases

During follow up, the patient's unstimulated TSH, serum TG was 0.8mg/ml and anti TG- antibodies was within normal. The follow-up ultrasound of the neck showed no thyroid gland which was in keeping with the previous therapy. The WBS with I-131 demonstrated no remnant tissue in the thyroid bed or the rest of the body. Clinically the patient presented with no persistent, recurrent or new symptoms related to DTC.

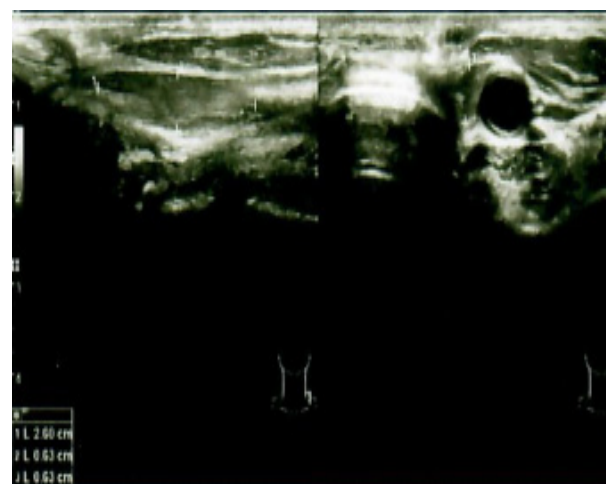


Figure 3. Thyroid Ultrasound post I131 therapy

Using the criteria in the EANM/ATA this was classified as an excellent response. At the time of publication, the patient was on a 2-5 years follow-up plan and suppression thyroid therapy.

Case 2

The patient was a 48-year-old female diagnosed with papillary thyroid cancer diffuse variant. She was referred from the medical admission ward with incidental findings of small painless lumps in the lower part of the right-side of the neck. The baseline thyroid function blood tests were within the normal ranges. Ultrasound of the neck was done which confirmed the presence of multiple nodules in the thyroid (Fig 4). MRI of the brain and neck was requested which revealed lesions in both thyroid lobes of varying sizes. The brain was normal. She had no other presentation or comorbidity.

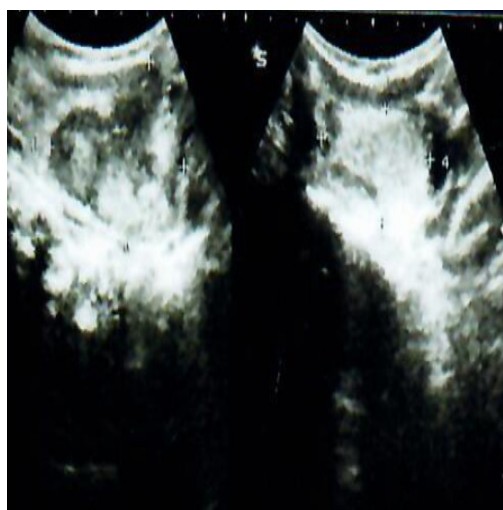


Figure 4. Staging Ultrasound-Multiple solid hypoechoic nodules

The patient had a right hemi-thyroidectomy in January 2017 for what was thought to be MNG, histopathology results showed papillary thyroid carcinoma, diffuse variant. Total thyroidectomy was done 3 months later. Following the aforementioned diagnosis, the patient was referred to Nuclear Medicine Department for ablation where further multiple investigations were conducted for staging, prognosis and risk stratification. A pre-ablation I131 whole body scan (I131-WBS) showed remnant tissue in the thyroid bed with no loco-region or distant metastases (Fig 5). ultrasound scan of the neck, computer tomography (CT) scan of neck and chest, Full blood count (FBC) results were normal and TSH was sufficiently raised at 63.21uIU/ml.

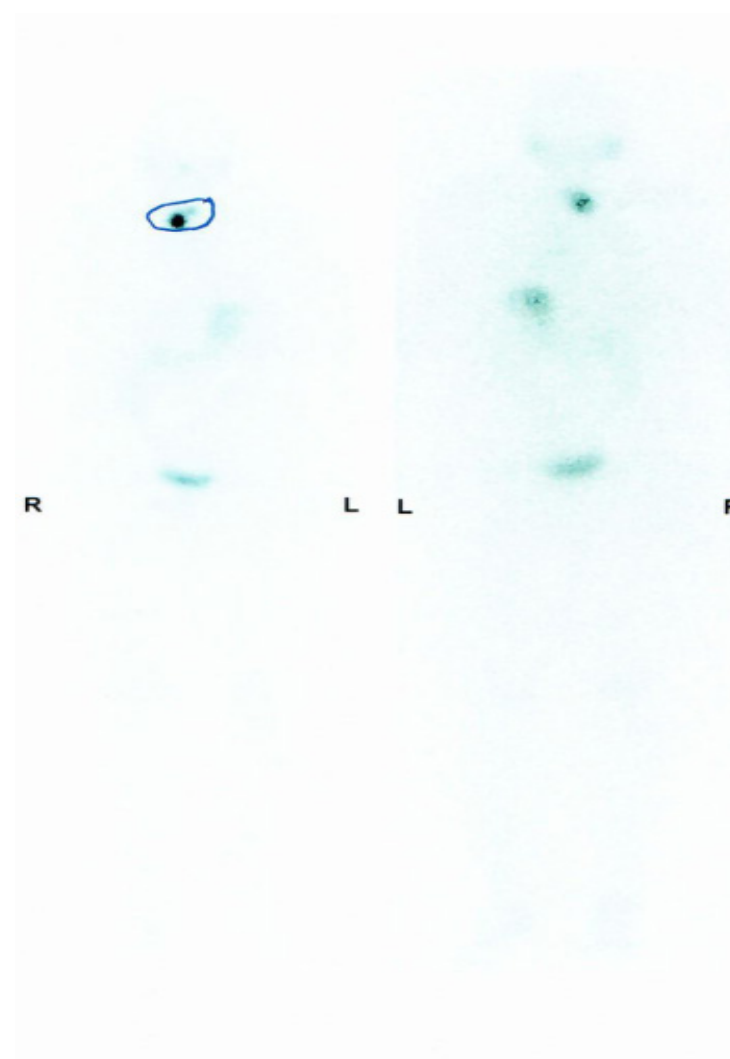


Figure 5. Pretherapy I131 scan showing residual thyroid tissue with no distant metastases

Using the history, examination and diagnostic and staging work up, the patient was categorized into the intermediate risk group and she was ablated with 2150MBq of I131. The post ablation WBS scan was done on day 2 and it showed uptake in residual tissue in thyroid bed and normal biodistribution in the rest of the scan. About a year post ablation, follow up assessment was done. Unstimulated TSH serum TG and anti TG- antibodies were done which were at 0.12ng/ml and within normal respectively. Additionally, on the follow up U/S of the neck no thyroid gland was seen in keeping with the previous therapy. The WBS with I-131 demonstrated no remnant tissue in the thyroid bed or the rest of the body (Fig 6). Using the criteria in the EANM/ATA this was classified as excellent response. At the time of publication, the patient was on a 2-5 years follow- up plan and suppression thyroid therapy (Haugen et al., 2015).

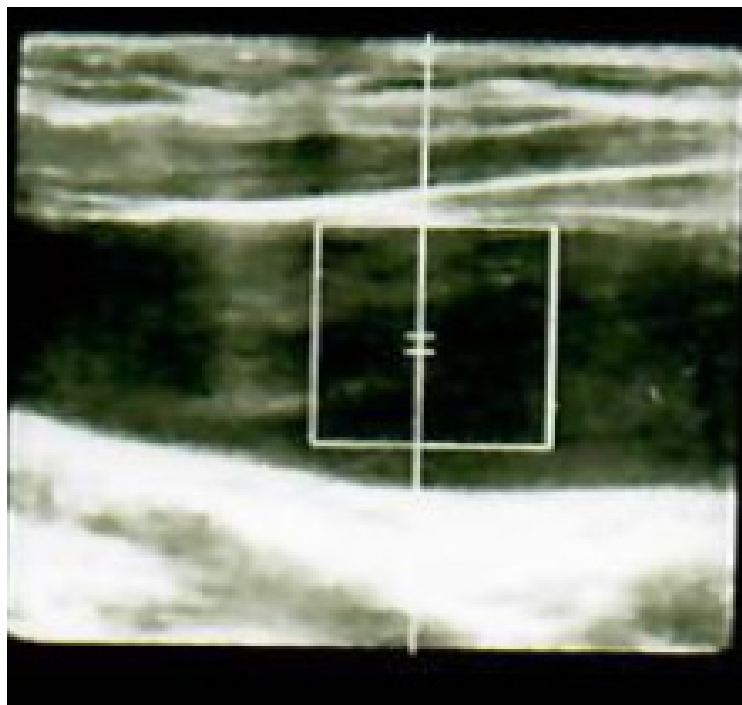


Figure 6. Post-I131 therapy-no thyroid gland

Discussion

Differentiated thyroid cancer patients can present with a varying degree of symptoms depending on the extent of the disease. Wartofsky L et al noted a wide range of presenting symptoms which included cough, dysphagia, odynophagia, haemoptysis, vocal cord paralysis and bone pain mostly in advanced disease (Nguyen et al, 2015). The patient may present with nodal metastases especially papillary thyroid cancer while lung and bone metastases are a rarer form of presentation (Nixon et al, 2012). Our patient who presented with occasional difficult to swallow was most likely due to compression symptoms as opposed to metastases since no local disease involvement was found. The other patient presented with a thyroid incidentaloma with no other presenting symptoms. A thyroid incidentaloma is an expected asymptomatic thyroid tumour discovered during the investigation of an unrelated condition (Russ, Leboulleux, Leenhardt, Hegedüs & 2014). The risk of malignancy in thyroid incidentaloma is similar to that of all thyroid nodules at 5 -13% in the absence of clinical risk factors (Russ, Bonnema, Erdogan, Durante, Ngu, Leenhardt, 2017; Yoon, Lee, Kim, Moon & Kwak, 2016).

A number of investigations are carried out to diagnose or confirm the diagnosis, stage, risk stratify and grade differentiated thyroid cancer diseases. This helps in planning for the most effective and appropriate individualised therapy for the patient. The investigations include Ultrasound scan of the neck (U/S), thyroid function test (TFT) for T3, T4, TSH, full blood count (FBC), ultrasound guided fine needle aspiration for cytology (FNAC)

or biopsy, Whole body scan with I 131 (I131 WBS), Chest x-ray, CT of neck and chest, Single photon emission computer tomography (SPECT) or SPECT/CT and Positron emission tomography (PET) or PET/CT (Luster et al 2008).

All our patients had pre-therapy U/S of neck and U/S guided FNAC. The main aim was to exclude thyroid cancer among nodules which occurs in 7- 15% depending on factors such as age, sex, neck radiation exposure history and family history. The U/S was performed to evaluate thyroid mass whether solid or cystic. U/S also assisted in diagnosing enlarged cervical lymph nodes (Nguyen et al, 2015). According to Haugen et al (2015), the thyroid nodules are a common problem with prevalence of palpable thyroid nodules approximated at (1-5 %) depending on gender in iodine sufficient parts of the world. This figure goes higher when a high-resolution U/S is used to 19- 68% of random selected individuals (Haugen, et al., 2015).

FNAC is an accurate and cost-effective method for evaluating thyroid nodules. When the procedure is performed under the guidance of U/S as compared to palpation, non- diagnostic and false – negative rates are reduced (Chung & Kim, 2019). The I131 WBS were done to stage the patients for loco-regional or distant metastases. These were pre-ablation and post-ablation scans to assess for iodine avidity and further assess the uptake and metastases respectively. CT of the neck and chest were performed in order to assess for metastases such as cervical lymph nodes as well as evaluate the anatomical extent of the tumour into the substernal region. Chest radiography is usually done if there are suspicious of lung metastases and in our set up this is routinely done before thyroidectomy. MRI is not routinely done in thyroid cancer evaluations but can be very instrumental in incidentaloma pick up (Sugianto et al., 2018). PET is more useful in recurrent or metastatic disease with negative I131 WBS but elevated serum thyroglobulin (TG) but not in routine usage (Leboulleux et al., 2007).

All our patients had their thyroid function tests done as part of the initial evaluation, in line with ATA 2015 (6). If serum TSH is subnormal, a radionuclide thyroid scan is done to ascertain the hot, warm, or cold nodules. A hot nodule has a low likelihood of harbouring malignancy and cytology may not be necessary. However, a high serum TSH level (even high normal) is associated with increased risk of malignancy in a thyroid nodule (Golbert et al., 2017). In the studies done by Biondi B et al, they reported that thyroid cell proliferation is TSH dependent to an extent that highly differentiated thyroid malignancies maintain that property. The principle of suppressive TSH therapy is based on this too (Golbert et al., 2017).

Management of DTC is based on the stage, risk stratification and prognostic factors which include Age > 55 years (AJCC8) or >45 years (AJCC7), tumour size, advanced stage, gender, extra thyroidal invasion and distant metastasis. Generally, DTC are not very aggressive tumours, with the best outcomes in low and intermediate risks.

Surgery has been recognized as the first line of therapy in DTC (Jayarangaiah et al., 2019). However, there are some exemption where surgery may not be indicated immediately such as, patients with very low risk tumour, patient at high surgical risk because of comorbid conditions, patients expected to have a short life span or those with medical or surgical conditions that need to be stabilised first (Haugen, et al., 2015). Most commonly used options for surgery include lobectomy, subtotal thyroidectomy depending on the stage, stratification, prognostication factors and the use of radioactive iodine therapy (RAIT). Many of our patients initially used to undergo lobectomy or subtotal thyroidectomy. This was because there was no RAIT being provided and many surgeons felt the need to avoid hypothyroidism by sparing some thyroid tissue. One problem with this approach is the high risk of recurrence associated with DTC especially in the intermediate and high-risk groups. However, with the current availability of RAIT, total or near total thyroidectomy is being performed more. Surgery is known to optimize disease free survival, overall survival, and quality of life in patients (Haugen, et al., 2015; Luster et al., 2008). Additionally, TT or near total thyroidectomy facilitates the use of radioactive iodine for ablation, adjuvant treatment and to utilise serum thyroglobulin in the follow up of patients. RAIT is given for ablation of remnant thyroid tissue, microscopic tumour foci and treatment of metastases thus reducing the chances of recurrence. The ablation of remnant thyroid tissues allows for the adequate follow up and early detection of recurrence with Tg and WBS (Bal & Ajit Kumar Padhy, 2015). The EANM recommends ablation of all differentiated thyroid cancer patients with tumour size above 1cm with RAIT (Cinar & Tas, 2015). Our patients were in the low to intermediate-risk disease and were given therapy in line with this EANM and ATA guidelines. In our patients, thyroid hormones supplements were not prescribed for 4 – 6 weeks post thyroidectomy in order to facilitate for the elevation of TSH to more than 30uIU/ml which stimulate RAI uptake and Tg release (Haugen et al., 2015). After TSH elevation, RAIT was administered in form of capsules (Haugen et al., 2015). In an event that TSH elevation is inadequate, and this is mostly due to extensive functioning thyroid cancer tissues left insitu post-thyroidectomy, recombinant human TSH (rhTSH) is used (Haugen et al., 2015). However, this option is not very practical in our resource constraint environment due to the cost

and limited availability of rhTSH, although it would be preferred by many patients. Post-ablation the patients were put on thyroid hormonal therapy. This serves to correct post-thyroidectomy and ablation hypothyroidism and also to suppress the growth of cancer cells by reducing TSH level.

Follow up assessments of our patients was done with the aid of clinical response, Tg with anti TG-antibodies, TSH, ultrasound scans and I131 WBS 6- 12 months post therapy. Tg as a tumour marker is supposed to be undetectable post TT and ablation. The first patient had Tg of 0.8ng/ml and the second it was 1.0ng/ml with normal anti TG anti-bodies on TSH stimulation. The neck ultra sounds and I131 WBS were negative for both case studies indicating excellent therapeutic responses. The ATA 2015 describes the status of the patient during follow up as excellent response, biochemical incomplete response, structural incomplete response or Indeterminate response depending on the clinical laboratory and imaging results (Haugen et al., 2015).

Conclusion

The use of radioactive iodine therapy in the management of DTC is well established and has been proven preceded by total or near total thyroidectomy. This reduces the risk of recurrence, improves the patients' quality of life and the overall survival rate. The success of this therapy depends on a multidisciplinary team approach and a well-structured follow up system. Case series have limitations such as none generalisation of findings. As such, there is need to conduct prospective studies based on larger sample sizes and interpretation with caution.

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