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Diagnostic Value of Serum Thyroglobulin in Differentiated Thyroid Carcinoma Patients to Monitor Persistence or Recurrence Disease

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Abstract

Serum thyroglobulin (Tg) is widely accepted as a tumor marker to evaluate the effectiveness of treatment for differentiated thyroid cancer (DTC) and to monitor for persistence or recurrence. However, Tg level can be misleading in the certain instances in which levels are low but have recurrence. The aim of this study to evaluate the diagnostic value of serum thyroglobulin in DTC patients to monitor persistence or recurrence disease

A retrospective study of 62 patients, 56 females and 6 males who had properly follow-ups after received I-131 ablation. Range of age was 19 to 73 years old. During the follow-ups, serum Tg, anti-thyroglobulin antibody (TgAb), chest X-ray and bone scintigraphy were examined. Serum thyroglobulin ≥ 2 ng/mL was used as positive for persistence or recurrence disease during thyroid hormone withdrawal.

Positive Tg and negative TgAb were found in 6 of 62 (9.67%) patients who showed abnormal uptake on bone scintigraphy. Negative Tg in 56 of 62 (90.03%) patients, 49 of 56 (87.5%) patients had both Tg and TgAb negative and bone scintigraphy also showed normal uptake. 6 of 56 (10.7%) patients had negative both Tg and TgAb but having abnormal bone scintigraphy which showed uptake at ribs in two patients, at lumbal spine in two patients, at sternum in one patient and the rest at both right-sacroiliac joint and parietal bones. One of 56 (1.7%) patient who had negative Tg, positive TgAb, normal bone scintigraphy and I-131 whole body scan showed an abnormal uptake at left and right area of the neck. Sensitivity and specificity for serum thyroglobulin were 46.15% and 100% respectively.

Serum thyroglobulin cannot be considered as a single indicator to monitor of thyroid cancer, furthermore TgAb examination should be included. Additional imaging tests such bone scintigraphy, I-131 whole body scan may improve diagnostic value to identify persistence or recurrence disease.

Keywords : Differentiated thyroid carcinoma, persistence, recurrence, serum thyroglobulin

Introduction

Primary treatment of differentiated thyroid carsinoma (DTC) consist of near-total thyrodectomy followed by Iodine-131 ablation therapy for thyroid tissue remnants and possible metastases.[1,2] After complete destruction of remnants, metastases or recurrence can be detected by measurement of the serum thyroglobulin (Tg) level as well as by radionuclide methods.[3]

Serum Tg is a glycoprotein that is produced exclusively by normal or neoplastic thyroid follicular cells (papillary and follicular cancer tissues). In the absence of the normal thyroid tissue, the only source of Tg production is metastases or local recurrences of follicular or papillary carcinomas.[4] It is widely accepted as a tumor marker to evaluate the effectiveness of treatment for DTC and to monitor for persistence or recurrence diseases. Some doctors have used as the first and only procedure to perform in low-risk patients, which is can reduce the need for whole body scan (WBS) or other imaging techniques.[5] However, Tg level can be misleading in the certain instances in which levels are low in the presence of metastases. Beside of that, there is no consensus about the precise level of serum thyroglobulin for clinical decision; detectable or undetectable.[6]

Furthermore, to increase the sensitivity of serum Tg in detection of metastases or tumour recurrence, measurement of serum Tg while patients are withdrawal of L-thyroxine (LT4) therapy (Tg-off) or during the use of recombinant human thyroid-stimulating hormone (rhTSH) to avoid the morbidity associated with hypothyroidism secondary to withdrawal of LT4.[7,8]

The objective of this study is to evaluate the diagnostic value of serum thyroglobulin to monitor persistence or recurrence of differentiated thyroid carcinomas.

Material and Methods

Patients

This retrospective study involved of 62 patients, 56 females and 6 males (range of age 19 to 73 years) with DTC who were referred to Nuclear Medicine Instalation Dr.M.Djamil Hospital Padang Indonesia. They had been treated by I-131 ablation therapy with doses (30-100 mCi) after 4-6 weeks near-total thyroidectomy. I-131 whole body scan was performed 3 days after I-131 therapy. Examinations were done 4-6 months after I-131 ablation therapy included serum Tg, anti-thyroglobulin antibody (TgAb), thyroid stimulating hormone (TSH), chest X-ray and bone scintigraphy. The presence of persistence or recurrence was confirmed clinically, radiology or scintigraphy.

Imaging

^{131}I whole-body scans and bone scans used a single-head gamma camera (sophy). ^{131}I scans were performed 72 hours after the administration therapeutic doses of (30 – 150 mCi) ^{131}I. High-energy collimator was used with photopeak centred on on 364 KeV±20%. For both ^{131}I whole-body scans and bone scans anterior dan posterior view were obtain. Bone scans used low-energy-high-resolution collimator with the photopeak centred on 159 keV±20%. Scans were performed 4 hours after the administration 20 mCi of ^{99m}TC- methylene diphosphonate (MDP).

Therapy

All patients were treated with accumulated dose range between 30- 250 mCi. Repetition therapy of ^{131}I based on serum Tg/TgAb and scintigraphy results after 4-6 months of initial therapy. ^{131}I whole body scan was performed 72 hours after administration of ^{131}I

Serum Tg, Tg Ab and TSH

Blood sample for measurements of Serum Tg was, TgAb and TSH were obtained after 4-6 weeks discontinued of LT4. Immunoradiometric assay (IRMA) was applied to measured serum Tg, Tg Ab and TSH. Serum thyroglobulin ≥ 2 ng/mL and positive Tg Ab were used for persistence or recurrence disease, while TSH levels above 30 uIU/mL.

Results

In 6 of 62 (9.67%) patients, serum Tg was positive and negative TgAb who showed abnormal bone scintigraphy results. Negative Tg in 56 of 62 (90.03%) patients, 49 of 56 (87.5%) patients who had Tg and TgAb negative, showed a normal bone scintigraphy results. 6 of 56 (10.7%) patients had negative both Tg and TgAb, on the contrary, the bone scans result showed high-uptake at ribs in two patients, at lumbal spine in two patients, at *sternum* in one patient and the rest at both *parietal bones, sternun, thoraco-lumbal spine, right sacroiliac joint and*. One patient of 56 (1.7%) had negative Tg, positive TgAb, normal bone scintigraphy, but on the other hand and I-131 whole-body scan showed an uptake at left and right area of the neck. Sensitivity and specificity for serum thyroglobulin were 46.15% and 100% respectively.

Many studies investigate both the sensitivity and specificity serum Tg. However measurement of specificity requires the capability to distinguish between true-and false-positive results, which is sometimes difficult.[9] Negative or Low Thyroglobulin level maybe due to presence of interfering anti-Tg antibodies in 40% of patients with DTC,[10,11] dedifferentiation of the tumor cells make they can still trap iodide but no longer make and release Tg, Hook Effect showed a normal or low serum Tg in sera with very high serum Tg, which it exceed the binding capacity of the Tg capture antibody and different standardization of Tg serum assay.

A neck ultrasound confirms recurrence due to isolated neck lymph-nodes metastase, furthermore the weakness of ultrasonography is high operator dependence. Another prodecures such as Tc-99m tetrofosmin, Tc-99m Sestamibi, FDG can be useful in patients with a high likelihood of persisten or recurrent DTC.

Conclusion

Serum thyroglobulin cannot be considered as a single indicator to monitor of thyroid cancer, furthermore TgAb examination should be included. Additional imaging tests such bone scintigraphy, I-131 whole body scan or FDG may improve diagnostic value to identify persistence or recurrence disease

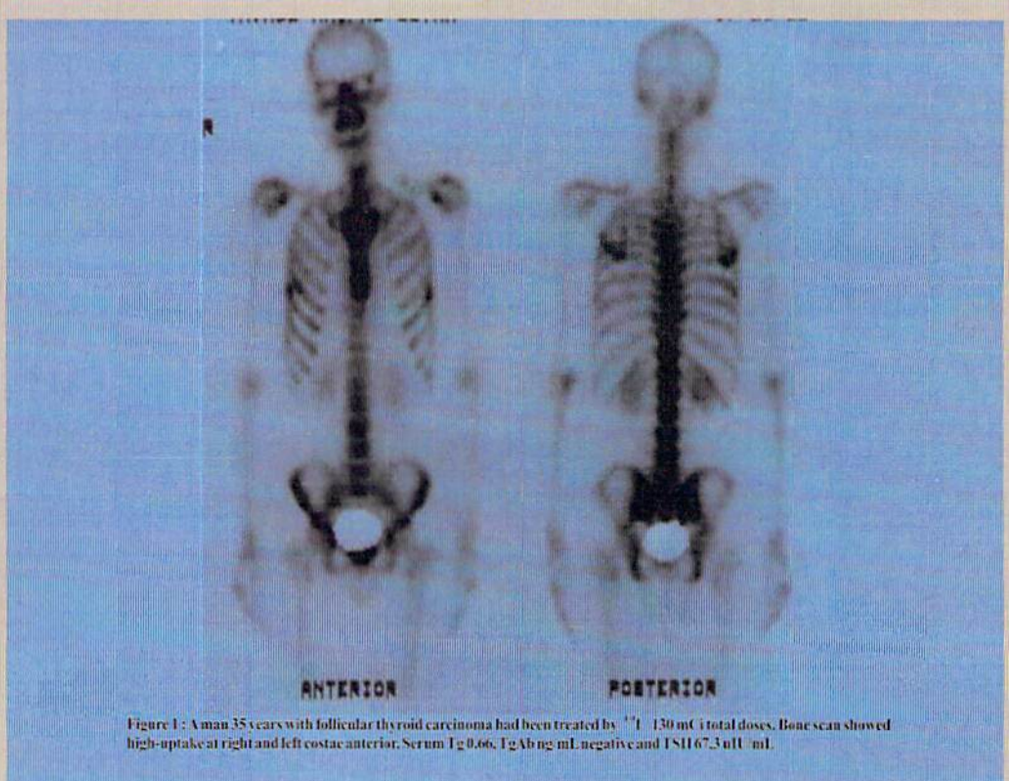

Figure 1 : A man 35 years with follicular thyroid carcinoma had been treated by ^{131}I 130 mCi total doses. Bone scan showed high-uptake at right and left costae anterior. Serum Tg 0.66, TgAb ng/mL negative and TSH 67.3 uIU/mL

Discussion

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