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Role of Thyroglobulin, Radioactive Iodine I-131, and Tc-99m Furifosmin "Q_{12}" in the Follow up of Post Ablated Well Differentiated Thyroid Cancer

Thesis

Submitted in partial fulfillment of the Degree of M. Sc. In Nuclear Medicine

By

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TO MY FAMILY

جامعة القاهرة / كلية الطب
القصر العيني

محضر

أجتماع لجنة الحكم على الرسالة المقدمة من
الطبيب / جوزيف اديب يوسف
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في الطب النووي

تحت عنوان : باللغة الانجليزية : Role of Thyroglobulin, Radioactive Iodine I-131 and Tc 99m Furifosmin "Q12" in the Follow up of Post ablated well differentiated Thyroid cancer

: باللغة العربية : دور الثيروجلوبولين ، اليود - ١٣١ المشع و التكنيشيوم ٩٩م فيروفوسمين في متابعة حالات سرطان الغدة الدرقية

بناء على موافقة الجامعة بتاريخ ٢ / ٩ / ٢٠٠٠ تم تشكيل لجنة الفحص والمناقشة للرسالة المذكورة أعلاه على النحو التالي :-

١) أ.د. [illegible]
٢) أ.د. [illegible] من المشرفين
٣) أ.د. [illegible] ممتحن داخلي
ممتحن خارجي

قامت اللجنة بفحص الرسالة بواسطة كل عضو منفردا وكتابة تقارير منفردة لكل منهم إنعقدت اللجنة مجتمعة في بتاريخ ٢٨ / ٩ / ٢٠٠٠ بقسم [illegible] بكلية الطب - جامعة القاهرة وذلك لمناقشة الطالب في جلسة علنية في موضوع الرسالة والنتائج التي توصل إليها وكذلك الأسس العلمية التي قام عليها البحث .

قرار اللجنة : قبول الرسالة [illegible]

توقيعات أعضاء اللجنة :-

المشرف الممتحن
المستحن الداخلي
الممتحن الخارجي

Title

Role of Thyroglobulin, Radioactive Iodine (I-131) and Tc-99 m Furifosmin "Q12" in the follow-up of post-ablative well-differentiated thyroid cancer.

Author

Moustafa H., Farag H., Omar W. and Iskander J.

Abstract

The purpose of the study was to evaluate the use of Tg as tumor marker and Tc-99m Q12 as non-specific tumor imaging agent versus the standard Radioiodine in assessment of follow-up of differentiated thyroid cancer. ***Methods:*** A prospective study was performed on 39 patients (25 females and 14 males) with DTC (24 papillary; 15 follicular) with near total thyroidectomy in 29 patients and block neck dissection in 10 of them. All patients were subject to serum Tg level estimation, whole body imaging using Tc-99m Q12 and I-131 after discontinuation of thyroid hormone replacement. ***Results:*** There were a negative concordant result of the three methods investigated in 11 patients and concordant positive result in 10 patients. Disconcordant results were seen in 18 patients with positive Tg. 6/17 had false negative results with I-131 WBS and 12/17 had false negative results with Tc-99m Q12. Only one patient showed false positive in serum Tg, with negative WBS by both isotopes. ***Conclusion:*** Serum Tg estimation as tumor marker is considered as the main method of follow-up in cases of post-ablated differentiated thyroid cancer. It showed 100% sensitivity and 97.2% specificity. Standard I-131 WBS is the main method for assessment of residual or recurrent thyroid lesions as well as metastatic bone lesions. In case of high serum Tg level and negative standard radioiodine scan, localization of metastasis can be made by a non specific tumor imaging agent such as Tc-99m Q12 which showed better assessment of metastatic cervical lymph nodes and metastatic lung lesions if compared to I-131.

Keyword

Thyroid cancer follow-up

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Josephine Adib Youssef.

CONTENTS

INTRODUCTION

Well differentiated thyroid carcinoma is a slowly growing tumor where local recurrence & distant metastasis may occur many years after the initial diagnosis. So, patient with well differentiated thyroid carcinoma requires long term follow up. Some lesions may recur in the remaining thyroid tissue and metastatic thyroid tissue don't concentrate radioiodine in the presence of normal thyroid tissue *(Mazzaferri, 1997).*

The total body scan with radioactive I-131 is the standard method for assessment of patients with differentiated thyroid cancer. However there are considerable variations in the affinity of thyroid carcinoma for radioactive I-131, about 25% of tumor lesions don't show I-131 uptake. This is often related to an inadequate period of thyroid hormone withdrawal; iodine intake in the diet; the size of the tumor & the administration of insufficiently large dose of I-131 for scintigraphy. So, as the results of I-131 scans are sometimes inconclusive. Attempts have been made to find alternative radiopharmaceutical.

Tc-99m furifosmin was developed as myocardial perfusion imaging but additional applications as non specific tumor imaging agent has been tried similar to methoxyisobutyl-isonitrile (MIBI) & TC-99m tetrofosmin. Tc-99m furifosmin "Q-12" has the advantage being available as kits using high dose of technetium four times that

used in radioactive I-131 which leads to better images. Also no need to stop thyroxin before the study.

Thyroglobulin (Tg) is a normal constituent of serum, detectable by radioimunuassay in 75-90% of healthy adults. Its level is altered in a number of physiologic & pathologic conditions. It may be elevated in non malignant conditions such as Grave's disease; thyroditis or modular goiter ***(Rafetoff and Lever 1983).*** Thyroglobulin (Tg) as a good tumor marker can be used in the follow up of differentiated thyroid cancer, Tg is low in patient underwent thyroid ablation & any elevation in Tg level may indicate the presence of recurrence or metastatic spread but it can't localize site of metastasis or recurrence, so better to be combined with other imaging technique.

Aim of the work:

- The use of Tg as tumor marker in the follow up of differentiated thyroid cancer & its correlation with other imaging techniques.
- Evaluation of Tc-99m-Q-12 as non specific tumor imaging agent versus the standard radioiodine in assessment of post-ablated thyroid cancer.

PHYSIOLOGY OF THE THYROID GLAND

The physiologic activity of the follicular epithelium is maintained by the thyrotropic hormone (TSH) of the anterior pituitary. With increased amounts of thyroxin (T_4), TSH is decreased and the thyroid gland becomes less active. Since some thyroid tumors are hormonally dependent on TSH. Thyroxin is usually administered therapeutically to patients with differentiated thyroid cancer in the hope that with suppression of TSH, the tumor may grow more slowly. With a deficiency of the thyroid hormone, TSH increases and stimulates the thyroid to become hyperplasic. Some thyroid tumors may be stimulated to greater activity with TSH therapy, a principle that may be useful in bringing about a greater uptake of radioiodine by the tumor *(Tonietti et al., 1967).*

The follicular cells perform many functions. They form colloid, which is essentially thyroglobulin. The cells trap and incorporate iodide into the thyroglobulin, and by secreting various oxidative enzymes bring about the iodination of tyrosine to transform it into the thyroid hormone. The same cells also elaborate a proteolytic enzyme that breaks the thyroglobulin-thyroxin bond so that thyroxin may be released and transported to the tissues. Since it has been demonstrated by autoradiography that various constituents of thyroglobulin as well as iodine are taken up by each cell of the follicle, it appears that all follicular cells perform the same functions *(Singer, 1990).*

PATHOLOGY OF CANCER THYROID

Virtually all-malignant neoplasms of the thyroid are epithelial in origin and hence are carcinomas. The currently utilized World Health Organization (WHO) pathologic classification of thyroid cancer formulated in 1974, divides all thyroid tumors into those arising from parafollicular (C-cell) elements and those arising from follicular epithelium or other sites. Those arising from the follicular epithelium may be differentiated (papillary, follicular) or undifferentiated (anaplastic, small cell), whereas the parafollicular epithelial carcinomas are usually moderately well differentiated "medullary" ***(Hedinger et al., 1989).*** The small cell carcinoma may represent a form of undifferentiated carcinoma arising from the follicular epithelium or may represent a primary lymphoma ***(Rayfield et al., 1971).*** Rarely the thyroid is the seat of a metastatic deposit or of a fibrosarcoma or lymphosarcoma, both of which are highly malignant. Metastases of extrathyroidal cancers to the thyroid are probably more common than is usually appreciated and occasionally present a problem in diagnosis ***(Woolner et al., 1961).***

PAPILLARY CARCINOMA

In most series, carcinoma that is either purely or predominantly papillary in structure is the most common; between 80-90% of the differentiated thyroid cancers are classified as papillary. They occur as a broad age range with a mean of about 45 years. Women are affected two to three times more commonly than men. Young patients with this disease sometimes give a history of having received x-ray therapy during childhood for cervical lymphadenitis or thymic enlargement, suggesting that radiation of the thyroid gland may play a pathogenic