

Original article

Lung metastases in patients with differentiated thyroid carcinoma and evaluation of response to radioiodine therapy

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ABSTRACT

Introduction: The most common site of metastases in differentiated thyroid carcinomas is the lungs. In our study, we aimed to determine the ratios of lung metastases in patients with differentiated thyroid carcinoma and response to radioiodine therapy.

Material and methods: A total of 542 patients with differentiated thyroid carcinoma who were admitted to our clinic were included in the study. High doses of ^{131}I were administered to the patients with lung metastases. Response to therapy were evaluated with ^{131}I scans and stimulated serum Tg levels were examined at least 6 months after therapy.

Results: Lung metastases were detected in 17 (3.1%) of 542 patients with differentiated thyroid carcinoma. Of these patients to whom high doses of ^{131}I therapy were administered, complete response to therapy was obtained in 5 (29.4%), partial response was obtained in 3 (17.6%) and no response could be obtained in 9 (53%) patients.

Conclusion: Although lung metastases from differentiated thyroid carcinomas are rare, those are more common in advanced ages and in males. High doses of ^{131}I therapy may be partially beneficial in these patients. Thus repetition of therapy is frequently required.

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Metástasis pulmonar en pacientes con cáncer diferenciado de tiroides y evaluación de la respuesta a la terapia con radioyodo

RESUMEN

Introducción: La localización más común de las metástasis a distancia en tumores diferenciados de tiroides es el pulmón. En este estudio se pretende determinar la proporción de metástasis pulmonares en el cáncer diferenciado de tiroides y su respuesta a la terapia con radioyodo.

Material y métodos: Quinientos cuarenta y dos pacientes con cáncer diferenciado de tiroides fueron incluidos en este estudio. Se administraron altas dosis de ^{131}I a los pacientes con metástasis pulmonares. La respuesta a la terapia se evaluó con estudios con ^{131}I y niveles de tiroglobulina estimulada al menos 6 meses después de la terapia inicial.

Resultados: Se detectaron metástasis pulmonares en 17 (3,1%) de los 542 pacientes. Tras la terapia con dosis altas de ^{131}I se observó respuesta completa en 5 (29,4%), respuesta parcial en 3 (17,6%) y no se obtuvo respuesta en 9 (53%) de los pacientes.

Conclusión: Aunque las metástasis pulmonares en los cánceres diferenciados de tiroides son raras, son más frecuentes en edades avanzadas y en varones. Altas dosis de ^{131}I pueden ser beneficiosas, aunque habitualmente esta terapia debe repetirse.

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Palabras clave:

Carcinoma diferenciado de tiroides

Metástasis pulmonares

Terapia con radioyodo

Introduction

Thyroid carcinomas are the most common endocrine tumors and yearly incidence has been reported as 7.1–8.8/100,000 in USA.^{1,2} This ratio may vary according to countries. Incidence has been suggested to increase in recent years (approximately 2.4-folds).^{3–5} Differentiated thyroid carcinomas (DTCs) constitute more than 90% of thyroid carcinomas.⁶ Although DTC usually has a good prognosis, recurrences and metastases may develop in years. Distant metastases are seen in 10% of papillary thyroid carcinomas

and 25% of follicular thyroid carcinomas.⁷ Lungs are the most common distant metastases localization followed by bones.^{8,9} Distant metastases in DTCs have been reported to lungs in the ratio 70% and to bones in the ratio of 20%.¹⁰ Lung metastasis is a important factor that effects the prognosis poorly.^{10,11}

Total thyroidectomy, radioiodine (^{131}I) therapy and TSH suppression are the most common ways for the treatment of DTCs. Risk of lung metastasis development is about 1.3% in patients who undergo total thyroidectomy followed by radioiodine therapy.¹² Amount of ^{131}I given in treatment of lung metastases cases should be more than 7.4 GBq (200 mCi) usually.¹³ Diffuse (miliary) lung metastases respond better to radioiodine therapy compared to nodular lung metastasis. Ratio of complete response to radioiodine therapy is not very high in DTC cases with lung metastases.

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The main complication of radioiodine therapy is pulmonary fibrosis. This complication is rare and especially seen in patients with diffuse lung metastases treated with high doses of ^{131}I .¹⁴ Limiting total dose and prolonging therapy intervals are recommended in order to prevent this complication.

In our study, we aimed to determine frequency of lung metastases and response to radioiodine therapy in DTC patients who were admitted to our clinic.

Material and methods

A total of 542 DTC patients (93 males, 449 females with mean age of 44 ± 13.5 years) who are treated and followed up in our clinic and 17 of these patients with lung metastases (4 males, 13 females with mean age of 48.7 ± 19 years) were included in the study. Histopathologic diagnosis of 518 patients revealed papillary thyroid carcinoma and for 24 patients it was follicular thyroid carcinoma.

Iodine free diet was applied for at least two weeks prior to ^{131}I therapy of patients with lung metastases and TSH was kept above $30 \mu\text{U/ml}$. Thyroglobulin (Tg) were measured using immunoradiometric analyzer that uses paramagnetic microparticles and chemiluminescent detection technology. Each individual sample was tested a single time for each analyte. Tg results above the manufacturer's reference limit were considered $0.4\text{--}4.1 \text{ ng/ml}$. Therapy doses were determined empirically. It was usually given as $7.4\text{--}11.1 \text{ GBq}$ ($200\text{--}300 \text{ mCi}$) ^{131}I oral capsules. Number, size, pathological subtype and iodine uptake of metastases were taken into consideration when determining therapy doses. Duration of follow-up was maximum 36 months. Iodine scan was done with 185 MBq (5 mCi) ^{131}I when $\text{TSH} > 30 \mu\text{U/ml}$ in patients whose stimulated serum Tg levels $< 2 \text{ ng/ml}$ six months after therapy. Iodine scan was done with ^{131}I in therapy doses in patients whose stimulated serum Tg levels $> 2 \text{ ng/ml}$ six months after therapy. Interval between two therapies was provided to be minimum 6 months in repeated therapies. Therapy was repeated maximum three times. Maximum cumulative dose was 2400 GBq (750 mCi). Patients were divided into three groups according to therapy results: Patients who responded to therapy completely were classified as Group I, partially responded as Group II and unresponsive ones were classified as Group III. Group I patients whose stimulated serum

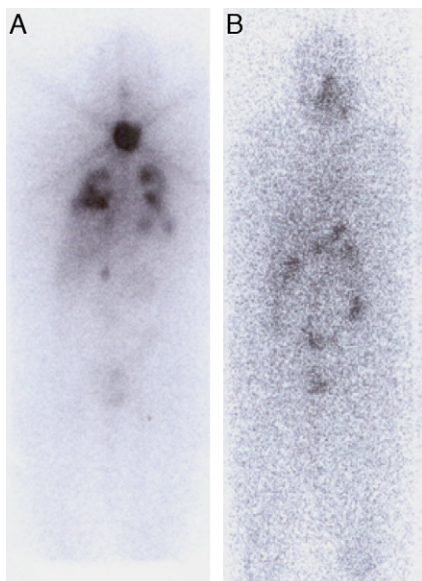


Fig. 1. Whole body scans before (A) and after (B) treatment in patients with lung metastases who completely responded to radioiodine therapy (Tg: 1.5 ng/ml).

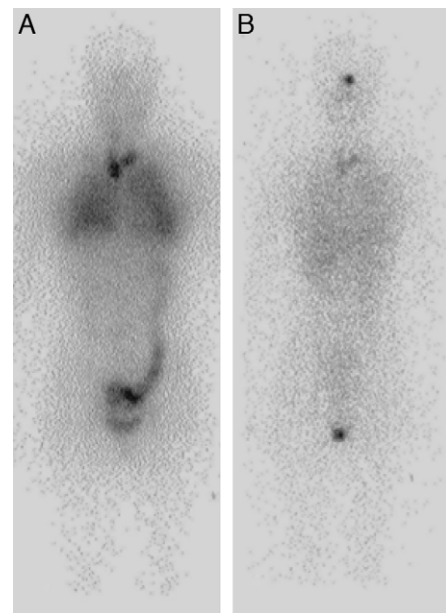


Fig. 2. Radioiodine uptake decreasing on the lungs was observed following the second therapy (B) in a patient with diffuse lung metastases (A) who treated radioiodine therapy two times (Tg $> 300 \text{ ng/ml}$).

Tg levels were below 2 ng/ml and iodine scans were negative were accepted to completely respond to therapy (Fig. 1). Group II patients whose iodine scan results were negative or positive but serum Tg levels reduced below initial values although above 2 ng/ml were accepted to partially respond to therapy (Fig. 2). Group III patients whose iodine scan results were negative or positive but serum Tg levels did not change or increase were considered not to respond to therapy (Fig. 3).

Results

Of 542 DTC patients included in the study, 518 (95.6%) had papillary cancer and 24 (4.4%) had follicular cancer. Lung metastases were detected in 17 (3.1%) patients. While mean age

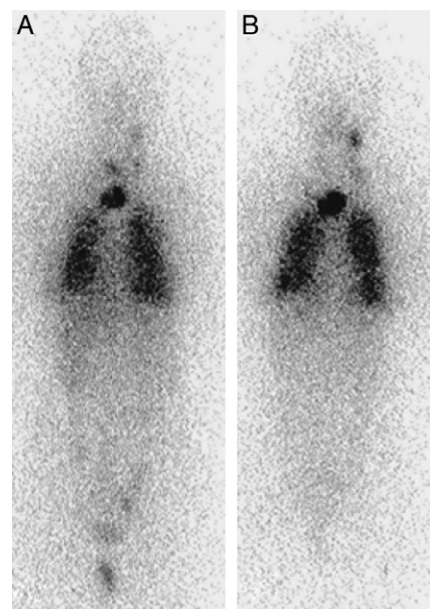


Fig. 3. Whole body scans before (A) and after (B) therapy in a patient with lung metastases who treated three times but not responded to radioiodine therapy (Tg $> 300 \text{ ng/ml}$).

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