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Original article

Expression profile of biomarkers altered in papillary and anaplastic thyroid carcinoma: Contribution of Tunisian patients

Asma Fourati [1], Olfa El Amine [1], Wided Ben Ayoub [2], Imen Cherni [1], Aida Goucha [1], Michèle Véronique El May [3], Amor Gamoudi [1], Ahmed El May [1]

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1. Salah Azaiez Cancer Institute, Department of Immuno-Histo-Cytology Salah Azaiez, Place Bab Saadoun, 1006 Tunis, Tunisia
2. Salah Azaiez Cancer Institute, Department of Epidemiology, Place Bab Saadoun, 1006 Tunis, Tunisia
3. University of Tunis El Manar, Faculty of Medicine, Research unit 01/UR/08-07, Tunis, Tunisia

Correspondence:
Asma Fourati, Salah Azaiez Cancer Institute, Department of Immuno-Histo-Cytology Salah Azaiez, Place Bab Saadoun, 1006 Tunis, Tunisia.
asma.fourati@rns.tn

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Molecular marker
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Summary

Aims > The objective of this study was to compare the protein expression profile between well-differentiated (papillary) and undifferentiated (anaplastic) thyroid carcinoma in Tunisian patients.
Methods > This first Tunisian retrospective study concerned data of 38 thyroid cancer cases (19 papillary carcinoma PTC and 19 anaplastic carcinoma ATC) collected at Salah Azaiez Institute of Tunisia. Immunohistochemistry was used to evaluate tumor expression of different molecular markers (p53, Ki67, E-cadherin, cyclin D1, bcl2, S100 and Her-2). The molecular expression was correlated with the clinicopathological characteristics of the tumors.
Results > There were 6 differentially expressed markers when comparing anaplastic thyroid carcinoma ATC with papillary thyroid carcinoma PTC. Expression of p53 and Ki67 were significantly increased in 16 and 18 ATC cases respectively, the Ki67 expression was lost in PTC. Cyclin D1, E-cadherin, bcl2 and S100 were overexpressed in PTC tumors; however, they were significantly decreased in ATC. The last marker, Her-2 was expressed in one case of PTC only.
Conclusion > Our results, similar with findings of other ethnic groups, showed alteration in expression of molecular markers associated with tumor dedifferentiation, indicating loss of cell cycle control with increased proliferative activity in ATC carcinoma. These data support the hypothesis that ATC may derive from dedifferentiation of preexisting PTC tumor.

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Original article

Mots clés
Marqueurs moléculaires
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et papillaires de la thyroïde
Immunohistochimie

Résumé

Profil d'expression des biomarqueurs altérés dans le carcinome papillaire et anaplasique de la thyroïde : contribution des patients tunisiens

Objectifs > L'objectif de cette étude était de comparer le profil d'expression protéique entre carcinomes thyroïdiens bien différenciés (papillaires) et indifférenciés (anaplasiques) chez des patients tunisiens.
Méthodes > Cette première étude rétrospective tunisienne a porté sur 38 cas de cancer de la thyroïde (19 carcinomes papillaires PTC et 19 carcinomes anaplasiques ATC) collectés à l'institut Salah Azaiez de Tunisie. On a utilisé l'immunohistochimie pour évaluer l'expression tumorale de différents marqueurs moléculaires (p53, Ki67, E-cadhérine, cycline D1, bcl2, S100 et Her-2). L'expression moléculaire a été corrélée aux caractéristiques clinicopathologiques des tumeurs.
Résultats > Une différence de l'expression de 6 marqueurs moléculaires a été montrée lors de la comparaison du carcinome anaplasique ATC avec le carcinome papillaire PTC de la thyroïde. L'expression de p53 et Ki67 a été significativement augmentée respectivement dans 16 et 18 cas ATC, l'expression du Ki67 a été complètement perdue dans PTC. La cycline D1, la E-cadhérine, la bcl2 et la S100 ont été surexprimées dans les tumeurs PTC, mais elles ont été significativement diminuées dans l'ATC. Le dernier marqueur, Her-2, a été exprimé dans un seul cas de PTC.
Conclusion > Nos résultats, semblables aux résultats d'autres groupes ethniques, ont montré une altération de l'expression des marqueurs moléculaires associés à la dédifférenciation tumorale, ce qui indique une perte de contrôle du cycle cellulaire avec une activité proliférative accrue dans le carcinome ATC. Ces données sont en concordance avec l'hypothèse que l'ATC peut dériver de la dédifférenciation de tumeur PTC préexistante.

Introduction

Anaplastic thyroid carcinoma (ATC) remains the most extremely aggressive cancer characterized by rapid, distant metastasis. This disease is very rare, and constitutes less than 2% of all thyroid tumors. Furthermore, it occurs in older patients, with an average survival rate of only 6 months after diagnosis [1]. ATC represents the poorest differentiated subtype of thyroid cancer, these characteristics make ATC resistant to the conventional treatment [2,3]. Due to this rarity, research of cellular origin and molecular etiology is needed to improve prognostic and therapeutic molecular markers of ATC. By pathological examination, some lesions showed undifferentiated tumors adjacent to well-differentiated tumors such as papillary or follicular carcinoma [4,5]; based on these observations, it has been hypothesized that ATC can arise de novo or by anaplastic transformation of preexisting differentiated thyroid carcinoma [6].
Several investigations focused to understand thyroid biological alterations by evaluating expression of protein markers involved in cell proliferation, apoptosis and adhesion. Multiple genetic changes have been implicated as helpful diagnostic and prognostic markers during initiation and progression in the pathogenesis of ATC and DTC [7–9].
Understanding prognostic variables in ATC remains poor because of the small number of patients. Until now, there are only a few previous reports of outcomes in large groups of ATC in different populations. For this reason, we proposed by the present study to contribute to the knowledge of ATC biomarkers by a Tunisian series. We compared the expression of a panel of molecular markers (p53, bcl2, Ki67, cyclin D1, S100, E-cadherin and Her-2) in ATC and PTC series, in order to clarify if differences in tumor phenotype reflect intratumoral molecular heterogeneity and if the Tunisian molecular profiles of ATC and PTC correlate with subtypes of patients of previous studies.

Materials and methods

Patients

This study was realized in Salah Azaiez Institute in Tunis (which is the only oncology hospital in Tunisia), and concerned 38 patients with thyroid carcinoma between 2000 and 2010. All patients underwent surgical treatment with curative intention. In the present study, we included archival specimens of all ATC collected between 2000 and 2010 (n = 19) and 19 classic well-differentiated PTC in the same period. Diagnoses were based on the final pathology report after total thyroidectomy or lobectomy, 6 ATC patients of our series underwent a biopsy for diagnosis. Specimens were included in paraffin and 3 µm sections were hematoxylin and eosin (H E) stained, or proceeded for immunohistochemistry; the slides were examined by two

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