



# Morphological and clinical presentation of papillary thyroid carcinoma in children and adolescents of Belarus: The influence of radiation exposure and the source of irradiation



Mikhail Fridman <sup>a,b,\*</sup>, Alfred King-yin Lam <sup>c</sup>, Olga Krasko <sup>d</sup>, Kurt Werner Schmid <sup>e</sup>, Daniel Igor Branovan <sup>f</sup>, Yuri Demidchik <sup>a,b</sup>

<sup>a</sup> Republican Centre for Thyroid Tumors, Prospect Nezavisimosti 64, 220013 Minsk, Belarus

<sup>b</sup> Belarusian Medical Academy of Post-Graduate Education, P. Brovki st. 3, 220013 Minsk, Belarus

<sup>c</sup> School of Medicine and Menzies Health Institute Queensland, Griffith University, Gold Coast, QLD 4222, Australia

<sup>d</sup> United Institute of Informatics Problems, National Academy of Sciences of Belarus, Surganova St. 6, 220012 Minsk, Belarus

<sup>e</sup> Institute of Pathology, University Hospital of Essen, University of Duisburg-Essen, Hufelandstraße 55, 45147 Essen, Germany

<sup>f</sup> Project Chemobyl Inc., Voorhies Av. 1810, Brooklyn, 11235 NY, USA

## ARTICLE INFO

### Article history:

Received 22 March 2015

Accepted 31 March 2015

Available online 1 April 2015

### Keywords:

Papillary thyroid carcinoma  
Children and adolescents  
Chernobyl disaster

## ABSTRACT

**Objective:** The aims were to analyse the features of papillary thyroid carcinoma in a large cohort of children and adolescents in Belarus and to study the influence of radiation exposure as well as the source of irradiation on the morphological and clinical presentations of tumours.

**Design and patients:** The clinical and pathological features of 1086 young patients (age range = 4 to 18 inclusive, followed up for  $\geq 18$  years) with papillary thyroid carcinoma diagnosed during the years 1990 to 2010 were reviewed. The patients were divided into three groups: “external radiation-related”, “post-Chernobyl” (internal irradiation-related) and “sporadic”. Besides, patients from “post-Chernobyl” cohort ( $n = 936$ ) were further divided into the three equal subgroups according to the dates of surgery, which were corresponding to the early (4–9 years), intermediate (10–12 years) and long (14–18 years) latency periods.

**Results:** Patients in the “external radiation-related” group often showed extra-thyroidal extension in tumours sized  $\leq 10$  mm ( $p = 0.002$ ). Distant metastases were more frequently ( $p = 0.006$ ) discovered in patients with papillary thyroid carcinoma in post-Chernobyl group (104 of 936, 11.1%) when compared to juveniles from other two groups. Lateral nodal disease and distant metastases were often noted in post-Chernobyl patients operated during the early and intermediate latency periods only.

**Conclusion:** Young patients in Belarus with papillary thyroid carcinoma in the “post-Chernobyl” group differed in many clinical and pathological parameters from those in the “sporadic” group. “External radiation related” papillary thyroid carcinomas were distinguished from other two groups of carcinoma in more advanced local spread and more aggressive behaviour of micro-carcinomas.

© 2015 Elsevier Inc. All rights reserved.

## 1. Introduction

Epidemiological surveys have shown that exposure to ionizing radiation (in particular intake of  $I^{131}$ ) in childhood or adolescence is a strong environmental risk factor for development of papillary thyroid carcinoma (Cardis and Hatch, 2011; United Nations, 2011).

Belarus is a country affected by an accident at the Chernobyl nuclear power plant in Ukraine on April 26, 1986. Thus, a comparative analysis

of clinical and pathological characteristics of papillary thyroid carcinoma in Belarus provides a unique opportunity to identify the key features of papillary thyroid carcinoma associated with internal irradiation in comparison to cases related to external irradiation as non-radiogenic carcinoma. The purpose of the study was to carry out a retrospective clinical and pathological analysis of papillary thyroid carcinomas in aetiologically divergent groups of patients in Belarus.

## 2. Material and methods

### 2.1. Study cohort and terms

The study subjects were children and adolescents (373 males and 713 females) who suffered from papillary thyroid carcinoma in the age range of 4 to 18 inclusive at surgery. The details of the patients'

\* Corresponding author at: Republican Centre for Thyroid Tumors, 64, Prospekt Nezavisimosti, 220013 Minsk, Belarus.

E-mail addresses: [kupriyan@rambler.ru](mailto:kupriyan@rambler.ru) (M. Fridman), [a.lam@griffith.edu.au](mailto:a.lam@griffith.edu.au) (A.K. Lam), [krasko@newman.bas-net](mailto:krasko@newman.bas-net) (O. Krasko), [kw.schmid@uk-essen.de](mailto:kw.schmid@uk-essen.de) (K.W. Schmid), [personal@doctorbranovan.com](mailto:personal@doctorbranovan.com) (D.I. Branovan), [yu.demidchik@gmail.com](mailto:yu.demidchik@gmail.com) (Y. Demidchik).

presentations, radiation exposure history, surgical and pathological findings as well as outcome were obtained from hospital papers and electronic medical records. Patients considered as having positive history of radiation exposure were identified according to medico-geographical data.

The patients were divided into three groups in the assessment. Among them, patients with papillary thyroid carcinoma attributed to external irradiation were labelled “external radiation-related” (after therapeutic radiation for malignancies during childhood). In total, 23 patients surgically treated during the period 1995 to 2010 were identified to belong to this group.

In cases of “external radiation-related” papillary thyroid carcinoma, the first primary malignancy was detected in the patients at a median age of 4.7 years (range, 1–12 years). For patients who developed papillary thyroid carcinoma after the treatment for lymphoma, the average latent period from completion of lymphoma management until the verification of papillary thyroid carcinoma was 8.6 years (range, 5 to 13 years). The median latent period for the development of papillary thyroid carcinoma in patients with leukaemia was 6.9 years (range, 4 to 12 years). Also, the median latent period for occurrence of papillary thyroid carcinoma in patients with sarcomas was 14.0 years (range, 10 to 16 years). The treatments for the primary malignant neoplasms (lymphoma/leukaemia, sarcoma and medulloblastoma) were in accordance with the standard protocols (including cytotoxic therapies). External irradiation was used in all the cases. The total absorbed radiation doses for the primary cancer varied from 12 to 54 Gy. As a rule, the thyroid gland was in or close to the treatment field. However, in two of the three patients in the sarcoma subgroup, the primary tumour was far away from the thyroid.

The second group was named “post-Chernobyl” and included 936 patients affected by internal radiation under various circumstances and to various amounts of  $I^{131}$  who were operated in the years 1990–2005 (post-Chernobyl period). The identification of these cases and the assessment of radiation exposure have been thoroughly discussed (Zablotska et al., 2011; Likhhtarov et al., 2014). In brief, according to the exposure conditions at the time of the accident, four groups of patients were noted. There were (1) subjects aged one year or more (exposed because of food/milk consumption); (2) subjects aged less than one year (exposed because of breast feeding); (3) subjects born in May–June 1986 who have been exposed partly in utero, and partly as a result of breast feeding, and (4) subjects born within the time period from July 1986 to March 1987 exposed in utero.

To reflect the duration of latency (from the April 26, 1986 to the age at surgery) and address clinical and morphological trends that were observed in the course of papillary thyroid carcinoma during these years, all cases were divided into three equal subgroups according to the time: operated for the period of January, 1990 to December, 1995; January, 1996 to May, 1999; and June, 1999 to September, 2005.

The “sporadic” group comprised 127 juveniles who were born during the years 1987–1992 (from April 1, 1987 to December 31, 1992) and having been operated for papillary thyroid carcinomas during the period of 1991–2010. There is no epidemiological evidence of radiation exposure in this group of patients. These patients were born long after the  $I^{131}$  full decomposition (April 26, 1986–July 28, 1986). They were not exposed to the internal irradiation and had no history of external therapeutic irradiation as well.

## 2.2. Pathological parameters

All the available histological slides were re-evaluated and the clinical records were reviewed. The Tumour–Lymph nodes–Metastasis (TNM) staging was determined according to the seventh edition of American Joint Committee on Cancer classification (American Joint Committee on Cancer, 2010). The dimensions of the papillary thyroid carcinoma were based on direct measurements of the resected thyroid specimens during macroscopic examination. Extra-thyroidal extension, infiltrative

versus circumscribed growth, co-existing pathologies (autoimmune thyroiditis, nodular goitre or follicular adenoma), histological architecture and dominant histological component in every case of papillary thyroid carcinoma were recorded as well. The histological variants were named after the World Health Organization (WHO) criteria (DeLellis and Williams, 2004).

## 2.3. Statistical analysis

The difference between the frequencies of each feature represented by categorical variable was established using Chi-square test or Fisher–Freeman–Halton exact test. The difference between values of each feature represented by continuous variable was compared using Kruskal–Wallis test.  $p$ -Value of  $<0.05$  was considered statistically significant.

For an analysis of clinical and morphological features of patients with aetiologically different papillary thyroid carcinomas, we used multivariate logistic regression with nominal variable with five category: (1) patients with “sporadic” papillary thyroid carcinoma; (2) patients with “external radiation-related” papillary thyroid carcinomas; (3) patients from post-Chernobyl group operated for the period of January, 1990 to December, 1995; (4) patients operated for the period January, 1996 to May, 1999 and (5) patients operated for the period June, 1999 to September, 2005. Age at presentation and gender of the patients with papillary thyroid carcinoma were included as two confounders in multivariate logistic regression. Patients with “sporadic” papillary thyroid carcinoma were considered as the baseline (reference group). The odds ratio (OR) with respect to baseline was calculated as exponential transformation of respective parameters and their 95% confidence intervals (CI). Analyses were conducted using R version 3.1.1 software (R Project for Statistical Computing, <http://www.r-project.org>).

## 3. Results

### 3.1. Papillary thyroid carcinomas in children and adolescents: age- and gender-related associations

The clinical and pathological features of patients with papillary thyroid carcinoma were listed in Table 1. There were significant differences in age and gender distribution. According to the results of multivariate analysis (Table 2), younger patients with papillary thyroid carcinoma are likely to have lateral (N1b) cervical lymph node metastases (OR = 0.92 [95% CI OR = 0.87–0.97];  $p = 0.002$ ) and distant metastases (OR = 0.83 [95% CI OR = 0.76–0.90];  $p < 0.001$ ).

Gender-connected differences in the characteristics of the whole group of young patients with papillary thyroid carcinomas were also noted (Table 2). Papillary thyroid carcinoma in boys was associated with higher frequency of distant metastases when compared with papillary thyroid carcinoma in girls (OR = 2.11 [95% CI OR = 1.41–3.21]);  $p < 0.001$ ). On the contrary, papillary thyroid carcinomas in boys are less frequently associated with co-existing pathologies (OR = 0.38 [95% CI OR = 0.25–0.56];  $p < 0.001$ ).

### 3.2. Descriptive characteristics of aetiologically different groups of papillary thyroid carcinoma in children and adolescents

On pathological examination (Table 1), many patients within the “external radiation-related” group revealed tumours in more advanced local spread (pT3–T4): (17 of 23, 73.9%,  $p < 0.001$ ). The frequency of papillary micro-carcinoma in patients of all aetiologically different groups has distinguished significantly ( $p = 0.025$ ). However, the prevalence of extra-thyroidal extension in tumours sized  $\leq 10$  mm apparently characterized patients within the “external radiation-related” group ( $p = 0.004$ ).

Distant metastases were more frequently ( $p = 0.006$ ) revealed in patients with post-Chernobyl papillary thyroid carcinoma (104 of 936,

Download English Version:

<https://daneshyari.com/en/article/5888049>

Download Persian Version:

<https://daneshyari.com/article/5888049>

[Daneshyari.com](https://daneshyari.com)