European Journal of Cancer 55 (2016) 74–80

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

Original Research

Ultrasound surveillance for radiation-induced thyroid carcinoma in adult survivors of childhood cancer

Enrico Brignardello [a,*], Francesco Felicetti [a], Anna Castiglione [b], Marco Gallo [c], Francesca Maletta [d], Giuseppe Isolato [e], Eleonora Biasin [f], Franca Fagioli [f], Andrea Corrias [g], Nicola Palestini [h]

[a] *Transition Unit for Childhood Cancer Survivors, Department of Oncology, Città della Salute e della Scienza Hospital, Turin, Italy*
[b] *Unit of Clinical Epidemiology, University of Torino and Centre for Cancer Epidemiology and Prevention (CPO Piemonte), Turin, Italy*
[c] *Oncological Endocrinology Unit, Department of Oncology, Città della Salute e della Scienza Hospital, Turin, Italy*
[d] *Pathology Unit, Department of Medical Sciences, University of Torino, Turin, Italy*
[e] *Diagnostic Imaging Department, Città della Salute e della Scienza Hospital, Turin, Italy*
[f] *Pediatric Onco-Hematology, Città della Salute e della Scienza Hospital, Turin, Italy*
[g] *Pediatric Endocrinology Unit, Department of Pediatric Sciences, Città della Salute e della Scienza Hospital, Turin, Italy*
[h] *Department of Surgery, Città della Salute e della Scienza Hospital, Turin, Italy*

Received 5 August 2015; received in revised form 4 November 2015; accepted 6 December 2015
Available online xxx

KEYWORDS
Childhood cancer survivors;
Thyroid cancer;
Ultrasound;
Surveillance;
Radiotherapy

Abstract ***Introduction:*** The optimal surveillance strategy to screen for thyroid carcinoma childhood cancer survivors (CCS) at increased risk is still debated. In our clinical practice, beside neck palpation we routinely perform thyroid ultrasound (US). Here we describe the results obtained using this approach.
Methods: We considered all CCS referred to our long term clinic from November 2001 to September 2014. One hundred and ninety-seven patients who had received radiation therapy involving the thyroid gland underwent US surveillance. Thyroid US started 5 years after radiotherapy and repeated every 3 years, if negative.
Results: Among 197 CCS previously irradiated to the thyroid gland, 74 patients (37.5%) developed thyroid nodules, and fine-needle aspiration was performed in 35. In 11 patients the cytological examination was suspicious or diagnostic for malignancy (TIR 4/5), whereas a follicular lesion was diagnosed in nine. Patients with TIR 4/5 cytology were operated and in all cases thyroid cancer diagnosis was confirmed. The nine patients with TIR 3 cytology also underwent surgery and a carcinoma was diagnosed in three of them. Prevalence of thyroid

* *Corresponding author*: Transition Unit for Childhood Cancer Survivors, AOU Città della Salute e della Scienza di Torino, Via Cherasco, 15 - 10126 Torino, Italy. Tel.: +39 011 6334531; fax: +39 011 6334703.
E-mail address: ebrignardello@cittadellasalute.to.it (E. Brignardello).

http://dx.doi.org/10.1016/j.ejca.2015.12.006

cancer was 7.1%. Tumour size ranged between 4 and 25 mm, but six (43%) were classified T3 because of extra-thyroidal extension. Six patients had nodal metastases; in eight patients the tumour was multifocal. At the time of the study all patients are disease free, without evidence of surgery complications.

Conclusion: Applying our US surveillance protocol, the prevalence of radiation-induced thyroid cancer is high. Histological features of the thyroid cancers diagnosed in our cohort suggest that most of them were clinically relevant tumours.

1. Introduction

Childhood cancer survivors (CCS) are a continuously growing population, with unique health problems that physicians will be facing more in the future. Due to modern chemotherapy and radiation therapy techniques, the 5 year survival rate of children and adolescents affected by tumours has improved steadily and is now estimated to be about 80% [1]. It has become evident, however, that the cure brings the risk of serious late effects [2–4], including the onset of second malignant neoplasms (SMNs).

SMNs are the most frequent cause of mortality for CCS who survived for more than 20 years [5,6], and their occurrence also has a dramatic impact on survival and quality of life.

The thyroid gland is a highly radiosensitive organ. In CCS, the risk of developing a thyroid cancer is closely related to radiation therapy to the head, neck or upper thorax, persists for several decades after treatment and is higher in patients who received radiotherapy at a younger age [7,8] and/or treated with doses ranging between 10 and 30 Gy [7,9–11]. These observations suggest that surveillance might be useful for those CCS at increased risk of thyroid cancer [12,13].

For this purpose, available guidelines [12,14,15] recommend annual palpation of the thyroid and restrict the use of ultrasound (US) to the characterisation of palpable nodules. Although the sensitivity of neck palpation to detect thyroid cancer is low, particularly in early stages, this approach is supported by the observation that radiation-induced thyroid carcinomas are usually well differentiated (i.e. papillary and, less frequently, follicular), generally behaving non-aggressively and with excellent survival rates in adults as well as in children [11,16]. Moreover, there is no evidence to date that an early diagnosis obtained by screening procedures is effective to reduce mortality for thyroid cancer in CCS.

On the other hand, it should be considered that radiation-induced thyroid cancer is suspected to be more aggressive [17,18]. American Association of Clinical Endocrinologists (AACE)–Associazione Medici Endocrinologi (AME)–European Thyroid Association (ETA) guidelines suggest to perform thyroid US in all patients with risk factors for thyroid malignancy (which include a history of head and neck irradiation), even if results of palpation are normal, and recommend fine-needle aspiration (FNA) biopsy for nodules of any size in patients with a history of neck irradiation in childhood or adolescence (grade designation B; best evidence level 3) [19]. American Thyroid Association (ATA) guidelines states that FNA may be warranted even in subcentimeter nodules of patients with a history of head and/or neck irradiation, since they have a greater potential to be clinically significant cancers [20].

Thus, while the international community is working to develop international survivorship follow-up guidelines [21], currently there is no consensus on the optimal surveillance strategy for thyroid cancer after radiotherapy in CCS and this issue is still matter of debate.

In 2008 we proposed neck US surveillance for CCS previously irradiated to the head, neck or upper thorax [22]. Here we describe the results obtained using this protocol in a cohort of young adults previously treated with radiotherapy for a childhood cancer and now enrolled in a long term follow-up program.

2. Methods

2.1. Study population

We considered all patients referred to the 'Transition Unit for Childhood Cancer Survivors' (part of the 'Città della Salute e della Scienza' Hospital in Turin, Italy) from November 2001 to September 2014. All clinical information (cancer diagnosis, therapies, relapses, second tumours, late toxicities, etc) of our CCS are recorded during follow-up. Data about demographic and treatment characteristics of this cohort have been previously published [23,24].

To the purpose of this study we selected all subjects who satisfied the following criteria: a) age at paediatric cancer diagnosis <18 years; b) at least 5 years of survival; c) at least one visit after the 18th birthday; d) previous radiotherapy involving the thyroid gland (i.e. radiation therapy to the head, neck or upper thorax) at age <18 years. Patients with a paediatric cancer diagnosis before 1985 were excluded from the analysis, to reduce the possible selection bias of the cohort.