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1

Radioactive iodine (RAI) therapy for metastatic differentiated thyroid cancer

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Differentiated thyroid cancer (DTC) is the most common endocrine malignancy. It usually has a comparatively benign course. If properly executed, radioiodine therapy can provide an effective treatment of even advanced, metastatic DTC. A major problem in determining the right RAI for a patient with metastatic disease is a comparative lack of evidence. There are no reports on randomized controlled trials in this patient group which can aid us in determining which way to treat which patient. Few non-randomized prospective observational studies have been performed. Most available evidence is based on retrospective analyses which, although often informative, still are hampered by the selection bias inherent to retrospective studies on a small, preselected sample of the total DTC population. The aim of the present review is to provide an overview of the relevant literature on the issues pertinent to the execution of RAI.

Radioiodine therapy of metastatic DTC in patients can be an effective treatment modality which will contribute significantly to a patients' life expectancy. However, much is unclear in the management of this malignancy, including which activity to use, how to determine this activity (empiric vs. dosimetric approach) as well as the potential long-term complications. In pediatric patients, special considerations apply with regard to weight-

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adaptation of activities as well the risk of pulmonary fibrosis in patients with diffuse miliary metastases.

Introduction

Differentiated thyroid cancer (DTC) is the most common endocrine malignancy. It usually has a comparatively benign course. Especially since the advent of radioiodine therapy (RAI), life expectancy in most patients (>85%) is unimpaired [1–4]. Only in patients with UICC/AJCC TNM stages IVa and higher at initial diagnosis, which fortunately includes only a minority of patients, life expectancy can be reduced [1–4].

If properly executed, radioiodine therapy can provide an effective treatment of even advanced, metastatic DTC. This is most evident in pediatric patients, where a complete remission of patients with extensive pulmonary metastases can be achieved – mostly without serious side effects. Although a complete remission is less often achieved in older patients, correctly indicated and administered radioiodine therapy can in many patients still lead to long lasting control of the disease without impairment of the patients' quality of life.

A major problem in determining the right RAI for a patient with metastatic disease is a comparative lack of evidence. There are no reports on randomized controlled trials in this clinical setting which can aid us in determining which way to treat which patient. Few non-randomized prospective observational studies have been performed. Most available evidence is based on retrospective studies which, although often informative, still are hampered by the selection bias inherent to retrospective studies on a small, preselected sample of the total DTC population.

Further complicating is the heterogeneous nature of metastatic DTC, leading to a pretherapeutically unpredictable behavior. Some patients will show a strong radioiodine uptake in most or all metastases, whereas others will only show a poor or even no storage of I-131 [5,6]. Even more difficult is the matter of radiation sensitivity: some patients will show progressive disease in spite of strong I-131 uptake, whereas other patients can show a response to RAI even though only a moderate I-131 uptake was seen.

The issues dealing with resistance against RAI, RAI refractory DTC and methods for handling such cases in clinical practice will be dealt with in focussed reviews of the relevant topics further on in this issue of Best Practice and Research in Endocrinology and Metabolism. Therefore the aim of the present review is to provide an overview of the relevant literature on the issues pertinent to the execution of RAI.

Historical perspective

The success story of radioiodine therapy specifically and nuclear medicine in general started in 1941 with the administration of radioactive iodine to patients with hyperthyroidism [7] and with the most effective treatment of a patient with very advanced metastatic DTC in Montefiore Hospital in New York by Seidlin et al. in 1943 [8]. Even in this first procedure Seidlin et al. included a crude form of dosimetry based on pre- and post-therapeutic measurements of I-131 uptake in tumors using a Geiger counter (which “revealed iodine retention by all the known lesions plus two previously unsuspected ones”) as well as activity measurements in whole body and urine. Though current-day equipment is more sophisticated and has a higher spatial resolution, the basic principles and additional procedures as performed by Seidlin et al. still distinguish a well-executed RAI.

Indications for I-131 therapy

Historically speaking, the aim of post-operative administration of I-131 therapy, also called “ablation” was threefold: 1. to treat any remaining, unknown cancer tissue in the thyroid remnant, lymph nodes or other locations and so 2. to prevent recurrence. Furthermore, 3. the destruction of any