European Journal of
Nuclear
Medicine

Case report

Visualization of the thymus with therapeutic doses of radioiodine in patients with thyroid cancer

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Received 14 May 1992

Abstract. Two cases of papillary carcinoma of the thyroid are presented in which whole-body scans following therapeutic doses of iodine-131 revealed intense anterior mediastinal uptake. In both cases, the mediastinal uptake was absent from scans obtained after removal of the entire thymus. Histologically, the resected thymus glands showed hyperplasia and contained neither thyroid tissue nor metastatic foci of thyroid carcinoma. We therefore concluded that anterior mediastinal uptake of radioiodine may be caused by hyperplasia of the thymus.

Key words: Thymus – Thyroid carcinoma – Iodine-131 treatment

Eur J Nucl Med (1993) 20:75–79

Introduction

Mediastinal uptake of iodine-131 has been reported in patients who have previously undergone surgery for differentiated thyroid carcinoma (Ramanna et al. 1985; Greenler and Klein 1989). It has been surmised that this uptake is the result of the accumulation of ectopic thyroid tissue in the mediastinum, but this has not been proven. In this article, we present two cases of papillary carcinoma of the thyroid in which whole-body scans with therapeutic doses of ^{131}I revealed intense anterior mediastinal activity presumably due to thymic hyperplasia.

Materials and methods

Patients with differentiated thyroid carcinoma who had undergone total or near-total thyroidectomy were placed on a low-iodine diet and ceased to receive triiodothyronine treatment 2 weeks before ^{131}I therapy. A therapeutic dose of ^{131}I was given every 6–7 months until no pathological ^{131}I uptake was seen on whole-body scans 4 days after administration of ^{131}I.

This report describes two patients with papillary carcinoma of the thyroid who showed anterior mediastinal uptake on whole-body scans with therapeutic doses of ^{131}I. Neither patient had a history of neck irradiation.

Whole-body scans (anterior and posterior views) were performed 4 days after administration of therapeutic doses of ^{131}I with a dual-headed digital scintillation camera (GCA-90B/E2, Toshiba Corp., Tokyo) equipped with a parallel-hole high-energy collimator. The energy peak was centered at 364 keV with a window of 20%. The scan speed was 15 cm/min. Data were collected on a computer (GMS-550U, Toshiba Corp., Tokyo) in 256 × 1024 matrices. Displays were visually and empirically controlled.

Case reports

Case 1. The patient was a 19-year-old woman born in November 1969. A total thyroidectomy with bilateral neck dissection revealed a papillary carcinoma with nodal metastases (5/15) in March 1989. She received 3.33 GBq ^{131}I in July 1989. Whole-body scans demonstrated faint accumulation in the anterior mediastinum as well as intense activity in the thyroid bed (Fig. 1a). Subsequently, she received 3.33 GBq ^{131}I in January 1990. Whole-body scans only revealed activity in the anterior mediastinum, without residual thyroid activity (Fig. 1b). Computer tomography (CT) demonstrated a diffusely enlarged thymus of normal shape, strongly suggesting thymic hyperplasia, which corresponded to the area of increased activity on the scans (Fig. 2). Cytological examinations disclosed a cervical node, which did not accumulate ^{131}I, to be a metastasis. Therefore, total thymectomy and additional left neck dissection were performed in May 1990. The thymus gland was enlarged, 13 cm × 10 cm in size, and histologically showed hyperplasia. Neither thyroid tissue nor metastatic foci of thyroid carcinoma were microscopically found in the gland. Nine of 12 excised nodes showed metastatic carcinoma. Finally, the patient was treated with 3.33 GBq ^{131}I in July 1990. Whole-body scans revealed only physiological distribution of the tracer (Fig. 1c). Positive thyroglobulin

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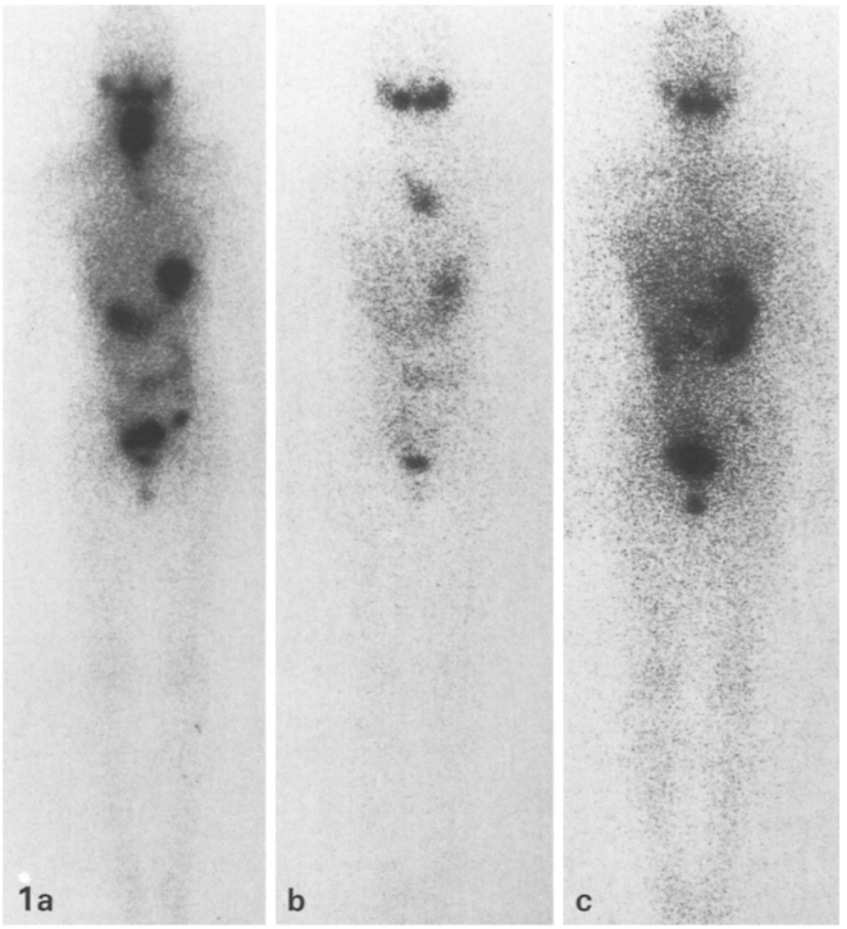


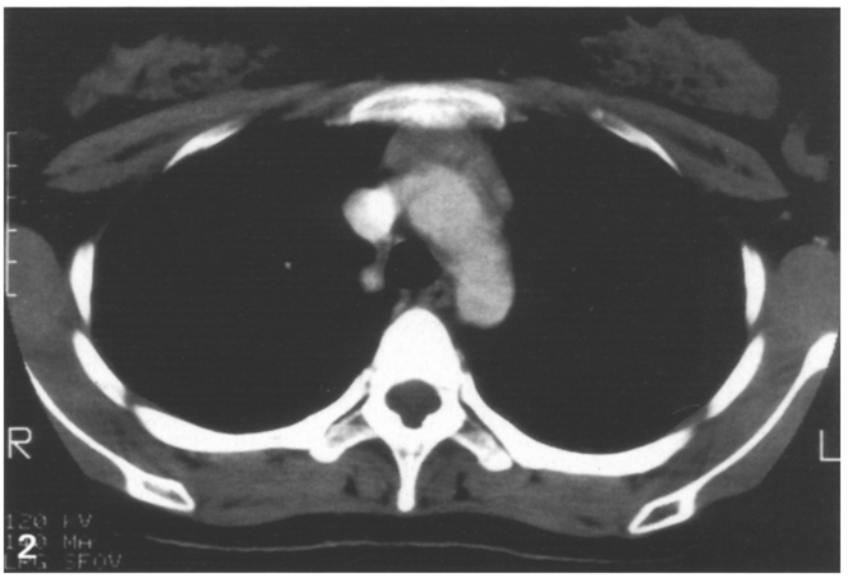
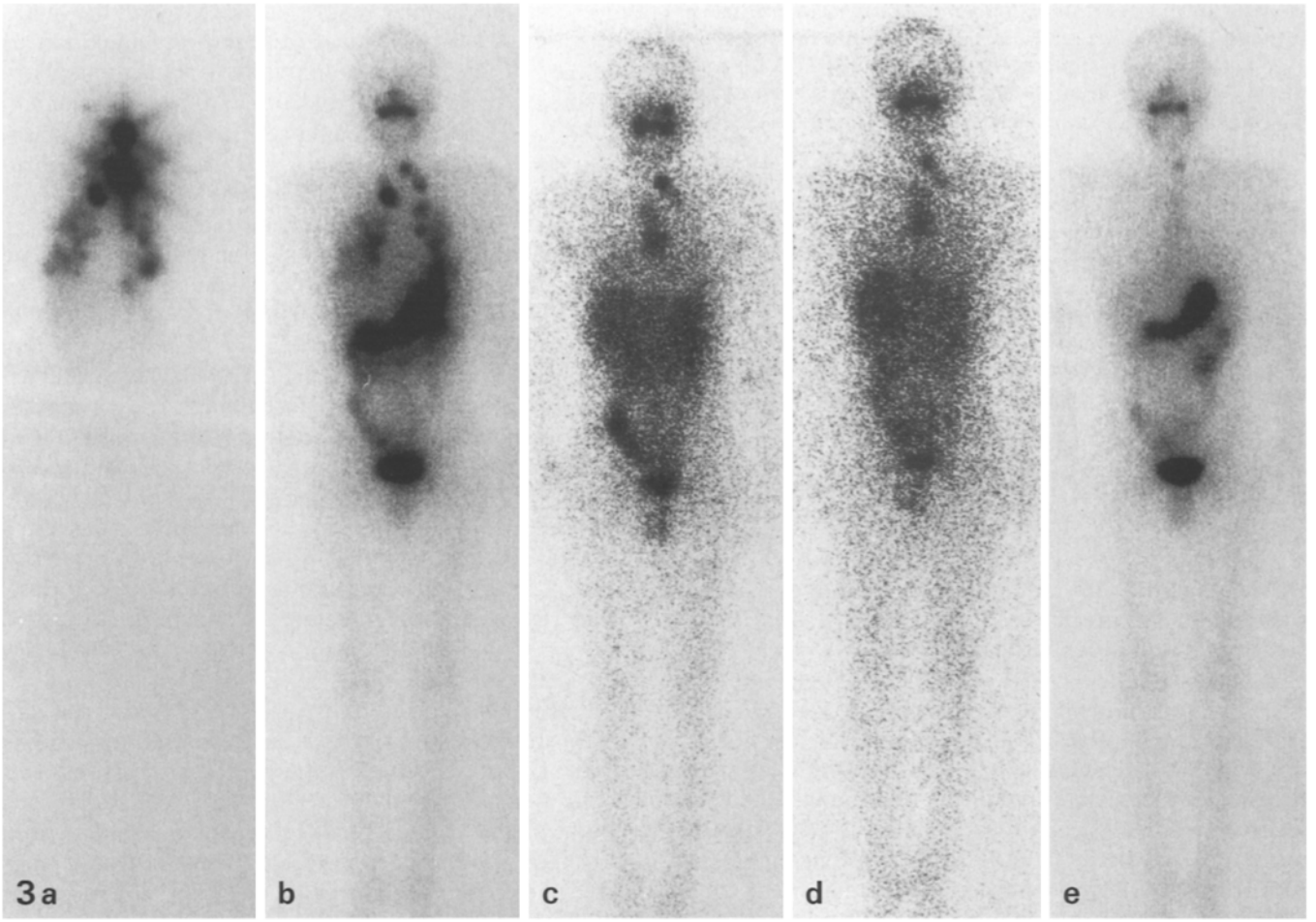


Fig. 1a–c. Case 1. **a** A whole-body scan 4 days after the initial treatment reveals intense activity in the thyroid bed. **b** Prominent mediastinal uptake with no thyroid activity following the second treatment. **c** Absence of abnormal uptake after total thymectomy

Fig. 2. Case 1. A diffusely enlarged thymus is seen anterior to the aortic arch on a post-contrast CT scan

(Tg) antibody interfered with serum Tg measurements. The patient has been given a suppression dose of levothyroxine, and to date there has been no evidence of recurrence on X-ray, ultrasound and CT examinations.

Case 2. The patient was a 28-year-old man born in May 1961. A subtotal thyroidectomy with right neck dissection revealed a papillary carcinoma with nodal metastases (13/18) in January 1981. In June 1989 he was referred to our department for ^{131}I therapy because of cervical metastases. He received 4.44 GBq ^{131}I, and whole-body scans demonstrated intense accumulation in the thyroid bed, cervical nodes and lung (Fig. 3a). Chest X-ray was normal. Since lung metastases were incidentally disclosed, he received an additional 5.55 GBq ^{131}I in January 1990. Whole-body scans



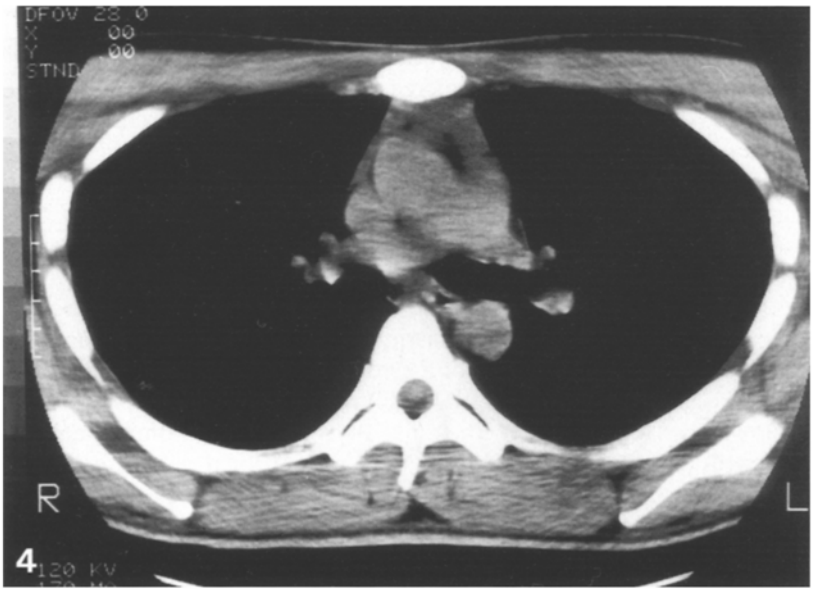


Fig. 3a–e. Case 2. **a** A scan 4 days after the initial treatment reveals intense activity in the thyroid bed, cervical nodes and lung. **b** Persistent lung and neck uptake following the second treatment. **c** New intense activity in the anterior mediastinum following the third treatment. The lung uptake is lost. **d** Unchanged uptake following the fourth treatment. **e** Very faint accumulation on the midline after total thymectomy

Fig. 4. Case 2. Diffusely enlarged thymus of normal shape on a plain CT scan

still revealed the lung and neck uptake (Fig. 3b). He again received 5.55 GBq ^{131}I in August 1990. Whole-body scans revealed new increased activity in the anterior mediastinum and persistent uptake in the neck, without residual lung uptake (Fig. 3c). CT showed a diffusely enlarged thymus of normal shape, strongly suggesting thymic hyperplasia, which corresponded to the area of increased activity on the scans (Fig. 4). The patient received 4.44 GBq ^{131}I in January 1991. Whole-body scans revealed the same findings as in August 1990 (Fig. 3d). The lack of residual lung uptake and the unchanged pattern of tracer distribution prompted total thymectomy and left neck dissection in May 1991. The thymus was enlarged to a size of 10 cm × 4 cm, weighed 34 g, and histologically

showed hyperplasia. Neither thyroid tissue nor metastatic foci of thyroid carcinoma were microscopically found in the gland. Excised nodes showed metastases. Thereafter, the patient was treated with 4.44 GBq ^{131}I in July 1991. Whole-body scans showed very faint accumulation on the midline, thought to represent the surgical scar of the chest wall, and persistent uptake in the left neck (Fig. 3e). The neck uptake was thought to have been caused by the unresected left upper part of the thyroid. The reasons for this conclusion were the location of the radioactivity, the history of subtotal thyroidectomy with complete neck dissection, and the location of a mass enhanced with contrast media on CT post-surgery. Tg antibody was negative and serum Tg concentrations, measured on the day of ^{131}I administration, gradually decreased from 270 ng/ml to 42 ng/ml as the number of treatment sessions increased. Additional ^{131}I therapy is planned as the Tg level remains high (normal: <10 ng/ml; Schneider et al. 1981; Ramanna et al. 1985).

Discussion

Of 85 patients with differentiated thyroid carcinoma who had undergone thyroidectomy, mediastinal ^{131}I uptake was found in ten (Ramanna et al. 1985). Only one of these latter patients had a very high Tg level(>100 ng/ml), and in this patient the mediastinal uptake was surgically confirmed to have resulted from ^{131}I accumulation in a mediastinal metastasis. In the remaining nine patients, the mediastinal uptake was demonstrated on scans with high tracer doses – 100 mCi (3.7 GBq) in five patients, 10 mCi (0.37 GBq) in three patients, and 2 mCi (0.074 GBq) in only one patient. None of these patients had clinical evidence of metastasis and seven of them had Tg values below 10 ng/ml. Therefore, the mediastinal uptake in these patients was considered to represent ^{131}I accumulation not in a mediastinal metastasis but rather in ectopic thyroid tissue which had migrated into the mediastinum during embryogenesis. There was, however, no definitive evidence for this speculation.

Greenler and Klein (1989) also reported several cases of thyroid carcinoma with mediastinal ^{131}I uptake. In a 20-year-old woman with papillary carcinoma of the thyroid, mediastinal uptake was shown on scans with a second dose of 150 mCi (5.55 GBq) and with a subsequent 8 mCi (0.296 GBq) dose 1 year later. In this patient, positive Tg antibody interfered with serum Tg measurements, and the uptake was not thought to represent mediastinal metastasis at the subsequent clinical follow-up. The mediastinal ^{131}I uptake was again tentatively considered to have been caused by thyroid tissue that had descended into the mediastinum as a developmental anomaly.

In our patients, in contrast, the mediastinal ^{131}I uptake disappeared from the scans after removal of the entire thymus. The resected thymus glands histologically showed hyperplasia. Significantly, neither thyroid tissue nor metastatic foci of thyroid carcinoma were found in the glands. These observations therefore indicated ^{131}I accumulation in thymic hyperplasia. To our knowledge, only one similar report has appeared in the literature. In 1979 Jackson et al. reported accumulation of radioiodine in the thymus in two patients with papillary carcinoma of the the thyroid. In a 24-year-old woman, microscopic thymus tissue contained in surgical specimens showed accumulation of ^{131}I, as verified by autoradiography. In another 43-year-old man with faint ^{131}I uptake in the region below the sternal notch, surgery revealed thymus tissue containing neither thyroid tissue nor malignant cells, and the radioactivity disappeared after the surgery. In addition, rat thymus glands were well demonstrated to accumulate ^{123}I non-specifically by means of autoradiography. Thus it was concluded that normal thymus cells can accumulate radioiodine.

Mediastinal thyroid without apparent connection to the cervical gland in the presence of a normal cervical thyroid is extremely rare (Kaplan et al. 1974; Salvatore and Gallo 1975). In the reported cases, the mediastinal thyroid was demonstrated concurrently with a normal cervical thyroid on scans with a conventional ^{131}I dose. After thyroidectomy, therefore, the mediastinal thyroid may be visualized on postooperative scans with a low dose of ^{131}I.

It is interesting that most of the reported cases with mediastinal uptake have been based on high radioiodine doses. The present cases were also revealed using therapeutic doses. Ramanna et al. (1985) considered that such uptake might represent small amounts of normal thyroid tissue. As another possibility, we postulate that the uptake may represent thymus tissue which has a weaker ability to accumulate ^{131}I than does thyroid tissue.

It is noteworthy that the mediastinal radioactivity in our cases became visually evident as the number of ^{131} therapy sessions increased. This finding may support the contention that the mediastinal uptake in our cases did not result from accumulation in ectopic thyroid tissue or metastatic thyroid carcinoma, since the radioactivity in these tissues should progressively decrease with progressive destruction by ^{131}I therapy as the number of treatment sessions increases.

CT should be the imaging method of choice for the evaluation of mediastinal abnormalities. One of the most common causes of a mediastinal mass is mediastinal thyroid. Glazer et al. (1982) reported five characteristic CT features of mediastinal thyroid: (1) anatomical continuity with a cervical thyroid, (2) focal calcification, (3) relatively high CT number, (4) rise in CT number with contrast enhancement and (5) prolonged enhancement after contrast administration. On the other hand, mediastinal involvement in recurrent thyroid carcinoma is reported to have a non-specific CT appearance, such as lymphadenopathy or chest wall invasion (Pearlberg et al. 1989). In contrast, normal thymus has a bilobed, arrowhead-shaped cross-section at all ages and can be detected by residual flecks of thymic parenchyma within the gradually increasing amount of parenchymal fat (Moore et al. 1983). Thymic hyperplasia is generally diagnosed on the basis of CT showing a diffusely en-

larged thymus with maintenance of the normal shape (Baron et al. 1982).

Serum Tg determination, especially in the hypothyroid state, is a sensitive and reliable method in the follow-up of patients with differentiated thyroid carcinoma, and normal Tg values in patients who have undergone total or near-total thyroidectomy have been reported to be less than 10 ng/ml (Schneider et al. 1981; Ramanna et al. 1985). Combined evaluation using serum Tg measurements and ^{131}I whole-body scans has been advocated.

We suggest that in patients with mediastinal uptake the following findings may be helpful in excluding the presence of mediastinal metastasis: (1) mediastinal uptake which becomes visually prominent as the number of ^{131}I therapy sessions increases, (2) mediastinal uptake which needs higher than usual doses of ^{131}I to be demonstrated, (3) detection of a diffusely enlarged thymus and no other abnormal appearance on CT scans, (4) a serum Tg value of less than 10 ng/ml 2 weeks following withdrawal of triiodothyronine, and (5) young age, since the residual amount of thymic parenchyma which can accumulate ^{131}I may not be small.

In conclusion, non-specific mediastinal uptake can be caused by thymic hyperplasia. This must be kept in mind to avoid unnecessary ^{131}I therapy, even though the therapeutic goal of ^{131}I treatment in patients with thyroid carcinoma is to ablate all detectable uptake.

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