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## Iodine Concentration by the Thymus in Thyroid Carcinoma

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A 14-yr-old boy underwent a total thyroidectomy with bilateral neck dissection for a papillary carcinoma with lymph node metastases. Total-body scanning with 3.7 GBq  $^{131}\text{I}$  revealed radioiodine accumulation in the anterior mediastinum. CT and MRI demonstrated a mediastinal mass which corresponded to the area of increased radioactivity. Five months later, another therapeutic dose of  $^{131}\text{I}$  was followed by a sternotomy and removal of the thymus because a hand-held radiodetecting surgical probe demonstrated that the thymus was the mediastinal structure which concentrated iodine. Thymus histology was negative for thyroid cancer metastases (as further confirmed by the negative immunostaining) and showed cystic Hassall's bodies. Secondary ion mass spectrometry microscopy demonstrated that iodine was located only in the Hassall's bodies, bound to proteins. This finding suggests that an acquired "thyroid follicle-like" structure, as that observed in cystic Hassall's bodies, could be responsible for the epithelial cell iodine uptake. In conclusion, we have provided evidence for the iodine-trapping property of the cystic Hassall's bodies of the thymus, which may be a possible cause of misleading mediastinal radioiodine uptake.

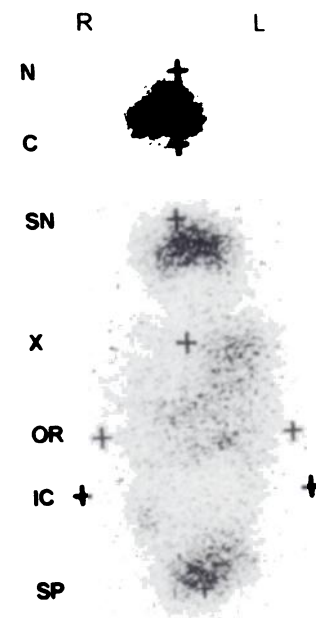
**Key Words:** thymus; iodine-131; total-body scanning

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Total-body scanning with  $^{131}\text{I}$  is a sensitive and specific method to localize foci of differentiated thyroid carcinoma. Nonetheless, only two-thirds of distant metastases concentrate radioiodine (1). Conversely, uptake of  $^{131}\text{I}$  has been reported in nonthyroid lesions such as inflammatory lung diseases, pericardial effusion, ovarian cyst, lymphoepithelial cyst, scrotal hydrocele, skin burn, fungal lesion, primary lung adenocarcinoma, bronchogenic carcinoma, gastric adenocarcinoma, Warthin's tumor and papillary meningioma (2).

Thymic uptake of  $^{125}\text{I}$ ,  $^{131}\text{I}$  and  $^{123}\text{I}$  has already been reported in rats (3–5). Mediastinal uptake observed in young patients has been presumptively attributed to the thymus because thymectomy resulted in the disappearance of the uptake (5–8).

In the present study, the mediastinal uptake was investigated



**FIGURE 1.** Total-body scan performed 5 days after administration of a therapeutic dose of 3.7 GBq  $^{131}\text{I}$  (100 mCi) (anterior view). R = right; L = left; N = nose; C = chin; SN = sternal notch X = xyfold; OR = outer rib; IC = iliac crest; SP = symphysis of pubis.

by the intraoperative use of a radiodetecting probe, histology and secondary ion mass spectrometry (SIMS) microscopy.

### CASE REPORT

A 14-yr old boy was referred in May 1993 to the nuclear medicine unit of the Gustave Roussy Institute. This patient had undergone total thyroidectomy and bilateral neck dissection because of a papillary thyroid carcinoma with bilateral lymph node metastases. The tumor infiltrated the thyroid in the form of a 5-cm in diameter nodule occupying the entire left lobe and a 3-cm in diameter nodule occupying most of the right lobe. There were seven metastatic neck lymph nodes (four on the right and three on the left). Intraoperatively, it was apparent that the tumor had infiltrated the muscles and the left recurrent nerve.

A  $^{131}\text{I}$  total-body scan performed 5 days after the administration of a therapeutic dose of 3.7 GBq  $^{131}\text{I}$  (100 mCi) revealed uptake in the anterior mediastinum, which accounted for 0.2% of the admin-

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istered activity. CT and MRI demonstrated an anterior mediastinal mass.

In November 1993, we administered a second therapeutic dose of 3.7 GBq (100 mCi)  $^{131}\text{I}$  and followed a protocol that allows total-body scanning on Day 3 (and thus visualization of abnormal iodine uptake), surgical removal of the source of uptake after its detection by a hand-held radiodetecting surgical probe (Cis Bio International, Gif sur Yvette, France) on Day 4, and control of the ablation of the iodine concentrating mass by repeating total body scanning on Day 6.

Figure 1 shows that, on Day 3, total-body scanning could detect mediastinal uptake. On Day 4, sternotomy was performed, and the surgical probe could demonstrate thymic activity concentration twice that in the surrounding tissues. Therefore, the thymus was removed and thymic radioactivity was no longer detectable (Table 1), as further demonstrated by a repeat total-body scan performed on Day 6.

Histology of the thymus was negative for normal and ectopic normal thyroid cells or cancerous and metastatic thyroid cells and showed cystic degeneration of thymic Hassall's bodies. Immunohistochemistry was negative for thyroglobulin (antithyroglobulin antibodies by DAKO; Tg6- M 75).

SIMS microscopy (9) was also performed. This is based on the sputtering phenomenon induced by the bombardment of a biological sample surface with an energetic primary ion beam. Part of the sputtered matter is composed of positive or negative, single or polyatomic ions which are peculiar of the atomic composition of the analyzed area. These "secondary ions" are then collected and separated, based on differences in their mass, in a mass spectrometer. SIMS microscopy demonstrated that the Hassall's bodies contained iodine (Fig. 2).

## DISCUSSION

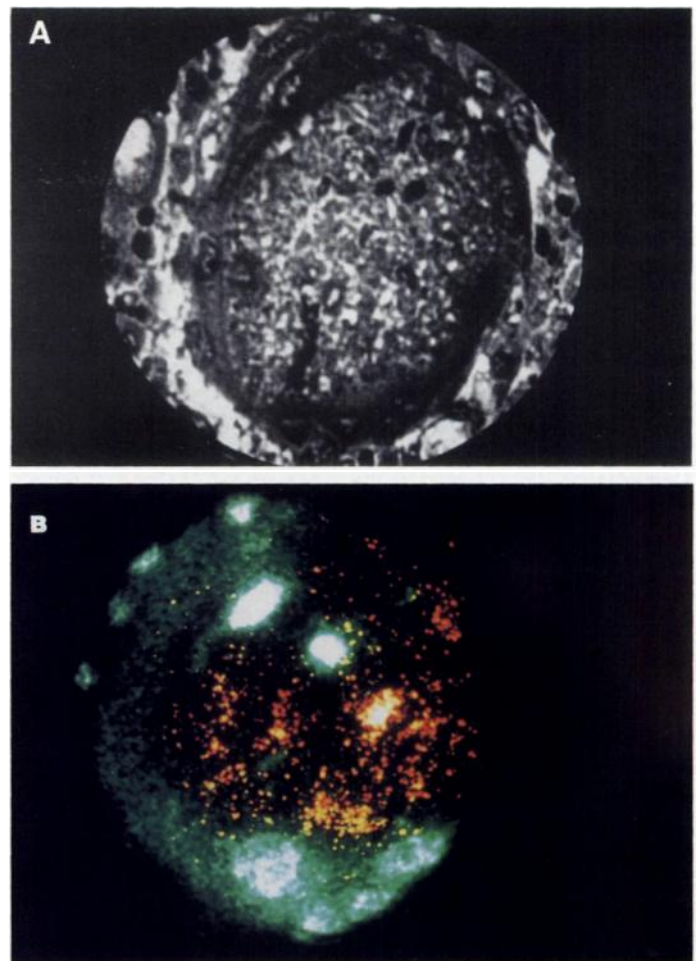
Hassall's bodies are constituted by epithelial cells which resemble keratinocytes; their function is unknown. At the time of the physiological thymic involution, Hassall's bodies decrease in number but increase in size and finally degenerate into corneal cysts (10). Such involutional changes occurred in our patient because histology of his thymus showed enlarged and cystic Hassall's bodies. To explain the iodine-trapping properties of these thymic cystic, corpuscles require a comparison with the thyroid follicles, keeping in mind that a follicular structure with cell polarization can take up iodine through the baso-lateral part of the epithelial cells (11). The basic architecture of both is that of a spheric structure containing a cluster of epithelial cells in the periphery and proteinaceous material in the center. The iodine-containing protein in the thyroid colloid is thyroglobulin; the equivalent protein in the cystic Hassall's bodies is unknown but could be a keratin-related protein. As consistently reported in the literature, thymic uptake of iodine is very low. Accordingly, thymic visualization requires high doses of  $^{131}\text{I}$  given for therapeutic purposes (1,2,5-8).

## CONCLUSION

Thyroid-unrelated mediastinal uptake can be caused by thymic involutional hyperplasia. This fact must be remembered when mediastinal uptake, undetectable Tg values and thymic hyperplasia are seen in young patients, as evidenced by CT and/or MRI.

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**FIGURE 2.** Images of serial sections of the surgical specimen with optical (A) and ionic (B) microscope. (A and B) Histological structure of Hassall's body is preserved during SIMS microscopy. (B) Superimposed computerized images of iodine (red) and phosphorus (green) in the Hassall's body. Phosphorus is located inside the cells while iodine is located inside the cystic lumen of the corpuscle.

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