

Limited value of delayed radiothallium image in the diagnosis of nodular goiter

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To test whether delayed thallium image can improve the diagnostic accuracy of thyroid tumor, we have reviewed 35 patients with cold nodules of proven histopathology. Early and delayed images were taken 10-20 min and 3-4 hr postinjection, respectively. In this study, a thyroid nodule was interpreted as malignant if it had normal or increased uptake on early scan and more residual radioactivity than paranodular tissue on delayed scan. In the eighteen patients who had carcinoma, a disappointing 44% false negative rate was observed. No significant difference was seen between retention-positive and negative cases in tumor size or histological type of cancer. Nor could any demographic bias explain the low sensitivity. Of the six false negatives, macroscopic cystic degeneration was seen in two cases, but tumors in the other four were grossly solid. Considering the histological heterogeneity often seen within a thyroid tumor, the portion with increased retention of radiothallium may be too small to be detected in the false negative cases. Furthermore, 3 false positive readings were obtained in 17 patients with benign conditions. We conclude that the contribution of the delayed thallium image was quite limited in predicting or ruling out malignancy in nodular goiters.

Key words: thallium-201, tumor scintigraphy, thyroid cancer, thyroid adenoma, delayed image

INTRODUCTION

THALLIUM-201 chloride is one of the most widely used radiopharmaceuticals, serving both in myocardial imaging and in tumor scintigraphy. In the diagnosis of nodular goiter, many authors have reported the accumulation of this radionuclide in thyroid cancers and their lymphnode metastasis.¹⁻⁷ Meanwhile, since a significant fraction of adenomas or other benign conditions also appear positive in the scintigram, a single radiothallium image could not be a satisfactory test to use in estimating the

histological nature of a given struma nodosa. The only general consensus in the literature appears to be that a thyroid nodule photopenic in a thallium study is most likely to be a benign cystic one. To overcome this poor specificity, some researchers have claimed that a delayed thallium image taken three to five hours after i.v. can improve the differentiating accuracy,⁸ whereas others have been more pessimistic about the value of this additional scan.^{9,10} In the past, while routinely taking both early and delayed thallium scintigrams for thyroid nodules, we have gradually become doubtful of the usefulness of this dual procedure. We have therefore retrospectively reviewed the cases with proven histological diagnosis to address this issue statistically. The consistency between radionuclear findings and histopathology was closely examined with particular attention to the contribution of the delayed image.

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MATERIALS AND METHODS

Patients

Thirty-five cases of untreated "cold nodules" in the thyroid were analysed in the present study. The tumorous lesions all appeared as trapping defects in the iodine-123 and technetium-99m scintigrams. Patients were excluded from the study if they had a history of previous thyroid surgery, or scintigraphically diffuse goiter, even if they showed nodularity on palpation. Histological diagnoses were made by two expert pathologists on surgical specimens. The whole patient group consisted of 6 men and 29 women, aged 20–85 (mean 50.2) years.

Thallium scintigraphy

Early and delayed images were taken 10–20 min and 3–4 hr, respectively, after i.v. injection of 74 MBq (2 mCi) of thallium-201 chloride (Nihon Mediphysics, Takarazuka, Hyogo). The scinticamera used was a Searl Pho/Gamma LFOV equipped with a pinhole collimator, with a window setting of $80 \text{ KeV} \pm 15\%$ and a preset count of 300 K. Interpretation of obtained scintigrams was done visually by a panel of three experienced specialists in nuclear medicine, and was unanimous on all occasions. To interpret early and delayed scintigrams combined, we followed the method of Ochi and colleagues:⁸ A thyroid nodule was considered malignant if it had normal or increased uptake on early scan and more residual radioactivity than paranodular tissue on delayed scan; a nodule without these findings was regarded as scintigraphically benign.

RESULTS

Table 1 summarizes the correlation between the diagnosis based on dual thallium imaging and final histopathology in the 35 subjects examined.

In the eighteen patients who had carcinoma, a 44% false negative rate was observed. No demo-

graphic bias could explain this low sensitivity, since there was little difference between scintigraphically "benign" and "malignant" groups as to age and sex. The same applies to the size of nodular lesions in these two groups. As for the histological type of malignant tumors, 4 out of 6 cases of follicular adenocarcinoma (FAC) were read as positive in the scintigrams, whereas the odds were 6 out of 12 for papillary adenocarcinoma (PAC). No other type of malignant goiter was observed in the present series. Of the six false negatives, macroscopic cystic degeneration was seen in two cases, one with FAC and another with PAC, but the other four were grossly solid.

Histological diagnoses in the three false positives were hyperplasia (adenomatous goiter) for two and follicular adenoma for one; in the 14 true negatives, follicular adenoma for 4, adenomatous goiter for 8, and Hashimoto thyroiditis for 2.

Representative cases of false positive and false negative are shown in Figs. 1 and 2, respectively.

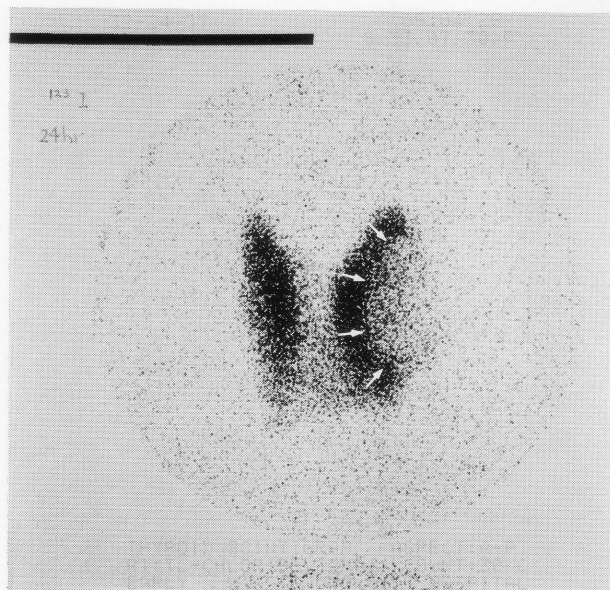
There were six cases in which combined reading of early and delayed scans differed from that of the early image only. The former gave correct radio-nuclear diagnoses in a false negative and two false positive cases of the latter, but was wrong in a true negative and two true positives. Hence, by adding delayed scan, specificity was slightly improved (from 76% to 82%) at the expense of sensitivity (from 61% to 56%), and overall accuracy remained the same at 69%.

DISCUSSION

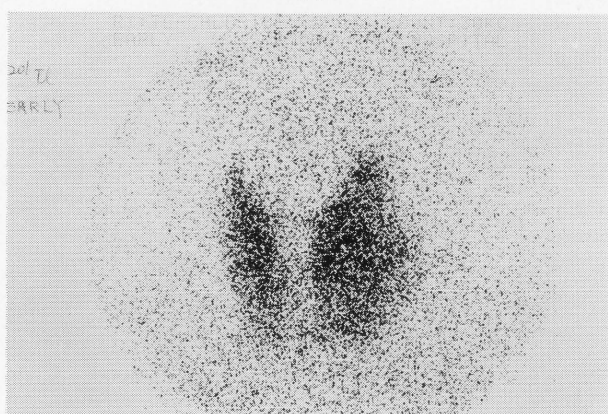
Contrary to some enthusiastic earlier reports, our present study showed discouragingly low sensitivity of the delayed radiothallium scan in differentiating malignant thyroid tumors from benign conditions. The false negative findings were solely attributable to neither cystic necrosis of large tumors nor to microinvasive FAC. In fact, there were 5 cases of

Table 1 Correlation of histopathology and scintigraphic diagnosis based on delayed image in cold thyroid nodules

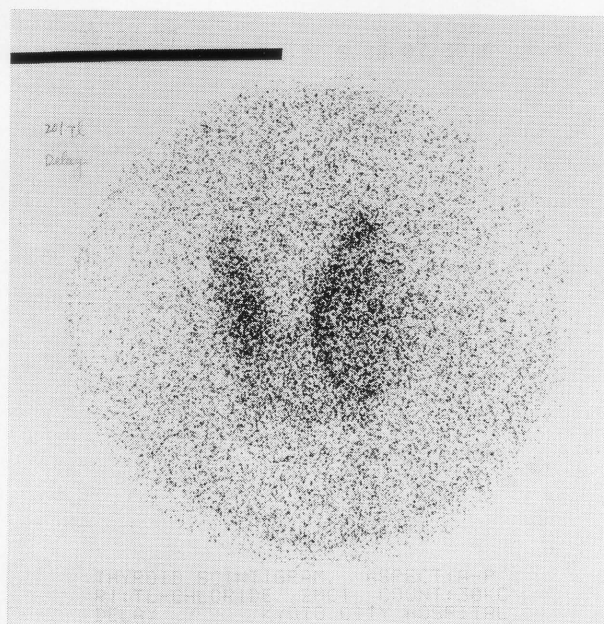
	Scintigraphy	Malignant	Benign	Total
Histology				
Malignant		10 (true positive)	8 (false negative)	18
Benign		3 (false positive)	14 (true negative)	17
Total		13	22	35
(sensitivity)	$10/10+8=56\%$			
(specificity)	$14/14+3=82\%$			
(overall accuracy)	$10+14/35=69\%$			



(a)



(b)



(c)

Fig. 1 A false negative case. In this 30-year-old female, iodine-123 image (Fig. 1a) showed a trapping defect at centrolateral portion of the left thyroid lobe (arrowheads) corresponding to a physically palpable nodule. This cold lesion accumulated similar amount of thallium-201 to the rest of thyroid in early scan (Fig. 1b) and less than the other parts in delayed one (Fig. 1c). This good washout lead to a radionuclear diagnosis of benign adenoma, but the final histopathology of resected tumor was papillary adenocarcinoma.

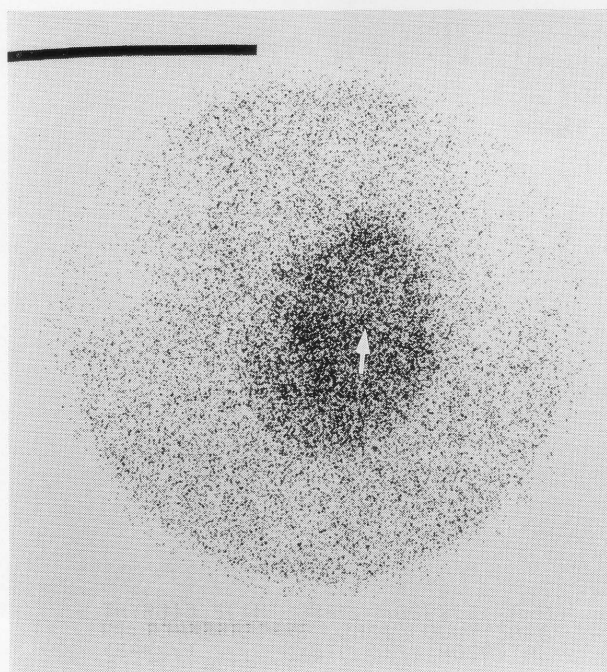
PAC without major cystic degeneration. We postulate that in those patients, partial vascular encasement by the tumors might have caused sufficient regional mild hypoperfusion to decrease the accumulation of radiothallium but still insufficient to necrotize the neoplastic tissue. Alternatively, as for the ability to accumulate thallium chloride, there may be two or more subsets within the "PAC" category. Concerning this point, it should be remembered that in current histopathology, thyroid carcinoma with both papillary and follicular components is classified as PAC.^{11,12} Furthermore, there often exists histological heterogeneity within a given thyroid tumor so that most of the mass appears cytologically benign while a small fraction of it is judged as malignant by pathologists. In these circumstances, it is no wonder that the nodule in question cannot retain enough radiothallium to be "positive" in a delayed scan, since the portion with increased ability to concentrate the radionuclide may be too small to be detected.

Considering these facts, dynamic studies with thallium-201^{13,14} seemed unlikely to be a fundamental solution for the low sensitivity.

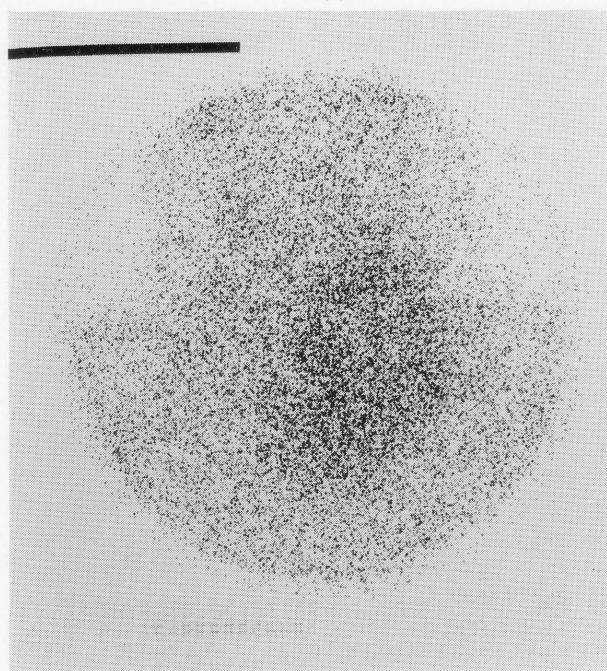
From the present analysis, we conclude that the contribution of the delayed thallium image was quite limited in forecasting malignancy in nodular goiters, and judgements based on its findings were sometimes even erroneous. For radionuclear evaluation of lymphnode metastasis, intrathoracic extension and cystic changes, early thallium image alone may be enough.^{6,7} Instead of an additional scintigram with inconvenient timing for patients and decreased patient throughput, other means, especially ultrasonography⁷ and fine needle aspiration biopsy,¹⁵ should be included in the initial diagnostic workup for nodular thyroid lesions, at least for now. Hopefully, future advances in tumor-specific radio-immunoscintigraphy or other nuclear medicine techniques will provide better presurgical prediction of the histology of thyroid nodules.

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(a)



(b)

Fig. 2 A false positive case. This female patient, aged 45 years, had a large painless left neck mass. Early thallium scan (Fig. 2a) showed prominent accumulation at the tumor site except a small focus of relative photopenia (arrow). This hot area was still more radioactive than the rest of the gland in delayed scan (Fig. 2b), and therefore read as scintigraphically malignant. The final histological diagnosis was follicular adenoma with a small portion of cystic necrosis.

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