Insular Carcinoma: A Distinct Thyroid Carcinoma with Associated Iodine-131 Localization

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Insular carcinoma, once considered a poorly-differentiated thyroid cancer, has been reclassified as a distinct thyroid neoplasm. Since this neoplasm is composed of follicular epithelial cells, it may concentrate radioiodide (^{131}I) making postoperative ^{131}I imaging for detection of metastases and radiotherapy possible. A 20-yr review of 35 cases diagnosed as anaplastic or undifferentiated thyroid carcinoma at this medical center revealed five patients with insular carcinoma. Four patients showed postoperative ^{131}I localization and received therapeutic doses of ^{131}I. Three of the four showed extrathyroidal ^{131}I localization in neoplastic lesions. In one patient, the resolution of metastatic lesions by magnetic resonance and ^{131}I imaging suggests that ^{131}I may have an important therapeutic role in this aggressive neoplasm.

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H istorically, thyroid carcinomas have been classified into two major groups: well-differentiated carcinomas composed of papillary or follicular cells and poorly-differentiated carcinomas composed of anaplastic and poorly-differentiated cells. The prognosis for papillary and/or follicular carcinomas is generally good, whereas for the latter group it is extremely poor. In 1984, Carcangiu et al. (*1*) reported a series of patients with poorly-differentiated thyroid carcinomas that demonstrated a less aggressive course of the disease. Their retrospective review revealed a characteristic histopathologic appearance consisting of nests or "insulae" of tumor cells in all cases.

A spectrum from well-differentiated to undifferentiated neoplasms, all with insular features, has been described in the literature (*1–4*). Some investigators have proposed that insular thyroid carcinoma be classified as a poorly-differentiated cancer that has a less aggressive course than undifferentiated or anaplastic thyroid carcinomas (*1,3*). Others have described this neoplasm as an aggressive var-

iant of well-differentiated thyroid cancer with insular features (*2,4*).

Two recent cases demonstrating similar pathologic features prompted a review of all 35 cases diagnosed as anaplastic or poorly-differentiated thyroid carcinoma during the past 20 yr at our institution. A review of the clinical course, including therapy and diagnostic studies, of five cases identified as "insular" carcinoma is presented.

MATERIALS AND METHODS

The histopathology slides of 35 cases diagnosed as anaplastic or poorly-differentiated carcinoma of the thyroid at our institution between 1968 and 1988 were reviewed by two pathologists (WPW, RAR) separately and without knowledge of diagnosis or clinical outcome. The hematoxylin and eosin-stained slides were available for all cases. Thyroglobulin and calcitonin immunohistology studies were available for three cases.

The criteria of Carcangiu et al. (*1*), as well as published photomicrographs of insular carcinoma, were used as the standard for diagnosis. A characteristic feature is groups or islands of tumor cells (insulae) surrounded by hypocellular fibrous tissue. The cells are small with indistinct nucleoli. The groups of cells appear homogeneous, showing minimal follicular growth. Necrosis is a common feature, which, when present, creates islands of viable cells surrounding small vessels (peritheliomatous pattern).

The medical records of each patient were reviewed and summarized. This included initial presentation, diagnostic studies, operative findings, and clinical course. Nuclear medicine and other radiologic studies were reviewed (EPJ, JES), and magnetic resonance images (MRI) were interpreted (DPH).

RESULTS

Table 1 summarizes the clinical, surgical, and histopathologic findings; radioactive iodide imaging; and therapy.

Case 1

A 72-yr-old man was found to have an asymptomatic, firm, fixed nodule (3 × 4 cm) in the right thyroid lobe. A [^{99m}Tc]pertechnetate thyroid scan showed a "cold defect" in the right thyroid lobe. Fine-needle aspiration biopsy for cytologic study suggested a follicular neoplasm. A right thyroid lobectomy revealed a hard mass intimately attached to the trachea and soft tissues of the right neck. A

TABLE 1
Summary of Patient Data

Patient	Age (yr/sex)	Clinical presentation	Operation	Pathologic findings	Lymph nodes	Postop ^{131}I images	[131]I therapy
1	72/M	3 × 4 cm firm mass, right lobe (1987)	Total thyroid-ectomy	Poorly-differentiated thyroid cancer with vascular invasion	Negative	Right thyroid bed, mid-thyroid bed, and left neck, proximal right humerus, proximal left femur	117 mCi 194 mCi
2	40/F	2.5 × 3 cm firm nodule, right lobe (1989)	Total thyroid-ectomy	Papillary (5%–10%) and poorly-differentiated thyroid cancer, no vascular or capsular invasion	Negative	0.3% right thyroid bed	130 mCi
3	41/F	2 × 2.3 cm firm nodule, right lobe (1956)	Right subtotal thyroidec-tomy	Papillary adenocarci-noma	Negative	Not done	None
		Enlarged left lobe (1966)	Left subtotal thyroidec-tomy	Hashimoto's thyroidi-tis	Negative	Not done	None
		Diffuse neck swelling (1972)	Mass excised	Poorly-differentiated thyroid carcinoma	Negative	3 neck foci, resid-ual neoplasms and both thyroid bed remnants	150 mCi
		Left neck mass (1975)	Radical neck dissection	Poorly-differentiated thyroid carcinoma	Multiple	Negative	None
4	75/F	Enlarged right lobe and dys-phagia (1988)	Right thyroid lobectomy	Poorly-differentiated thyroid cancer with capsular invasion	Negative	Not done	None*
5	19/F	Diffuse neck swelling (1985)	Total thyroid-ectomy	Poorly-differentiated thyroid cancer with tracheal invasion	Multiple	Cervical and sub-sternal lymph nodes	150 mCi 146 mCi

* 3000 cGy of external irradiation of vertebral metastases.

total thyroidectomy was completed at a second operation with preservation of two parathyroid glands. The histologic diagnosis was extensive poorly-differentiated carcinoma with features of insular carcinoma and vascular invasion (Fig. 1). The anterior resection margin was positive for malignant cells. Immunohistochemical studies were posi-tive for thyroglobulin and negative for calcitonin.

Two months postoperatively, the patient underwent whole-body imaging after injection of 2 mCi (74 MBq) of [131]I. Tracer localized in the cephalad aspect of the right thyroid bed (0.5%, 96 hr uptake) and in the mid-neck (neoplasm), overlapping into the left thyroid bed (5.4%, 96 hr uptake). Serum thyroid-stimulating hormone (TSH) was 74 units/ml. Foci of abnormal localization also were noted in the left proximal femur and the right proximal humerus. The patient was treated with 117 mCi (4329 MBq) of ^{131}I postoperatively, and post-therapy ^{131}I uptake was again seen in the neck, left femur, and right humerus,
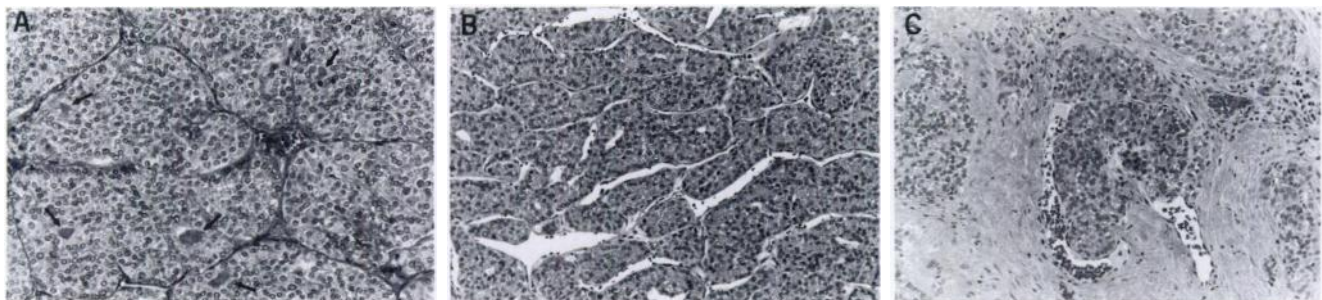

FIGURE 1. Histopathology for Case 1 showing classic features of insular carcinoma. (A) Well-defined insulae of tumor cells with focal follicular differentiation (arrows) surrounded by delicate fibrovascular septa (hematoxylin and eosin, 160×). (B) Insular carcinoma showing focal trabecular growth with intervening cleft-like spaces (hematoxylin and eosin, 160×). (C) Insular carcinoma with focal vascular invasion (hematoxylin and eosin, 400×).
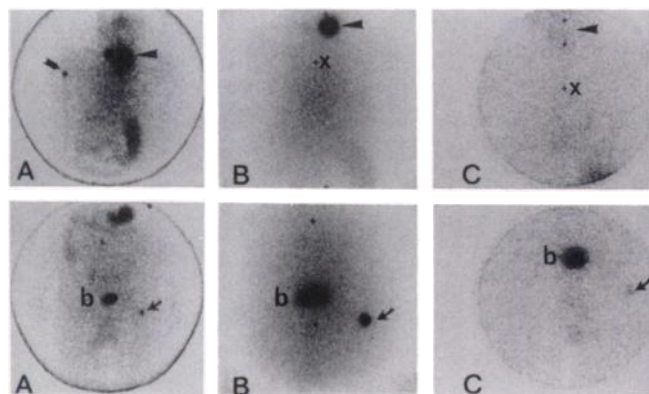
FIGURE 2. (A) Pinhole images 72 hr after initial ^{131}I therapy show abnormal uptake in the left mid-neck (arrowhead) and right thyroid bed, proximal right humerus (wide arrowhead), and left proximal femur (arrow). b = bladder activity. (B) Pinhole images 72 hr after second ^{131}I therapy show less uptake in the neck foci (arrowhead) and left femur (arrow). The right humeral focus is no longer visible. + = thyroid cartilage; +× = xyphoid process; and b = bladder activity. (C) Images 6 mo after second ^{131}I therapy show no focal uptake in the neck (arrowhead) and proximal right humerus and progressive decreased uptake in the proximal left femur (arrow). +× = xyphoid process; b = bladder activity; upper + = thyroid cartilage; and lower + = suprasternal notch.

FIGURE 4. (A) Pre-therapy coronal T1-weighted (TR/1t = 583/20) image through the mid-intertrochanteric portion of the left femur shows a focal lesion (arrow) with decreased signal relative to that of marrow but greater than that of muscle. (B) STIR (TR/TE/TI = 2233/40/125) image corresponding to A shows increased signal in the lesion (arrow) consistent with a metastatic lesion.

but nowhere else (Fig. 2A). Only after MRI was it realized that part of the ^{131}I localization in the mid-neck was due to a metastatic lesion in the cervical spine.

MRI of the neck using a 0.5-T superconductive Vista scanner (Picker International) displayed a focal lesion in the C5 vertebral body, suggesting skeletal metastases (Fig. 3). The pelvis was studied using T1-weighted and short tau inversion recovery (STIR) imaging (Fig. 4) to clarify the abnormal ^{131}I uptake in the proximal left femur. Additional T1-weighted images after the intravenous injection of gadolinium-diethylenetriaminepentaacetic acid

(Gd-DTPA) showed mild enhancement of the lesion, also indicating probable neoplasm.

Whole-body images 6 mo later showed no localization in the humerus and less localization in the neck (uptake of 0.6%) and left femur (uptake of 0.2%) 96 hr after a 2-mCi dose of ^{131}I. A bone scan showed abnormal focal bone remodeling in the proximal left femur, which was "cold" on a ^{99m}Tc-albumin colloid marrow scan (Fig. 5). Both findings corresponded to the same site as the ^{131}I and MRI abnormalities. A second dose of ^{131}I (194 mCi or 7178 MBq) was administered, and post-therapy images were obtained (Fig. 2B). The calculated radiation dose delivered to the C5 lesion was 242,000 rads with 36,000 rads to the left femoral lesion for this therapy.

Radioiodide imaging 8 mo after the second ^{131}I therapy no longer showed localization in the neck, and uptake in the proximal left femur (Fig. 2C) had decreased to 0.02% 96 hr after 2 mCi of ^{131}I. A repeat MRI revealed almost
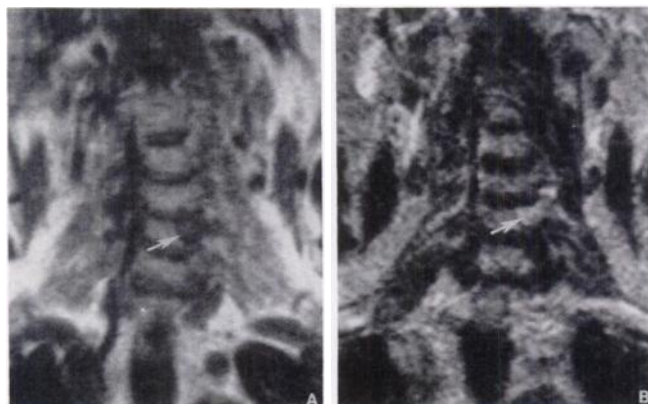

FIGURE 3. (A) Pre-therapy coronal T1-weighted (TR/TE = 383/20) image through the mid-neck shows a focal lesion (arrow) in the left C5 vertebral body. (B) Coronal T2-weighted (TR/TE = 200/100) image corresponding to A. The low signal on T1-weighted and high signal (arrow) on T2-weighted images relative to the cervical marrow is consistent with a metastatic lesion.
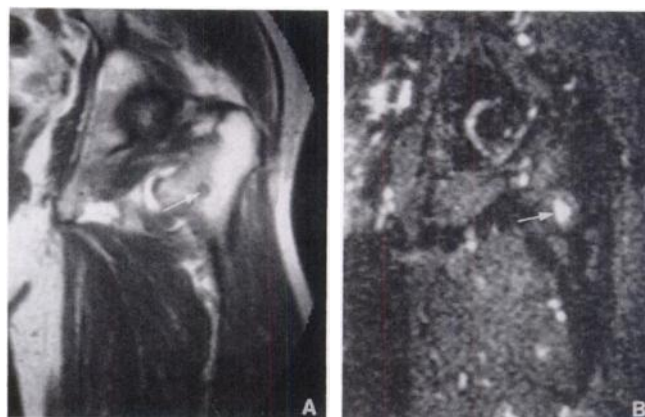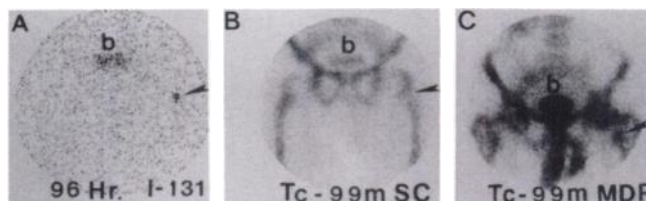

FIGURE 5. (A) Iodine-131 image of the pelvis and upper legs obtained 96 hr after a 2-mCi dose shows focal uptake (arrowhead) in the proximal left femur and residual bladder activity (b). (B) Technetium-99m-sulfur colloid bone marrow image obtained the same day as A (without moving the patient and using a 10% window) shows a "cold" focus (arrowhead) corresponding to the region of ^{131}I uptake. b = bladder activity. (C) Technetium-99m MDP bone image obtained before the ^{131}I scan shows a focus of slightly increased bone remodeling (arrowhead) in the proximal left femur. b = bladder activity.

complete disappearance of the focal abnormality in the C5 vertebral body. The left femoral lesion was visible with a very low signal on T1-weighted images (Fig. 6A) and a homogeneously very bright signal on STIR images (Fig. 6B). Gadolinium-DTPA failed to enhance the lesion (Fig. 6C). These findings suggest necrosis of the metastatic focus leaving only a fluid-filled cavity. The patient is asymptomatic, and a follow-up ^{131}I scan 22 mo after the second therapy still showed only a small focus of uptake in the proximal left femur.

Case 2

A 40-yr-old woman had an asymptomatic firm nodule in the inferior right thyroid lobe without cervical lymphadenopathy. A total thyroidectomy revealed an encapsulated right inferior pole neoplasm (2.5 × 3 cm) with a trabecular and papillary architecture. Approximately 5%–10% of the neoplasm had distinct components of papillary carcinoma, and the remainder had an insular carcinoma pattern. There was no evidence of capsular or vascular invasion, and two resected lymph nodes showed no metastatic neoplasm.

Iodine-131 images obtained 6 wk postoperatively demonstrated a focus in the right thyroid bed with 0.25% uptake at 96 hr. Total-body pinhole images 2 days after therapy with 130 mCi (4810 MBq) of ^{131}I demonstrated no abnormal foci outside the right thyroid bed. Iodine-131 6 mo later showed no evidence of residual functioning tissue in the neck or elsewhere. The patient has no clinical evidence of residual neoplasm, and follow-up ^{131}I imaging is planned in 1 yr.

Case 3

A 41-yr-old woman had a 2 × 2.3-cm papillary adenocarcinoma of the thyroid removed by a right subtotal thyroidectomy in 1956. A left subtotal thyroidectomy in 1966 for an enlarged left lobe revealed Hashimoto's thyroiditis. She noted diffuse swelling of the neck in 1972,
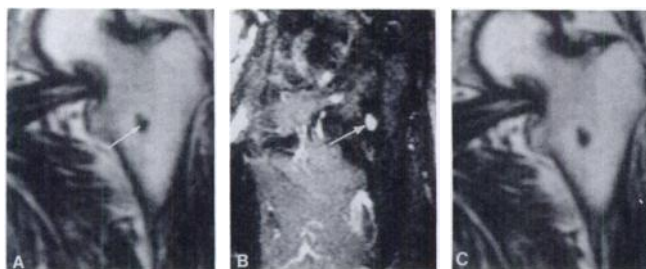

FIGURE 6. (A) Post-therapy coronal T1-weighted (TR/TE = 600/20) image of the proximal left femur shows further loss of signal within the focal lesion (arrow) to less than that of muscle. (B) Coronal STIR (TR/TE/TI = 2067/40/125) image shows very bright signal in the lesion (arrow). These T1 and STIR signal characteristics suggest a fluid-filled cavity. (C) Coronal Gd-DTPA-enhanced T1-weighted image shows no evidence of contrast enhancement indicating probable necrosis of the metastatic lesion.

and tracheal deviation was noted on a chest radiograph. Biopsy showed possible papillary recurrence. An esophagram demonstrated invasion of esophageal muscle. Right and left thyroid lobe remnants and a neoplastic mass of poorly-differentiated thyroid carcinoma were removed in May 1973.

A postoperative ^{131}I scan showed uptake in three neck focii (both thyroid beds and midline residual neoplasm), which were treated with 150 mCi (5550 MBq) of ^{131}I in July 1973. A post-therapy scan revealed approximately 4% uptake in the neck. A radioiodine scan in January 1974 showed no remaining activity in the neck or elsewhere in the body. A sternocleidomastoid muscle mass was noted in March 1975, and a ^{131}I scan was negative. A repeat ^{131}I scan after two doses of TSH was also negative. A classic radical neck dissection in April 1975 revealed poorly-differentiated thyroid carcinoma in the superior mediastinal lymph nodes. Review of the 1973 histologic material revealed features of insular carcinoma. This patient has moved out-of-state and has been lost to follow-up.

Case 4

A 75-yr-old woman with multiple sclerosis and a long-standing goiter noted intermittent episodes of tenderness plus progressive enlargement of the right thyroid lobe associated with dysphagia for 1 yr. A [^{99m}Tc]pertechnetate thyroid scan showed a discrete 5-cm focus of decreased uptake in the mid-lateral right lobe. A chest radiograph was unremarkable except for tracheal deviation to the left. A right lobectomy revealed a poorly-differentiated carcinoma with insular features and vascular invasion. Immunohistochemical staining for thyroglobin was focally positive, whereas an antibody stain for calcitonin was negative.

She refused to have a left lobectomy and has been followed for 2 yr with subsequent development of lower extremity weakness due to biopsy-proven poorly-differentiated metastatic cancer to L1 and L3. This has been treated with external beam irradiation (3000 cGy). Review of the histologic material revealed the characteristic findings of insular carcinoma.

Case 5

A 19-yr-old woman presented with a second episode of painless neck swelling. Physical examination revealed bilateral, enlarged, mobile, nontender cervical lymph nodes. Both lobes of the thyroid were enlarged and felt indurated. An open lymph node biopsy showed mixed papillary and follicular carcinoma most likely of thyroid origin. A [^{99m}Tc]pertechnetate thyroid scan showed a discrete focus of decreased localization in the lower left lobe with non-uniform uptake throughout an enlarged gland. Computed tomography (CT) of the neck revealed enlargement of both thyroid lobes with a mass lesion in the left lower lobe and multiple, bilateral, enlarged lymph nodes. A total thyroidectomy and bilateral lymph node dissections were

performed in June 1985. The neoplasm was adherent to the trachea and could not be resected entirely. Histologic examination revealed a poorly-differentiated thyroid carcinoma with all the features of insular carcinoma with bilateral lymph node involvement. This neoplasm also contained a distinct component of papillary carcinoma.

A postoperative ^{131}I scan in August 1983 showed 0.4% uptake in the right thyroid bed and 1.7% in the midline overlapping the left thyroid bed (TSH of 217 μ units/ml). She received a 150-mCi (5550 MBq) dose of ^{131}I, and post-therapy images showed multiple additional foci in lymph nodes outside the thyroid bed (Fig. 7A). In January 1986, the patient had palpable enlargement of two cervical lymph nodes. These were excised, revealing metastatic insular carcinoma. A radioiodide scan (TSH = 137 μ units/ml) revealed several new foci (total uptake 1.2%) in both sides of the neck, including the suprasternal area with resolution of uptake in the thyroid bed. A second therapeutic dose of ^{131}I (146 mCi or 5402 MBq) was given in June 1986, and post-therapy images again showed multiple foci in the neck and substernal region (Fig. 7B). Follow-up imaging is planned for this patient.

Microscopic Findings

All five cases showed features that have been described with insular carcinoma, including well-defined insulae of tumor cells often surrounded by thin connective tissue fibers (Fig. 1). Thick bands of fibrous tissue frequently separated some of the larger islands. Frequently, artifactual clefting between the fibrous connective tissue rim and the tumor cells was identified. The small nests often showed small dense colloid accumulations in small follicles. Variable amounts of necrosis were also seen in all five neoplasms, ranging from a small focus to widespread necrosis throughout the tumor, accounting for 10% of the tumor volume. All of these small insular nests were well defined. Broad sheets of cells were noted in Cases 1 and 3, and

FIGURE 7. (A) Pinhole image 48 hr after initial ^{131}I therapy shows uptake in both thyroid beds plus multiple additional foci (arrows) in bilateral cervical metastases not visualized on the pre-therapy images. (B) Pinhole image 48 hr after second ^{131}I therapy shows much less uptake in the thyroid beds, but marked increased uptake in additional cervical and substernal lymph node metastases.

a trabecular arrangement of cells was seen in Cases 2, 4, and 5.

Pleomorphism was virtually absent in all of the cases. Only rare cells showed marked changes in cytoplasmic size. No giant cells or multinucleated cells were present. Nuclear overlapping was not prominent in any of the areas classified as insular carcinoma. The mitotic index was low in all of the tumors, approximately 1 per 10 high-power fields.

There was no associated follicular carcinoma in any of our cases. However, Case 3 had a papillary carcinoma of the thyroid excised 16 yr before presenting with a poorly-differentiated thyroid carcinoma. This patient also had a coexistent adenoma in the contralateral lobe of the main neoplasm. Portions of the neoplasms in Cases 2 and 5 also contained distinct components of papillary carcinoma as well.

DISCUSSION

Despite the variance in clinical course and differing histologic classifications, a feature that is common to all insular carcinomas is the presence of cells that arise from follicular epithelium. These small neoplastic cells are arranged in an insular pattern and have the distinct potential to concentrate radioiodine. This allows postoperative radioiodide imaging and the potential for adjuvant radioiodine therapy. Until the recent reclassification in 1984 of insular carcinomas as a distinct thyroid cancer, many patients were considered to have anaplastic or poorly-differentiated neoplasms that would not be expected to localize ^{131}I (1). They were therefore unlikely to be considered for postoperative radioiodide imaging or radiotherapy.

Radionuclide bone imaging has shown a high sensitivity for detection of skeletal metastases, but it is frequently unable to distinguish metastases from benign processes (5). MRI has been shown to be useful in clarifying the nature of skeletal abnormalities seen on radiographs and/or radionuclide scans (6–9). In the spine, the multiplanar capabilities of MRI and its ability to image the entire spine make this modality superior to CT imaging (6,7). The STIR sequence is especially helpful in the evaluation of marrow pathologic processes (8,9). In Case 1, the MRI studies were helpful in confirming the skeletal metastasis in the femur and an unsuspected C-spine lesion obscured by uptake in and adjacent to the thyroid bed on the ^{131}I images (Fig. 2A). Subsequent MRI studies confirmed a favorable response to ^{131}I therapy of the metastatic foci.

Four of our patients showed postoperative ^{131}I localization and received ^{131}I therapy. One patient was not studied. Extrathyroidal ^{131}I localization in neoplastic lesions occurred in three of the four cases. The fourth patient showed ^{131}I uptake in the right thyroid bed only. Carcangiu et al. (1) reported that 7 of 25 patients with insular carcinoma received prophylactic ^{131}I therapy shortly after a total thyroidectomy. All seven apparently developed recurrent
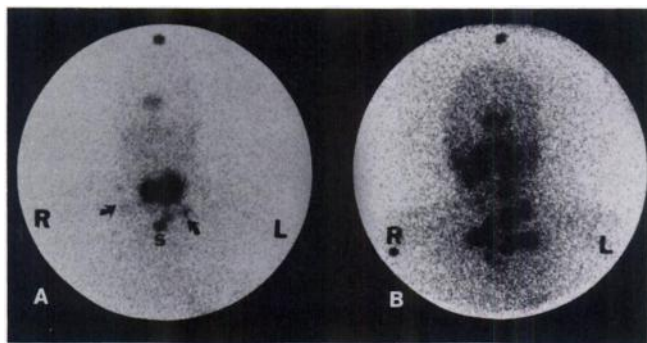
disease; however, it is unclear how many of their patients initially showed ^{131}I localization in neoplasm outside the thyroid bed or if any showed ^{131}I uptake in the recurrent lesions. In the series of Flynn et al. (4), three of four patients with insular carcinoma received postoperative ^{131}I ablative therapy. Two (one with a prior diagnosis of metastatic follicular thyroid cancer and one with papillary carcinoma containing foci of insular carcinoma metastatic to bone) received more than one therapeutic ^{131}I dose. The percent of ^{131}I uptake was not given in either case.

Both reports documented the propensity of insular thyroid carcinoma to recur locally and as distant metastases (1,4). In addition, total thyroidectomy, nodal resection, and prophylactic radioactive iodide therapy "failed to control disease" in several patients. Currently, the percent of insular carcinomas that have sufficient ^{131}I concentration to allow postoperative ^{131}I therapy is unknown. Nevertheless, postoperative ^{131}I ablation of residual functioning thyroid tissue usually allows ^{131}I uptake in remaining neoplastic deposits or metastases that may not be identified on pre-therapy images (10). Furthermore, ^{131}I localization in residual thyroid bed tissue and/or in differentiated cell components of metastatic lesions may allow ablation of adjacent neoplastic cells that have poor ^{131}I uptake (11).

Although additional documentation is needed, it is likely that early detection of metastases will enhance ^{131}I therapeutic intervention and subsequently improve survival and/or palliation in patients with insular thyroid carcinoma. For this reason, postoperative ^{131}I imaging is recommended for all patients with insular carcinoma of the thyroid.

REFERENCES

1. Carcangiu ML, Zampi G, Rosai J. Poorly differentiated ("insular") thyroid carcinoma. A reinterpretation of Langhans' "wuchernde Struma." Am J Surg Pathol 1984;8:655–668.
2. Sakamoto A, Kasai N, Sugano H. Poorly differentiated carcinoma of the thyroid. A clinicopathologic entity for a high-risk group of papillary and follicular carcinomas. Cancer 1983;52:1849–1855.
3. Limbert E, Soares J, Botelho L, Sobrinho-Simoes M. "Insular" thyroid carcinoma—clinicopathological study of 12 cases. In: Jaffiol C, Milhaud G, eds. Thyroid cancer. New York: Elsevier; 1985:317–319.
4. Flynn SD, Forman BH, Stewart AF, Kinder BK. Poorly differentiated ("insular") carcinoma of the thyroid gland: an aggressive subset of differentiated thyroid neoplasms. Surgery 1988;104:963–970.
5. McNeil BJ. Value of bone scanning in neoplastic disease. Semin Nucl Med 1984;14:277–286.
6. Colman LK, Porter BA, Redmond J III, et al. Early diagnosis of spinal metastases by CT and MR studies. J Comput Assist Tomogr 1988;12:423–426.
7. Pettersson H, Gillespy T, Hamlin DJ, et al. Primary musculoskeletal tumors: examination with MR imaging compared with conventional modalities. Radiology 1987;164:237–241.
8. Ehman RL, Berquist TH, McLeod RA. MR imaging of the musculoskeletal system: a 5-year appraisal. Radiology 1988;166:313–320.
9. Unger EC, Summers TB. Bone marrow. Top Magn Reson Imag 1989;1:31–52.
10. Beierwaltes WH, Rabbani, R, Dmuchowski C, Lloyd RV, Eyree P, Mallette S. "An analysis of ablation of thyroid remnants" with I-131 in 511 patients from 1947–1984: experience at University of Michigan. J Nucl Med 1984;25:1287–1293.
11. Tubiana M, Lacour J, Monnier JP, et al. External radiotherapy and radioiodine in the treatment of 359 thyroid cancers. Br J Radiol 1975;48:894–907.

EDITORIAL
Differentiating Anaplastic Thyroid Carcinomas

Differentiated thyroid carcinomas of follicular cell origin (pure papillary, papillary-follicular, and follicular carcinomas) are amenable to treatment with the combination of surgery, thyroxine suppression, and radioiodine ablation of thyroidal remnants and metastases, with excellent results relative to morbidity, recurrence, and survival in the overwhelming majority of patients. Medullary thyroidal carcinoma of C-cell origin tends to be a more aggressive tumor with unremitting progression and metastases to cervical lymph nodes, liver, bone, lungs, and adrenals unless early surgical intervention results in total removal and cure. Ten-year survival rates are about 50%.

On the other hand, undifferentiated, anaplastic carcinomas, until recent years, have been considered to be extremely aggressive and rapidly and almost universally fatal. The few survivors of these cancers were considered to result from removal, sometimes fortuitously, of small anaplastic carcinomas at a very early stage. In the last dozen or so years, electron microscopic and immunohistochemical techniques have been developed, permitting the recognition of a number of tumors of differing origin that have been included under the rubric of anaplastic thyroid carcinoma. Correctly categorizing and specifically treating these tumor types have a salubrious effect in a number of circumstances. Whereas the majority of anaplastic large-cell carcinomas (of follicular cell origin) still carry an extraordinarily grave prognosis, most of the anaplastic small-cell thyroid carcinomas are of the diffuse type and really represent primary malignant lymphoma (1-3); these primary thyroidal non-Hodgkins extranodal lymphomas are often confounded with

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