Aspiration Cytology of ^{131}I-Induced Thyroiditis

A Case Report

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BACKGROUND: Fine needle aspiration (FNA) has become an indispensable diagnostic tool for the investigation of thyroid nodules. Although ^{131}I may induce morphologic changes similar to those associated with external radiation, a known diagnostic pitfall, the cytology literature on the subject is very sparse. This case exemplifies the thyroid cytologic changes associated with ^{131}I exposure.

CASE: A 50-year-old male with a remote history of ^{131}I exposure had an indurated thyroid on routine physical examination. FNA was interpreted as positive for malignant cells, and subsequently a total thyroidectomy was performed. Review of the cytologic sample revealed follicular cells with focal, marked cytologic atypia, abundant colloid, stromal fragments, and lymphocytes. The thyroidectomy specimen consisted of an indurated and nodular gland showing architecture distortion by micronodule formation, lymphocytic infiltrates, interstitial fibrosis and follicular atrophy. Marked nuclear atypia was seen in the follicular cells.

FNA of ^{131}I-exposed thyroid glands may reveal large, atypical cells in addition to classical changes of nodular goiter and/or chronic thyroiditis.

CONCLUSION: FNA of thyroid glands exposed to ^{131}I may show significantly large, atypical follicular cells in addition to classical changes of nodular goiter and/or chronic lymphocytic thyroiditis. Although the clinical history and the diffuse nature of the process may favor a benign process in most cases, the presence of marked atypia could lead to a malignant diagnosis. Pathologists, therefore, should exercise extreme caution in interpreting cases with ^{131}I exposure. (Acta Cytol 1997;41:1369–1372)

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Pathologists are frequently called on to help clinicians select patients with thyroid nodules for

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surgery through the interpretation of fine needle aspiration (FNA) specimens. Some of the recognized pitfalls associated with this technique are the cytologic changes following radiation therapy. ^{131}I therapy, currently the most popular treatment for adults with Grave's disease,[18] may induce similar cytologic changes. These findings, therefore, may impose a serious interpretive challenge for a pathologist unaware of the patient's past medical history. The current literature on aspiration cytology of the thyroid exposed to ^{131}I is very sparse. Below we describe a case that exemplifies the clinical problems that one can face with such cases.

One cannot make an unequivocal benign diagnosis in cases where the cytologic atypia is pronounced.

Case Report

A 50-year-old African American male had an indurated thyroid gland on routine physical examination. The patient had a long history of Grave's disease treated with ^{131}I 30 years prior to this presentation. He denied having any symptoms. Physical examination revealed a firm, right thyroid lobe with no cervical adenopathy. FNA was performed on the right thyroid lobe using a 22-gauge needle. Three direct smears were made, fixed in 95% ethanol and subsequently stained with Papanicolaou stain. The smears were moderately cellular and composed predominantly of follicular cells, abundant colloid, fibrovascular stroma and lymphocytes. The follicular cells were grouped mainly in loose, monolayered clusters with occasional formation of microfollicles. There was marked anisonucleosis and nuclear pleomorphism (Figures 1 and 2). Abundant, large, atypical cells, mainly singly or in loose clusters, were intermixed with fibroblasts and blood vessels. The nuclear chromatin of these cells was coarse, and occasional prominent micronucleoli were present. No nuclear grooves or intranuclear inclusions were identified. The nuclear/cytoplasmic ratio was slightly increased, and the cytoplasm was abundant and clear. Many nuclei were giant and appeared "naked" due to disintegration of their cytoplasm. Because of the marked anisonucleosis, the smears were interpreted as malignant, favoring an anaplastic carcinoma. Because of the cytologic diagnosis, a frozen section from the right lobe interpreted as a follicular neoplasm and the presence of additional nodules in the left lobe, a total thyroidectomy was performed.

The thyroidectomy specimen consisted of a 9.5-g, firm thyroid gland measuring 10×5.3×2.5 cm. The capsule appeared intact. A 2.0-cm nodule in the right lobe and two nodules in the left lobe, measuring 1.0 and 0.5 cm, were identified. The remainder of the parenchyma was diffusely indurated. Microscopically, the overall glandular architecture was distorted by the formation of nodules; patchy, lymphocytic infiltration; interstitial fibrosis; and follicular atrophy. Abundant lymphocytes and occasional plasma cells were present throughout the gland, without germinal center formation. The nodules were entirely encapsulated by an irregular, thick fibrous capsule and were composed of large, dilated follicles admixed with tightly packed, small follicles with scanty colloid. No evidence of capsular or vascular invasion was identified. The follicular cells showed marked nuclear pleomorphism (Figure 3). The nuclei were markedly enlarged and hyperchromatic, with occasional prominent nucleoli. There was no evidence of nuclear clearing, intranuclear inclusions or nuclear grooving. The nuclear/cytoplasmic ratio was slightly increased, and the cytoplasm contained large vacuoles. Occasional atypical multinucleated giant cells were also seen. Cellular atypia was seen throughout the gland but more prominently within the nodules (Figure 4). Areas of hemorrhage, hemosiderin-laden macrophages and foreign body multinucleated giant cell reaction were seen in the right lobe nodule, the subject of preoperative FNA.

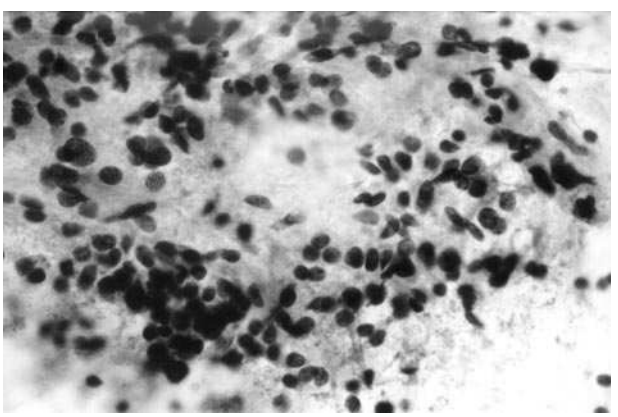

Figure 1 Follicular cell population in area of increased cellularity (Papanicolaou stain, ×400).

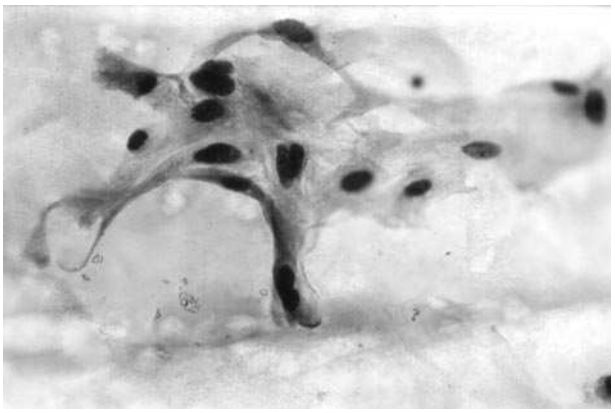

Figure 2 Atypical cells with marked hyperchromatism and nucleomegaly (Papanicolaou stain, ×400).

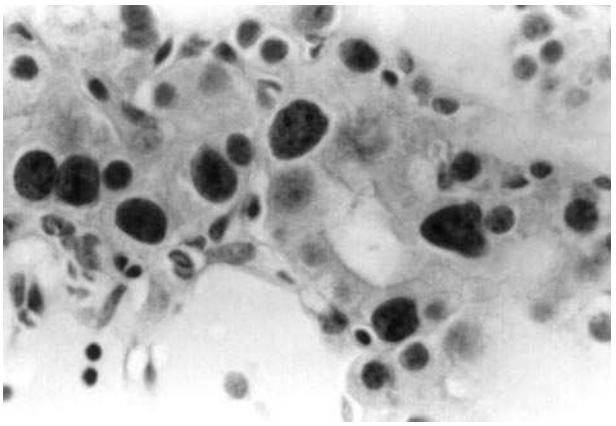

Figure 4 Histologic section from thyroidectomy specimen showing marked atypia and anisocytosis of follicular cells (hematoxylin-eosin, ×400).

Discussion

FNA is a preferred diagnostic method for patients presenting with thyroid nodules since it allows the selection of surgical candidates with a high degree of accuracy. This method is simple, safe, cost effective and relatively atraumatic. When the performance and interpretation are in experienced hands, the false negative rate is very low, as low as 2%, depending on the series, and the false positive cases are even lower.[14] However, in thyroid FNA, as in any other diagnostic medical procedure, certain limitations and pitfalls exist. The changes associated with radiation exposure may be difficult to differentiate from those of malignant neoplasms, even among the most experienced cytopathologists. The changes induced by ^{131}I and its consequences have not been studied well, and the cytology literature on the subject is sparse.[4,5]

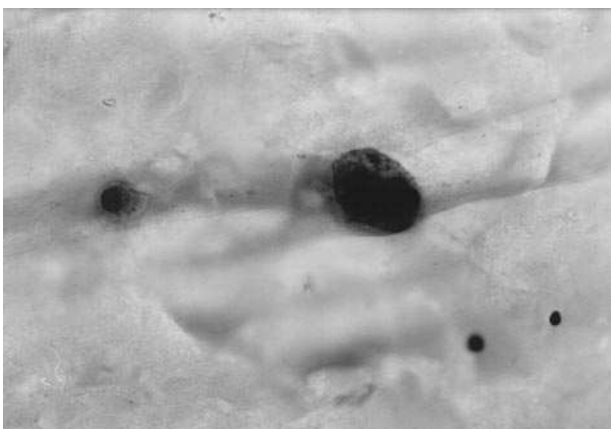

Figure 3 Atypical cell in a background of "watery" colloid. Note the size of this cell as compared to that of the histiocyte next to it (Papanicolaou stain, ×400).

The association between external beam radiation and thyroid cancer has been well documented.[2,6,8,12,16,17] There is considerable controversy regarding whether internal radiation induced by ^{131}I also increases the risk of thyroid cancer. Tezelman et al suggested that ^{131}I may increase slightly the risk of thyroid cancer and that these resultant neoplasms may behave especially aggressively.[18] It seems that long-term follow-up studies are needed to confirm this hypothesis since other large, cooperative studies from the United States and Sweden have found no increased risk.[3,9]

The pathologic changes following ^{131}I therapy have been described as non–dose dependent and can occur months to years after administration of the radioactive drug.[1,4,7,16] The changes recapitulate those created by external radiation.[1,6,8,12,15] Fibrosis, follicular disruption and atrophy, Hürthle cell change, nuclear atypia, nodule formation and lymphocytic infiltration are the most common findings.[4,11,13,16] Early studies by Freeberg and Dailey described the histologic changes in the thyroid glands of patients receiving ^{131}I for intractable angina pectoris, congestive heart failure and hyperthyroidism.[1,7] In addition to chronic thyroiditis, diffuse follicular atrophy and fibrosis, they found bizarre, hyperchromatic cells to be one of the most prominent features.[10,11] Kennedy and Thomson, howev-

er, described Hürthle cell change and follicular breakdown with abundant extrafollicular colloid as the most specific findings. They found that nuclear pleomorphism was not a distinguishing feature since it was also found, along with fibrosis, telangiectasia and eosinophilic cuffing of vessels, in the nonirradiated, control groups.[10]

To our knowledge, Droese and colleagues published the only article on aspiration cytology of thyroid glands exposed to ^{131}I.[5] They studied fine needle aspirates from 27 patients treated with ^{131}I for Grave's disease, toxic nodular goiter, and euthyroid goiter. The changes described by these authors are similar to those associated with low-dose external radiation exposure: colloid goiter, chronic thyroiditis, and large, atypical cells. These features were found at least two months after exposure, but the atypia was not as prominent as in cases of external radiation. Our findings are very similar to those of Droese and colleagues. The morphologic changes present on FNA and in the thyroidectomy specimen were very prominent despite the remote, 30 year-history of ^{131}I exposure. Although the presence of large, atypical cells was worrisome in our case, the overall pattern was that of nodular goiter characterized by abundant colloid, a moderate amount of follicular cells in monolayered clusters, stromal fragments and lymphocytes. Since we were aware of the patient's history of ^{131}I exposure, the diagnosis of radiation-induced-thyroiditis could easily be favored over cancer.

In summary, FNA of ^{131}I-exposed thyroid glands may reveal large, atypical cells in addition to classical changes of nodular goiter and/or chronic thyroiditis. Although clinical information and the diffuse nature of the changes in some cases favor a benign process secondary to radiation damage, one cannot make an unequivocal benign diagnosis in cases where the cytologic atypia is pronounced. Pathologists, therefore, should exercise extreme caution in interpreting cases with previous exposure to ^{131}I. Surgical exploration may still be needed in a large number of cases, especially if a trial of thyroid hormone does not completely resolve the nodular disease.

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