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Accumulation of Iodine-131-Iodocholesterol in Renal Cell Carcinoma Adrenal Metastases

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Adrenocortical scintigraphy is a useful technique for differentiating between types of nonhyperfunctioning adrenal masses. Metastatic tumors do not normally accumulate radioiodocholesterol and show discordant uptake on scintigrams. We present two patients who showed accumulation of ^{131}I-6β-iodomethyl-19-norcholesterol (NP59) in the adrenal metastases from renal cell carcinoma. In one patient with bilateral adrenal metastases, accumulation in the primary tumor as well as adrenal metastases was demonstrated. The adrenal metastases in both patients were resected and were histologically proven to be metastases from clear-cell renal carcinoma. Accumulation of NP59 in metastatic adrenal tumors, although a very rare finding, suggests a pitfall in the differential diagnosis of adrenal cortical tumors.

Key Words: adrenal metastases; adrenocortical scintigraphy; renal cell carcinoma; iodocholesterol

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Adrenocortical scintigraphy is a useful tool for the differential diagnosis of nonhyperfunctioning adrenal masses (*1–3*). In patients with malignant neoplasms, it is crucial to distinguish between metastatic adrenal tumors and other benign tumors to assess tumor staging and plan further management. Accumulation in the adrenal gland decreases (discordant uptake) when it is replaced with neoplasms, because malignant and metastatic tumors do not accumulate the radiolabeled cholesterol analog (*4,5*). Although several cases of adrenal metastatic tumors coexisting with an adenoma have been reported showing increased uptake (concordant uptake) on adrenocortical scintigraphy (*6–8*), no cases with concordant uptake have been reported in patients with only adrenal metastatic tumors.

We have performed adrenocortical scintigraphy on patients with malignant neoplasms for the evaluation of their adrenal tumors, seven of which were histologically proven to have had adrenal metastatic tumors. Of these patients, five showed discordant uptake consistent with cases in previous literature; the other two, however, demonstrated accumulation of radioiodocholesterol. We present these two cases and discuss the possibility of accumulation of NP59 in the malignant neoplasms.

CASE REPORTS

Patient 1

A 58-yr-old woman entered the hospital for resection of a left renal cell carcinoma (RCC). CT scan demonstrated a huge right adrenal mass and the left renal tumor (Fig. 1A). Hormonal measurements revealed no adrenocortical or medullary dysfunction. Adrenocortical scintigraphy was performed for the evaluation of the right adrenal tumor. She received 37 MBq of ^{131}I-6 β-iodomethyl-19-norcholesterol (NP59). Posterior and anterior abdominal images taken 8 days after injection demonstrated increased uptake (concordant uptake) in the right adrenal gland compared to the left side (Fig. 1B). In addition, diffuse distribution of radioactivity was shown in the vicinity of the left adrenal gland. This radioactivity persisted for 10 days after injection, suggesting radiotracer accumulation in some parts of the primary renal tumor. The right adrenal gland (7 × 3 cm, 36 g) was resected and was histologically proven to be metastatic from the RCC (Fig. 2). No

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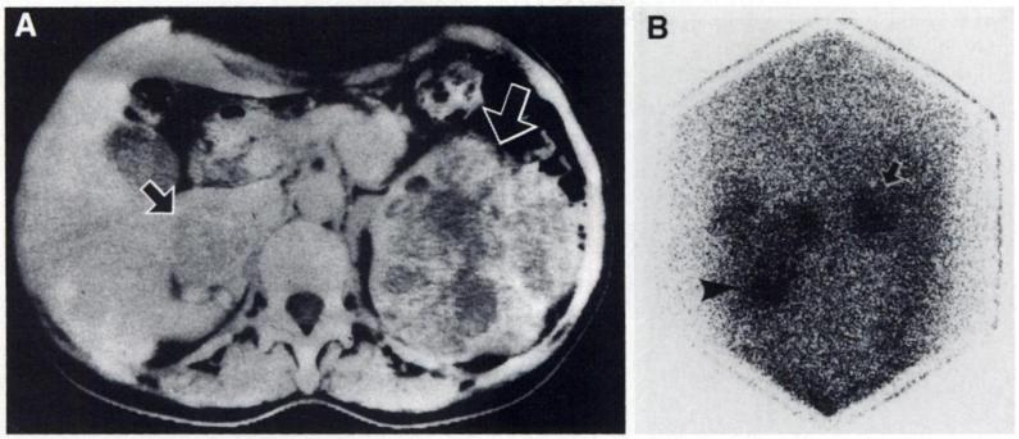

FIGURE 1. CT scan (A) demonstrates a left renal tumor (large arrow) and a right adrenal tumor (small arrow). A posterior image 8 days after injection of NP59 (B) shows increased uptake in the right adrenal gland (arrow) and diffuse distribution of radioactivity (arrowhead) under the left adrenal gland.

adrenal adenoma tissue coexisted. The left adrenal gland was also resected along with the left RCC and a small metastatic lesion (5 mm) was found.

Patient 2

A right adrenal tumor was found on a CT scan in a 68-yr-old man with left RCC. A loss of plasma cortisol circadian rhythm was observed, although his peripheral concentrations of cortisol and aldosterone were normal. He was examined with NP59 for the evaluation of the adrenal tumor. Only the right adrenal gland was visualized on the scintigrams (Fig. 3). The findings were interpreted as right adrenocortical adenoma with left adrenal suppression. The tumor (3 × 3 cm, 8 g) was resected and was histologically demonstrated to be metastatic from the RCC. No metastatic lesions in the left adrenal gland were found visually or in the part of the tissue resected with left RCC microscopically. He received cortisol postoperatively for 1 wk. With 4 days' withdrawal of cortisol, adrenocortical scintigraphy was performed for the re-evaluation of the left adrenal gland. There was no accumulation in the left adrenal gland. A left adrenal tumor, which was progressive and diagnosed as metastasis, developed 6 mo after the operation.

FIGURE 2. Metastatic tumor from clear-cell renal carcinoma (arrow). Rich lipid content in the cells are noted. Normal adrenocortical cells (arrowhead) are in the lower layer. (Hematoxylin and eosin, 100x).

DISCUSSION

Two cases demonstrating accumulation of radioiodocholesterol in the RCC metastatic tumor are presented. In previous articles, no such accumulation in the metastatic tumor has been demonstrated except when those tumors coexisted with adrenocortical adenoma (*6–8*). Coexistence of adenoma was not demonstrated in these cases.

In the first patient, the adrenal mass discovered on CT scan was large and metastases were suspected. Increased uptake in the tumor suggested adrenocortical adenoma. The uptake in the right adrenal tumor was prominent but the contralateral adrenal gland was not suppressed. We suspected the coexistence of adenoma and asked the pathologists to re-evaluate the specimens. Three pathologists from different departments confirmed the diagnosis. They reported that the tissue contained lipids and resembled adrenal tissue. In this patient, diffuse uptake in the

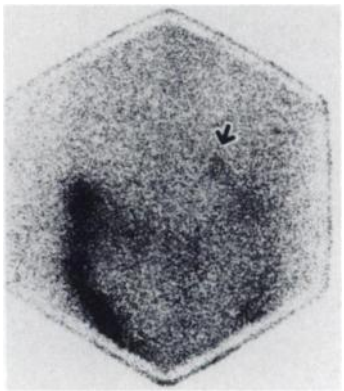

FIGURE 3. Adrenocortical scintigram 8 days after injection. Tracer uptake in the right adrenal gland (arrow) is demonstrated while no accumulation of tracer in the left adrenal gland is evident.

vicinity of left adrenal gland was also demonstrated and it was suspected to be a part of the primary tumor.

Scintigraphic findings in the second patient were interpreted as concordant uptake because the contralateral adrenal gland was not visualized. However, uptake in the tumor was rather faint. We suspected hypofunction of the contralateral adrenal gland but the patient did well without steroid hormone replacement. Adrenal metastasis in the contralateral side was also suspected. However, the resected left adrenal gland was normal and no macroscopic metastatic lesion was found during the operation. There might be some connection with the left adrenal mass that developed later. However, we could not find a good explanation for nonvisualization of the left adrenal gland.

Accumulation of iodocholesterol was shown only in patients with RCC. Clear cells of RCC contain a large quantity of cholesterol ester and histologically resemble adrenal glands. We suggest that this large lipid pool is involved in accumulation of NP59. Clayman et al. (*9*) injected RCC patients with NP59 and measured uptake in various tissues. The highest accumulation of the tracer was shown in the adrenal glands followed by RCC tissue. Tracer activity in RCC was about two times higher than in the kidneys or the liver, although tracer activity in the adrenal glands was 10 times higher than that of RCC. In addition, one patient showed faint activity in the area of his renal mass on radionuclide imaging.

NP59 binds to low-density lipoproteins (LDL) in the circulation and enters the tissue by LDL receptor-mediated transport (*10,11*). It has been reported that some forms of human solid tumor express an increased amount of LDL receptors (*12,13*). Rudling and Collins (*14*) showed that some RCC expressed higher LDL receptor levels compared to normal kidney tissue although they were usually low. Although we were not able to measure the level of LDL receptors in our cases, these tumors may have had an increased number of LDL receptors compared to adrenal glands. An increase in LDL receptors in the tumors is not specific to RCC (*12,13*), and other tumors have been reported to have an increase in LDL receptors.

CONCLUSION

We report two cases of adrenal metastatic tumors from RCC that accumulated NP59. Although it is not clear why this occurs, there may be some connection with the rich cholesterol content of RCC. This finding, although rare, represents one of the pitfalls of differential diagnosis of adrenal tumors with adrenocortical scintigraphy using iodocholesterol.

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