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A case of ganglioneuroma in which ^{131}I-6β-iodomethyl-19-norcholest-5(10)-en-3β-ol scintigraphy showed high uptake in the adrenal gland leading to a misdiagnosis

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We experienced a case in which ^{131}I-6β-iodomethyl-19-norcholest-5(10)-en-3β-ol (^{131}I-adosterol) scintigraphy showed high uptake in the right adrenal gland. We diagnosed functional cortical adenoma because of the finding of ^{131}I-adosterol scintigraphy. However, no positive findings for the existence of cortical adenoma were obtained in other examinations and we performed right adrenalectomy. Unexpectedly, pathological finding showed the right adrenal gland was occupied with a large ganglioneuroma. This is an instructive case in which ^{131}I-adosterol scintigraphy showed abnormal high uptake in the adrenal gland, in spite of the fact that the adrenal gland was occupied by a tumor derived from adrenal medulla.

Key words: ^{131}I-6beta-iodomethyl-19-norcholest-5(10)-en-3beta-ol, adrenal gland, ganglioneuroma

INTRODUCTION

ADRENAL-SPECIFIC RADIOLIGAND, ^{131}I-6β-iodomethyl-19-norcholest-5(10)-en-3β-ol (^{131}I-adosterol)[1] was developed in the 1970s. Increased uptake of the agent in tumor regardless of visualization of the contralateral gland suggests that the adrenal mass is usually a benign cortical adenoma.[2] This agent has the potency to diagnose lesions of the adrenal cortex and has been widely used to diagnose lesions which are derived from adrenal gland.[3,4] However, this agent has some pitfalls when used for diagnosis and we sometimes encounter patients whose scintigraphic findings are not consistent with their clinical ones. We experienced a patient who had an adrenal gland tumor derived from adrenal medulla in whom ^{131}I-adosterol scintigraphy showed high uptake in the adrenal gland. Here, we report a patient with ganglioneuroma whose ^{131}I-adosterol scintigraphy showed high uptake in the adrenal gland resulting in a misdiagnosis.

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CASE REPORT

A 37-year-old man was admitted for evaluation of an incidentally discovered right adrenal tumor. His physical findings, biochemical and endocrinological data had no significant abnormalities. The levels of plasma cortisol, aldosterone, noradrenaline, and adrenaline were within normal limits.

Abdominal CT imaging showed an oval-shaped tumor in the right adrenal gland (Fig. 1). The tumor had a maximum diameter of approximately 4 cm and had homogeneously soft tissue density. Residual adrenal cortex was found in the top portion of the right adrenal gland. T1-weighted MRI showed homogeneous hypo-intensity in the right adrenal tumor. Both in-phase and out-of-phase studies equally showed hypo-intensity, suggesting that

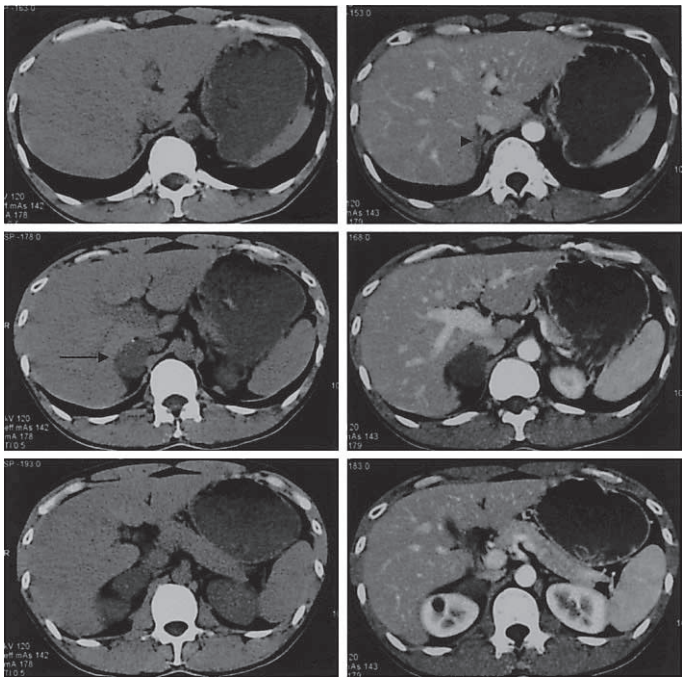

Fig. 1 *Left:* plain CT, *Right:* contrast enhanced CT, *Top:* upper (*top*) portion, *Middle:* middle portion, *Bottom:* lower portion. Abdominal CT image showed an oval-shaped mass in the right adrenal gland (→). Residual adrenal cortex was found in the top portion (►). Contrast enhanced CT did not show significant enhancement effect.

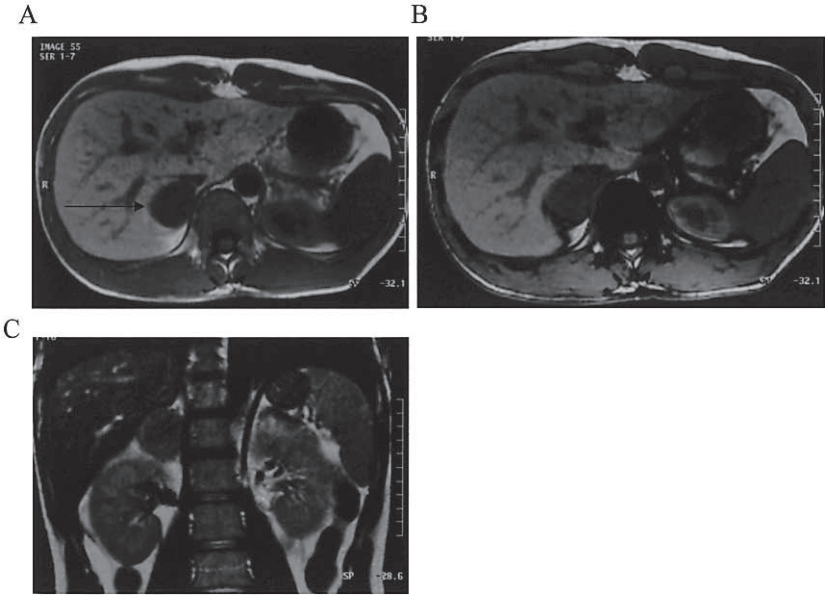

Fig. 2 A: axial image (in-phase), B: axial image (out-of-phase), C: coronal image (in-phase). Abdominal T1-weighted MRI showed homogeneous hypo-intensity mass in the right adrenal gland both in in-phase and out-of-phase studies (→). The intensity of the right adrenal gland was not significantly different from that of left one.

cortical adenoma could be excluded (Fig. 2). ^{123}I-meta-iodobenzylguanidine (MIBG) scintigraphy was done. We used ^{123}I-MIBG instead of ^{131}I-MIBG because we planned both examinations about adrenal cortex and medulla and the half-life of ^{123}I was shorter than that of ^{131}I. Back image was obtained 6 and 24 hours after 111 MBq of ^{123}I-MIBG was injected. ^{123}I-MIBG scintigraphy showed no abnormal uptake in bilateral adrenal glands, suggesting that tumor derived from adrenal medulla would be largely excluded (Fig. 3).

Then, ^{131}I-adosterol scintigraphy was done. A single detector scintillation camera (ZLC-7500, SIEMENS Co., Tokyo, Japan) fitted with high energy collimator was used to take images. Back image was obtained 7 days after 18.5 MBq of ^{131}I-adosterol was injected. ^{131}I-adosterol scintigraphy showed apparently high uptake in the right adrenal gland (Fig. 4). The uptake area was wide and not extremely localized. The uptake in the right adrenal gland was predominately high in the top portion and relatively low in the other portions.

We calculated the quantitative ^{131}I-adosterol uptake ratio. The method used was similar to that of Morita et al.[5] First, adrenal phantoms were prepared by placing 5 m*l* of solutions of Na^{131}I (37 MBq/m*l*) in a glass vial. The vial

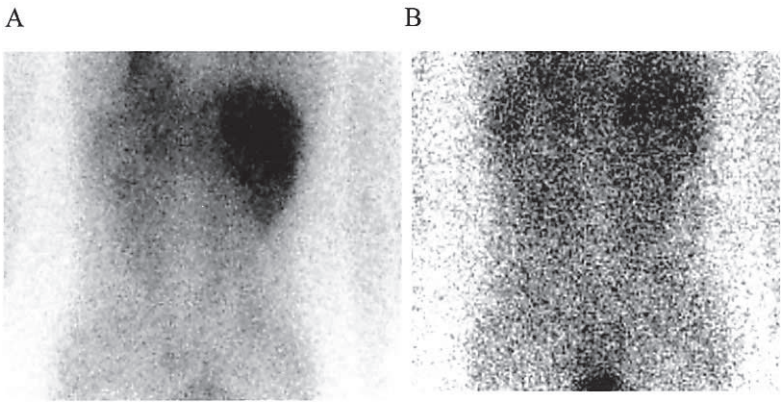

Fig. 3 A: 6 hours, B: 24 hours. ^{123}I-MIBG scintigraphy showed no abnormal uptake in bilateral adrenal glands.

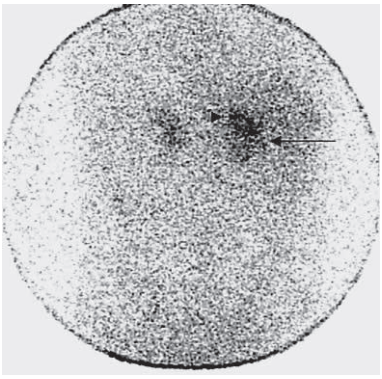

Fig. 4 ^{131}I-adosterol scintigraphy showed high uptake in the right adrenal gland (→). The uptake in the upper portion of the right adrenal gland was predominately high (►). The uptake in the left adrenal gland was within normal limits.

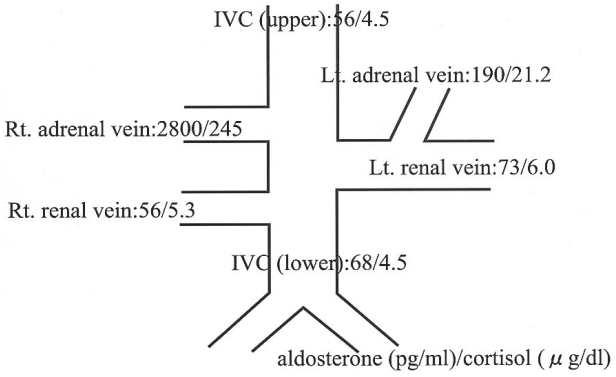

Fig. 5 A scheme of aldosterone/cortisol venous sampling.

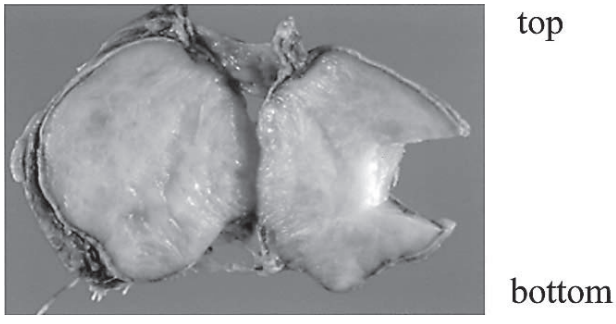

Fig. 6 Macropathological specimen showed a large gray-white round nodule with elastic hardness, occupying over half of the medulla, and compressing the covering adrenal cortex in an outward direction. The residual portion was noticed as a small appendix.

was placed in a tissue equivalent simulated body phantom prepared with water so that radioactivity counts were made at distances of 0, 2, 4, 6, 8, 10, 12 cm from the detector equipped with 365 keV high energy collimator. Radioactivity counts were measured at each distance. We calculated the exponential functional equation from the distance and counts per minute (cpm). Second, net adrenal counts were calculated by the cpm and the distance between the back surface and center of adrenal gland obtained from CT using the exponential functional equation. Total administered dose was obtained by subtraction of the post from pre radioactivity (Bq) in the syringe and attenuation correction made for 7 days. The quantitative ^{131}I-adosterol uptake ratio was calculated as radioactivity in the adrenal gland (Bq) divided by total administered dose (Bq) × 100 (%). The quantitative ^{131}I-adosterol uptake ratio was 15.03% in the right adrenal gland and 6.74% in the left adrenal gland (8.48 ± 4.59% is mean value ± standard deviation in our institute).

Because ^{131}I-adosterol scintigraphy suggested the possibility of a functional cortical adenoma, we postponed operation and decided to perform selective adrenal venous blood sampling. Selective adrenal venous blood sampling showed that the aldosterone/cortisol ratio[6,7] in the right adrenal vein was 11.4 (2800 (pg/m*l*)/245 (μg/d*l*)) and comparable to those of inferior vena cava 12.4 (56 (pg/m*l*)/4.5 (μg/d*l*)) in upper, 15.1 (68 (pg/m*l*)/4.5 (μg/d*l*)) in lower, respectively (Fig. 5), suggesting that existence of a functional cortical adenoma would be excluded. We considered that there was little possibility of this adrenal tumor being a functional cortical adenoma and performed right adrenalectomy.

Macropathological specimen showed that the right adrenal gland was occupied by a large tumor, which compressed the covering adrenal cortex in an outward direction. Adjacent adrenal cortex was noticed as small appendix (Fig. 6). Micropathological specimen was proved to be ganglioneuroma and adjacent adrenal cortex was circumferentially compressed around the tumor (Fig. 7). Immunohistopathological examination showed normal expression pattern of c17,[8] dehydroepiandrosterone sulfotransferase (DHEA-ST),[9] c21,[10] c11,[11] scc,[12] and 3 beta-hydroxysteroid dehydrogenase (3β-HSD)[13] in the

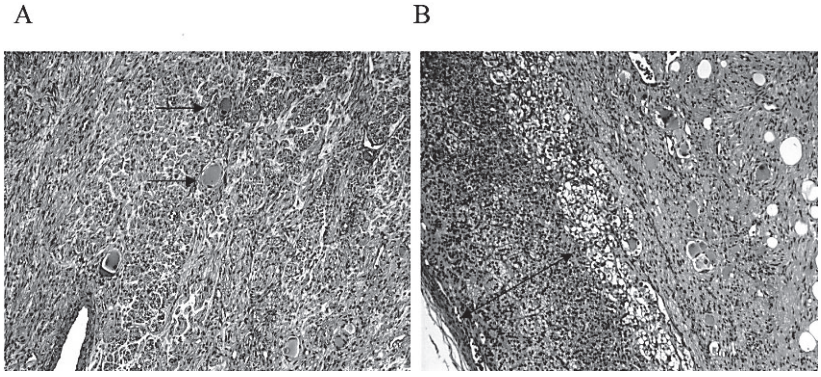

Fig. 7 A: central area (Hematoxylin-eosin stain (× 40)), B: peripheral area (Hematoxylin-eosin stain (× 10)). Histologically, the tumor was composed of neurofibromatous compact tissue and a scattered mixture of large neuroganglionic cells (→). These cells assumed a non-atypical figure similar to the physiological one, and their origin was identified by means of immunohistology: the former positivity of S-100, NSE, and the latter positivity of synaptophysin. The residual adrenal cortex was circumferentially compressed around the tumor and loss of lipoid (⟷).

residual adrenal cortex. These immunohistopathological findings suggested that cortical function in producing steroid was kept within normal limits and cortisol-hypersecreting adenoma was not present.

DISCUSSION

We speculated three possible mechanisms explaining why ^{131}I-adosterol scintigraphy showed abnormal high uptake in the right adrenal gland in this case.

First, ^{131}I-adosterol scintigraphy might show abnormal high uptake in the right adrenal gland because of the anatomical location of normal adrenal cortex. For example, normal adrenal cortex might be compressed behind the tumor and the quantitative ^{131}I-adosterol uptake ratio of the right adrenal gland became high. Because the quantitative ^{131}I-adosterol uptake ratio is calculated using the distance between the center of the adrenal gland and back surface, assuming that adrenal cortex is homogeneously distributed around adrenal medulla and the center of adrenal gland is most appropriate for the distance. However, if residual adrenal cortex was compressed at the backside of the tumor and the distance between the adrenal cortex and back surface was much shorter than that between the center of adrenal gland and back surface, the calculated quantitative ^{131}I-adosterol uptake ratio would be much higher than the essential quantitative ^{131}I-adosterol uptake ratio. However, in this case, macro and micropathological findings showed that residual adrenal cortex was circumferentially compressed around the tumor and not necessarily localized at the backside of the right adrenal gland, and ^{131}I-adosterol uptake was widely distributed and predominately high in the top portion. In addition, we calculated the quantitative ^{131}I-adosterol uptake ratio (15.03%) using the distance between the center of the right adrenal gland and back surface. The quantitative ^{131}I-adosterol uptake ratio in the right adrenal gland would be 12.69% and high, even if we had assumed that uptake of ^{131}I-adosterol had been localized at the backside of the right adrenal gland and the ratio had been calculated using the distance between the back edge of the right adrenal gland and back surface. Another possible mechanism related to anatomical location is overlapping of the top portion of the right adrenal gland and liver. However, the radioactivity in the top portion in the right adrenal gland (233 cpm) was higher than the sum of the lower portion of the right adrenal gland (128 cpm) and liver (69 cpm). Although the anatomical location of normal adrenal cortex might to some extent affect the high uptake in ^{131}I-adosterol scintigraphy, we think that the theory in which anatomical location of normal adrenal cortex alone caused high uptake in ^{131}I-adosterol scintigraphy lacks sufficient evidence.

Second, a small functional nodule might be present in the residual adrenal cortex. However, this contention can be largely excluded. Because, even though we cut about 10 slices in the right adrenal gland, no nodular lesions were detected. In ^{131}I-adosterol scintigraphy, uptake of ^{131}I-adosterol was widely distributed and not extremely localized in the right adrenal gland. In addition, selective adrenal venous blood sampling in which aldosterone/cortisol ratio in the right adrenal vein was comparable to that of inferior vena cava was also a crucial reason against the existence of a micro nodule.

Third, ^{131}I-adosterol was accumulated in the ganglioneuroma. However, to our knowledge, there is no report of high uptake of ^{131}I-adosterol or extremely activated cholesterol metabolism in ganglioneuroma. The theory that high blood flow in the ganglioneuroma caused high uptake of ^{131}I-adosterol is deniable, because no significant enhancement effect in CT or flow void in MRI was found.

In this case, a planned operation was postponed be-

cause ^{131}I-adosterol scintigraphy showed high uptake in the right adrenal gland, and selective adrenal venous blood sampling was added. In the selective adrenal venous blood sampling, the aldosterone/cortisol ratio in the right adrenal vein was comparable to that of inferior vena cava as mentioned above. Because no positive finding was found in selective adrenal venous blood sampling and various endocrinologic studies, we considered that there was little possibility of this adrenal tumor being a functional cortical adenoma and performed right adrenalectomy.

To our knowledge, there is no report in which ^{131}I-adosterol showed high uptake in the adrenal gland in which tumor derived from adrenal medulla was present. Although we have not determined the definite reason why ^{131}I-adosterol scintigraphy showed high uptake in the right adrenal gland in this case, we speculate that several factors, for example anatomical location of adrenal cortex, volume of adrenal gland, or physical stimulation to residual adrenal cortex might be at work and caused high uptake in ^{131}I-adosterol scintigraphy. ^{131}I-adosterol scintigraphy has some pitfalls that may lead to a misdiagnosis through these and other factors. This was a rare and instructive case for the reason that ^{131}I-adosterol scintigraphy showed abnormal high uptake in the adrenal gland in which tumor derived from adrenal medulla was mainly present.

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