Metastatic Medullary Thyroid Cancer: Localization with Iodine-131 Metaiodobenzylguanidine

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A patient in whom metastatic medullary thyroid cancer was diagnosed underwent a scintigraphic examination using [^{131}I]MIBG. Multiple hot lesions and diffuse hepatic uptake were noted corresponding to bone and liver metastases. Iodine-131 MIBG may prove to be useful for scintigraphic localization and for the treatment of medullary thyroid cancer as in pheochromocytoma and neuroblastoma.

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In 1980 the striking affinity of iodine-131 metaiodobenzylguanidine ([^{131}I]MIBG) for the adrenal medulla was reported, which is structurally similar to noradrenaline and taken up by adrenergic storage vesicles (*1*). Thereafter, [^{131}I]MIBG has been found to accumulate in benign and malignant pheochromocytoma (*2*), adrenal medullary hyperplasia (*3*), and neuroblastoma (*4*). Recently, a patient in whom uptake of [^{131}I]MIBG was observed by medullary thyroid cancer has been reported (*5*). We describe the localization of disseminated medullary thyroid cancer using this substance.

CASE REPORT

A 51-yr-old woman was admitted for the investigation of a 5-mo history of watery diarrhea. Twenty years earlier she had undergone left hemithyroidectomy and postoperative irradiation for thyroid cancer. She also had noticed back pain and swelling over the lumbar vertebra during the last 3-yr. She had never had hypertension. There was no family history of endocrinopathy.

Findings of physical examination included: blood pressure 140/80 mmHg supine; pulse 76 and regular; heart auscultation, normal S1 and S2 with no murmurs or gallops: a fixed mass of 2 cm in diam in the left supraclavicular region; several small palpable lymph nodes in the right anterior neck; a large lobular hard mass extending from the thyroid bed down to the mediastinum behind the sternum; and two body hard lumps with indistinct boundary in the middle of the lower back region. There was no evidence of neurofibromas of the eyelids or the lips or the tongue. Laboratory results showed a very high serum calcitonin level of 288 ng/ml (normal below 0.3) and raised plasma levels of carcinoembryonic antigen; 33.3 ng/ml (below 10) and $PGF_{2\alpha}$; 797 pg/ml (55–292). Routine urinalysis, complete blood count with differential, and electrolytes were normal. Other significant normal tests included plasma epinephrine of 28 pg/ml (normal below 100), norepinephrine of 110 pg/ml (below 350), urinary epinephrine of 4 μg/day (below 30), norepinephrine of 15 μg/day (below 120), metanephrine of 21 μg/day (below <165), normetanephrine of 3 μg/day (below 80) and vanillylmandelic acid of 1.5 mg/day (below 11.8).

On x-ray films coarse, stippled, calcific deposits were found in the regions of the anterior neck; coarse, coalescent, calcified lesions were found in the liver; a large calcified mass located between L_3 and L_4, and multiple sclerotic lesions throughout the lumbar and thoracic spine and the pelvis were observed (Fig. 1). X-ray computed tomographic (CT) examination showed a coarse coalescent calcific deposit of 2 cm by 3 cm in the right lobe of the liver and numerous stippled deposits throughout both lobes of the liver (Fig. 2). CT scan of the adrenals could rule out an enlarged adrenal suggesting pheochromocytoma.

On bone scintigrams with technetium-99m methylene diphosphonate([^{99m}Tc]MDP), markedly increased radioactivity was seen in the areas of the anterior neck extending from the thyroid bed down behind the sternal body, the lower lumbar

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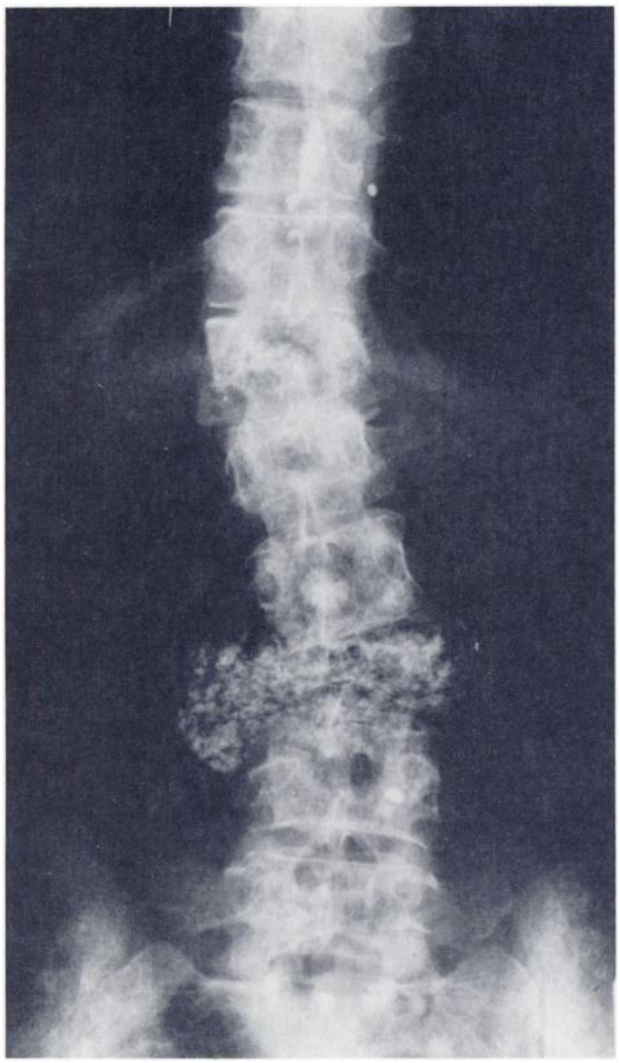

FIGURE 1
Plain x-ray film shows large calcified mass located between L_3 and L_4 and multiple sclerotic lesions throughout thoracic and lumbr spine and pelvis. Contrast media lies in spinal canal

spine expanding laterally to both sides, the upper lumbar spine, the middle thoracic spine, and the liver (Fig. 3). Biopsy specimen obtained from the cervical lymph node revealed the histology of medullary thyroid cancer. The large retrosternal mass confirmed by the oblique view was thought to be the recurrent medullary thyroid cancer and the calcified lesions in the lumbar and thoracic spine and the liver strongly suggested that the lesions might be the metastases from the medullary thyroid cancer. Whole-body scanning using iodine-123 showed a sole accumulation in the remaining right lobe of the thyroid gland but no uptake by the vertebra nor the liver.

Scintigraphy with [^{131}I]MIBG was performed at 24, 48, and 72 hr after the administration of 0.5 mCi of this tracer, thyroid uptake of ^{131}I being prevented by Lugol's solution. The images were obtained using a large-field-of-view gamma camera with high-energy collimator interfaced with a microcomputer. Scintigrams taken at 72 hr after administration of the tracer showed areas of increased radioactivity in an area from the suprasternal region to the antero-superior mediastinum, in the three distinct areas of lower and upper lumbar spine and thoracic spine, and diffusely in the liver (Fig. 3).

DISCUSSION

Medullary thyroid cancer (MTC) is not common, comprising only a small percentage of all thyroid malignancy. Ten percent of the cases are familial, usually appearing as a component of multiple endocrine neoplasia (MEN) Type IIa or MEN Type IIb. MTC tends to metastasize locally and at a distance more frequently than differentiated thyroid adenocarcinoma. Recurrence occurs in half of patients after surgery. External radiotherapy is not helpful in disseminated MTC. Chemotherapy may only promise partial remission. In recent years, there have been several reports of treatment of MTC with ^{131}I. However, the response to radioiodine treatment is transient (*6*). The possible accumulation of a specific radiopharmaceutical in the metastatic lesion of MTC offers a clinical importance from a view of

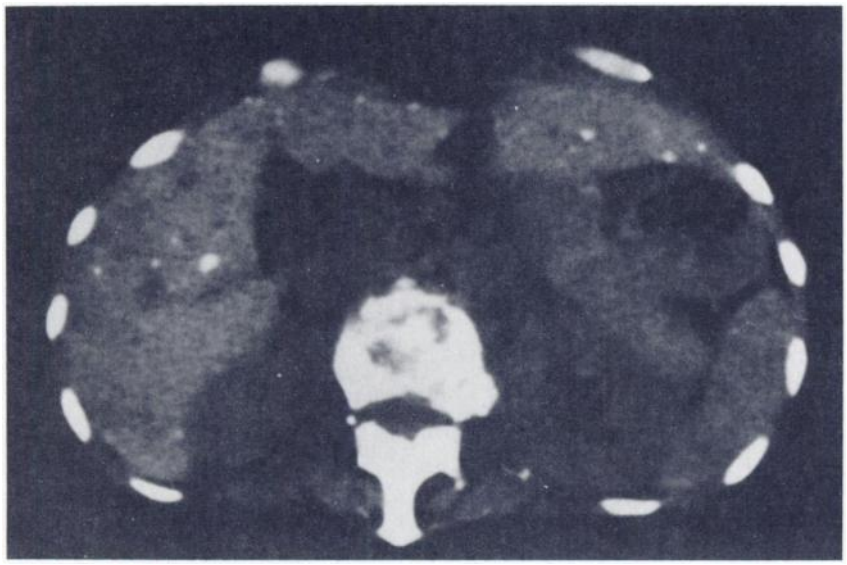

FIGURE 2
Numerous stippled calcific deposits are scattered throughout both lobes of liver. Vertebral body is also affected

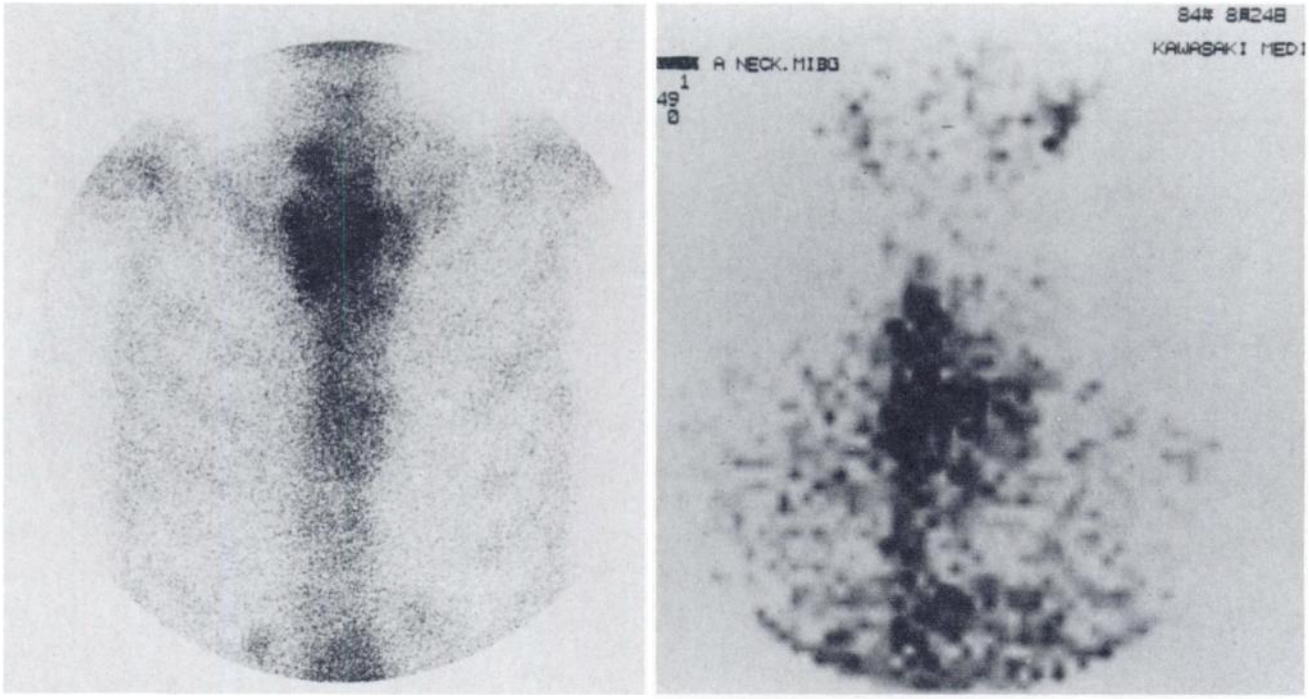

FIGURE 3A
Scintigrams using [^{99m}Tc]MDP (left) and [^{131}I]MIBG (right). On anterior thoracic view, area of increased activity of both tracers extending from suprasternal region down to mediastinum is noted

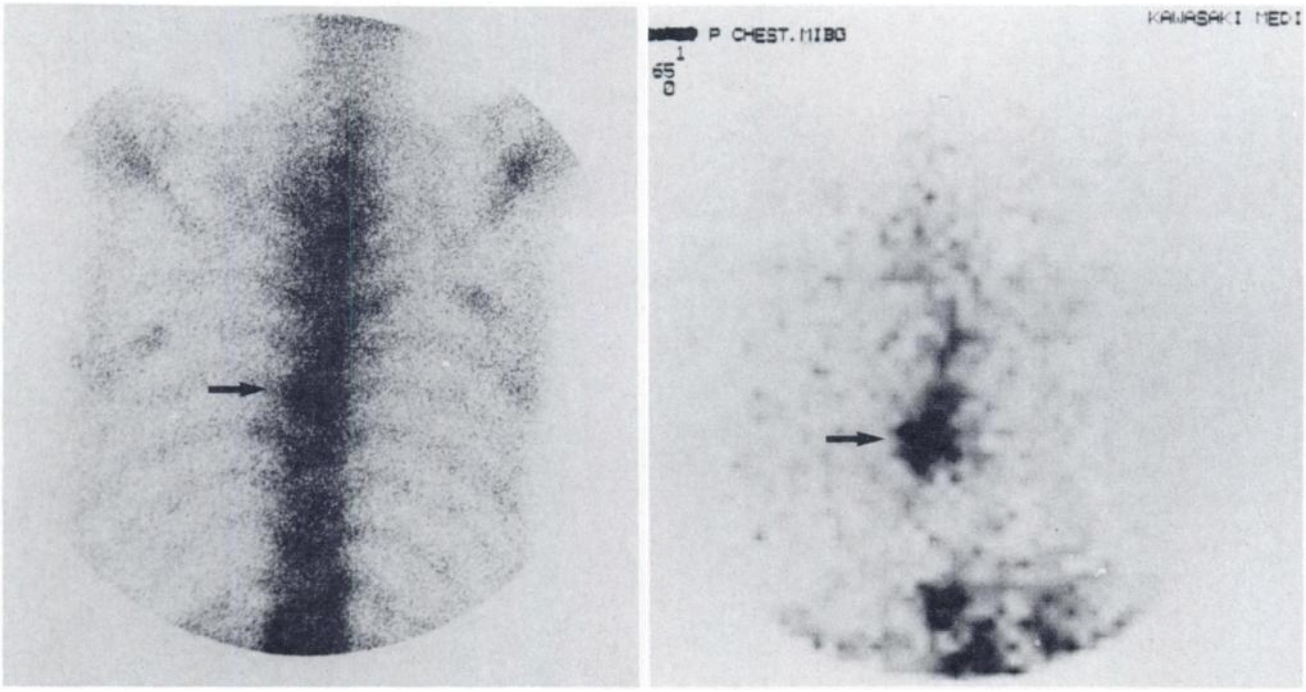

FIGURE 3B
Scintigrams using [^{99m}Tc]MDP (left) and [^{131}I]MIBG (right). On posterior thoracic view, area of increased activity of both tracers is noted in thoracic spine (arrows)

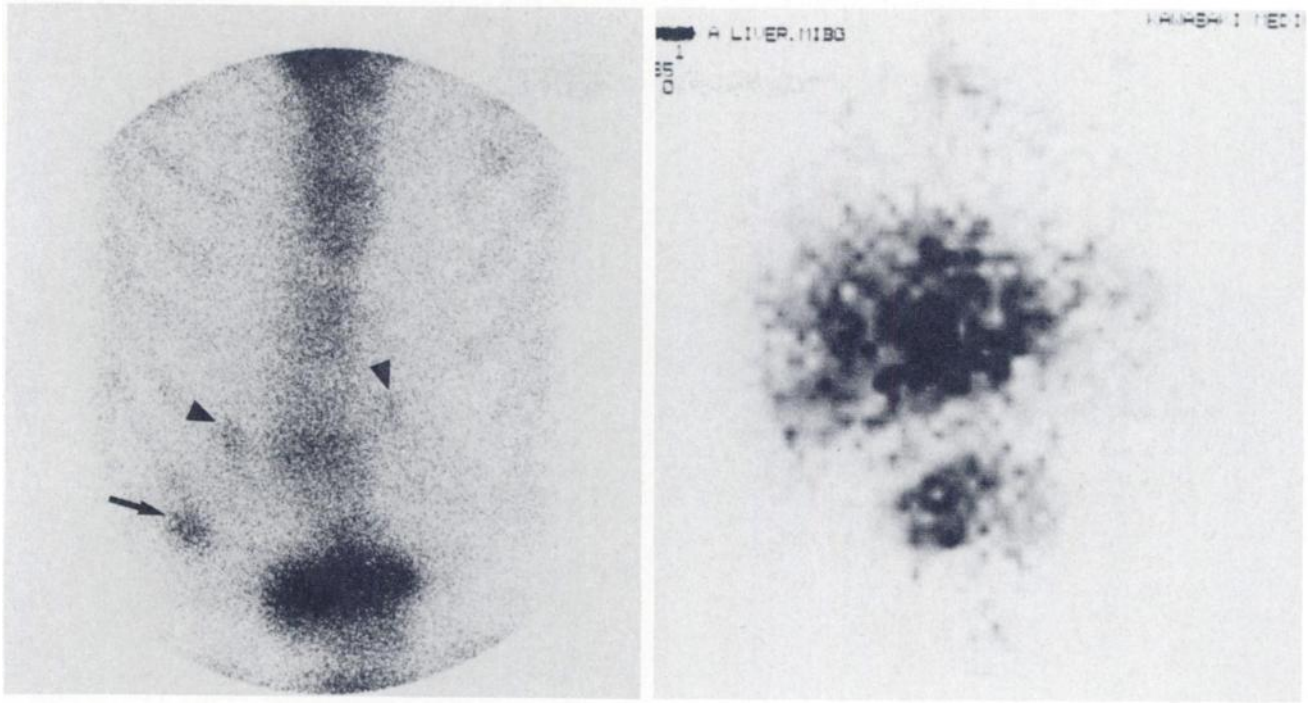

FIGURE 3C
Scintigrams using [^{99m}Tc]MDP (left) and [^{131}I]MIBG (right). On anterior abdominal view, [^{99m}Tc]MDP accumulates clearly in area of right hypochondrium (arrow) and slightly in two areas of epigastrium (arrowheads), whereas [^{131}I]MIBG accumulates diffusely in liver

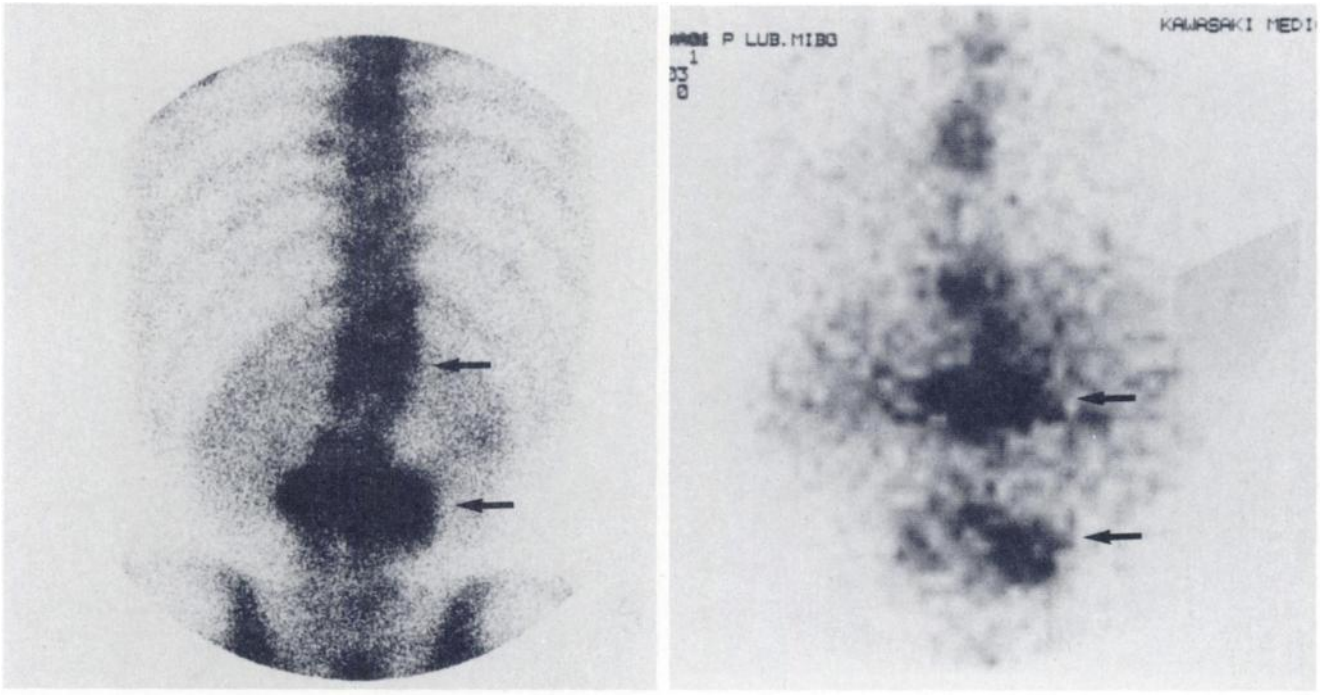

FIGURE 3D
Scintigrams using [^{99m}Tc]MDP (left) and [^{131}I]MIBG (right). On posterior lumbar view, two areas of increased uptake of both tracers is noted in lumbar spine (arrows)

surveying metastases and also therapeutic application.

In our case, recurrence of MTC was suspected by the symptom of diarrhea and high serum calcitonin levels. It was proved by the biopsy of the cervical lymph node and the large retrosternal mass was thought to be the local recurrence of MTC. Based on the patient history and the pattern of calcification on x-ray films and CT, the calcified lesions in the lumbar and thoracic spine and in the liver were appropriately thought to be the metastases of MTC. Iodine-131 MIBG accumulated not only in the lesions that was shown by bone scintigraphy but also in the extraosseous lesions; in the liver, [^{99m}Tc]MDP accumulated only in the large calcified lesions, whereas the uptake of [^{131}I]MIBG by the liver was increased diffusely comparing with the normal cases; in the mediastinum, the area of increased uptake of [^{131}I]MIBG extended more lower than the area shown by bone scintigraphy.

Iodine-131 MIBG has been found useful for the localization and the treatment of pheochromacytoma (*7*)(*8*) and neuroblastoma (*9*). Although the local recurrent lesion of MTC has been reported to accumulate [^{131}I]MIBG (*5*), to our knowledge there have been no papers dealing with the uptake by distant metastatic lesions. This report described the accumulation of [^{131}I]MIBG in the bone and liver metastasis of MTC. Iodine-131 MIBG scintigraphy may prove to be useful for surveying metastasis, for the postoperative follow-up of recurrence, and also for the treatment of MTC.

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