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Retroperitoneal Malignant Fibrous Histiocytoma Mimicking Pheochromocytoma

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We report the case of a 52-yr-old man with a mass in the area of the left adrenal. The clinical features, MIBG uptake, and elevated urinary dopamine levels suggested the diagnosis of pheochromocytoma. He presented with unstable hypertension, tachycardia, weight loss, and the "inflammatory syndrome" (fever, leukocytosis, and high sedimentation rate). Clinical findings, preoperative radiographic (sonography, CT scan, [^{131}I]MIBG scintigraphy), and endocrine evaluations (elevated 24-h urinary dopamine) were suggestive of a dopamine-secreting adrenal tumor. The mass was resected and on histologic examination showed the characteristic features of a malignant fibrous histiocytoma (MFH). The tumor cells were immunopositive for neuron-specific enolase (NSE), vimentin, CD-68, S-100, desmin, and immunonegative for chromogranin A, synaptophysin, neurofilament protein, and low-molecular-weight keratin, indicating that this tumor was not able to synthesize catecholamines. The prolonged retention of the tracer (MIBG) was interpreted as a consequence of obstructive hydronephrosis, while elevated urinary dopamine levels were assumed to be due to compression of the renal vessels by the large retroperitoneal mass.

Key Words: Malignant fibrous histiocytoma; [^{131}I]MIBG scintigraphy; dopamine pathology; retroperitoneal neoplasm.

Introduction

Radiolabeled ^{131}I-metaoiodobenzylguanidine ([^{131}I]MIBG) scintigraphy is known for its high specificity (98.9%) in detecting pheochromocytoma and other tumors of neural crest origin *(1)*. A misleading positive MIBG scan is very rare. There are data on adrenal adenomas and carcinomas with misleading positive MIBG scans *(2)*. Focal [^{131}I]MIBG uptake adjacent to the adrenal has been reported in patients with obstructive hydronephrosis, dilated renal pelvis, renal failure, and unilateral renal artery stenosis *(3,4)*.

Malignant fibrous histiocytomas (MFH) are rare tumors, frequently associated with leukemoid reaction, attributed to tumor production of unidentified hematopoietic factors *(5,6)*.

We present the case of a 52-yr-old man with a large retroperitoneal mass assumed to be a malignant dopamine-secreting adrenal tumor based on positive MIBG and elevated urinary dopamine levels. The mass was surgically resected and histology revealed malignant fibrous histiocytoma.

Case Report

A 52-yr-old man was admitted into our Institution with a large retroperitoneal mass thought to be an adrenal tumor. Initially he presented with abdominal pain, hypertension (up to 190/120 mmHg) with postural hypotension (100/70 mmHg), palpitations with tachycardia (up to 160/min), profuse sweating, pallor, nervousness and anxiety, intermittent fever (38–39°C), and severe weight loss (20 kg in 6 months).

Laboratory findings where compatible with "inflammatory syndrome": WBC 72.500 × 10^9 with granulocytosis (78% of neutrophils), high sedimentation rate, and elevated leukocytic alkaline phosphatase (APL; Table 1). Serum cortisol, T4, TSH, calcitonin, PRA, aldosterone, urinary noradrenaline, and adrenaline levels were within normal range (Table 1). Urinary dopamine concentrations were elevated two- to threefold (518–1005 µg/24 h, normal up to 300 µg/24 h). Serum NSE was elevated twofold. Ultrasonography and computed tomography (CT) scan of the abdomen demonstrated a 10 × 7.5 cm mass in the region of left adrenal (Fig. 1). After 1 mo, scintigraphy with 768 µCi [^{131}I]MIBG showed uptake in the region of left adrenal (Fig. 2). After pretreatment with phenoxybenzamine (4 × 10 mg) and metoprolol (50 mg/d) for 2 wk the patient underwent surgery. Intraoperative findings confirmed hydronephrosis of the left kidney and compressed renal vessels due to compression by the large retroperitoneal mass. Postoperative evaluation was not possible due to rapid clinical deterioration. Autopsy was not performed.

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Table 1
Preoperative Laboratory
and Hormonal Analysis, Compared with Normal Range

Parameter	Patient values	Normal range
Sedimentation rate (h^{-1})	105	<20
Fibrinogen (g/L)	15	2–4
Hemoglobin (g/L)	86	115–170
Erythrocyte ($\times 10^{12}$/L)	3.36	3.30–5.80
Haematocrite (%)	27	35–53
Leukocyte ($\times 10^{9}$/L)	72.5	4.0–10.0
Trombocyte ($\times 10^{9}$/L)	735	130–400
Leukocyte alkaline phosphatase	232	<90
AST (U/L)	13	<27
ALT (U/L)	40	<30
Alkaline phosphatase (U/L)	393	30–90
Creatinine (μmol/L)	88	53–124
T4 (nmol/L)	85.3	55–160
TSH (mU/L)	0.51	0.15–5.0
Cortisol (9 h)	814	154–638
Noradrenaline (μg/24 h urine)	19.7...20.8...17.9	10–25
Adrenaline (μg/24 h urine)	3.4...4.1...2.5	1–6
Dopamine (μg/24 h urine)	628.9...1005.3...518.1	100–300
Neuron specific enolase (ng/mL)	31.12	0.0–15.2
Calcitonin (ng/L)	<5	0.0–13.0
Plasma renin activity (ng/mL/h)	0.78	0.2–2.8
Aldosterone (ng/L)	136.1	42.0–201.5

Pathologic Findings

The removed tissue was fixed in buffered formalin and embedded in paraffin. By light microscopy a cellular mesenchymal tumor was identified (Figs. 3A,B). The tumor cells were elongated and exibited a diffuse pattern. Several scattered multinucleated giant cells were also apparent. In some areas focal inflammatory infiltration was seen. Cellular and nuclear pleomorphism was marked and mitotic figures could be encountered. For immunohistochemistry the streptavidin-biotin-peptidase complex method was applied. The tumor cells were strongly immunopositive for NSE and vimentin (Fig. 4). Many scattered tumor cells were immunoreactive for CD-68, a macrophage (histiocyte) marker. Few scattered tumor cells were immunopositive for desmin and S-100 protein. The tumor cells were immunonegative for chromogranin A, synaptophysin, neurofilament protein, low-molecular-weight keratin, and smooth-muscle actin. The MIB-1 index was very low. The tumor demonstrated cellular and nuclear pleomorphism, with large areas of necrosis. No vascular invasion was found. Based on histologic and immunohistochemical findings, the diagnosis of malignant fibrous histiocytoma was made.

Discussion

Clinical features, in particular the unstable hypertension, postural hypotension, paroxysmal tachycardia, and the "inflammatory syndrome," high urinary dopamine levels, and the tumor mass in the left adrenal suggested the diagnosis of dopamine-secreting adrenal tumor. It is noteworthy that scintigraphy with [^{131}I]MIBG was positive.

[^{131}I]MIBG adrenal scintiscan is a reliable, safe, highly specific, and noninvasive morphofunctional method to investigate neural crest tumors, mainly pheochromocytomas and neuroblastomas *(1,7)*. MIBG, an analog of guanethidine, has a molecular structure similar to that of noradrenaline, and is concentrated and stored in chromaffin granules and is largely (90%) excreted unchanged in the urine over several days after intravenous administration. Misleading positive findings of MIBG results are considered to be rare.

The misleading positive MIBG results could be divided into three categories. The first category consists of those due to tracer uptake in various neuroendocrine lesions other than pheochromocytomas, namely, tumors of the APUD series *(8)*. The second category consists of those with tracer uptake in various primary adrenal tumors other than pheochromocytoma, such as adrenocortical adenoma and adrenal metastases of choriocarcinoma *(1,2,9)*. The third category consists of extraadrenal tracer uptake due to abnormalities in the route of excretion. Radiopharmaceutical accumulation may be demonstrated in obstructive hydronephrosis due to compression by a large retroperitoneal mass *(1)*. Misleading focal [^{131}I]MIBG accumulation in the renal area has been reported in the presence of dilated renal pelvis, acute focal pyelonephritis, and unilateral renal artery stenosis, possibly due to increased sympathetic innervation or activity resulting from severe renal artery stenosis *(3,4)*.

Malignant fibrous histiocytoma is a soft tissue sarcoma of adults, primarily localized in the extremities. It is rare in the retroperitoneum. The clinical, radiographic, and CT signs are nonspecific. The tumors show immunophenotypic heterogeneity and ultrastructural variations, with several subtypes (fascicular, storiform, inflammatory, and pleomorphic). They can be diagnosed only by histology and various tumor markers aid the differential diagnosis. In a study of four malignant fibrous histiocytomas, 100% exhibited immunoreactivity for vimentin, desmin, CD68, 75% were positive for synaptophysin, and 50% for NSE *(10)*. Froehner et al. *(11)* reported a patient with malignant fibrous histiocytoma producing NSE and human beta-chorionic gonadotropin, masquerading a germ cell tumor *(11)*. Our patient had high circulating NSE levels and the tumor was immunopositive for NSE, suggesting that the tumor was the source of the elevated NSE. Furthermore, tumor cells were negative for chromogranin A, indicating that they were not able

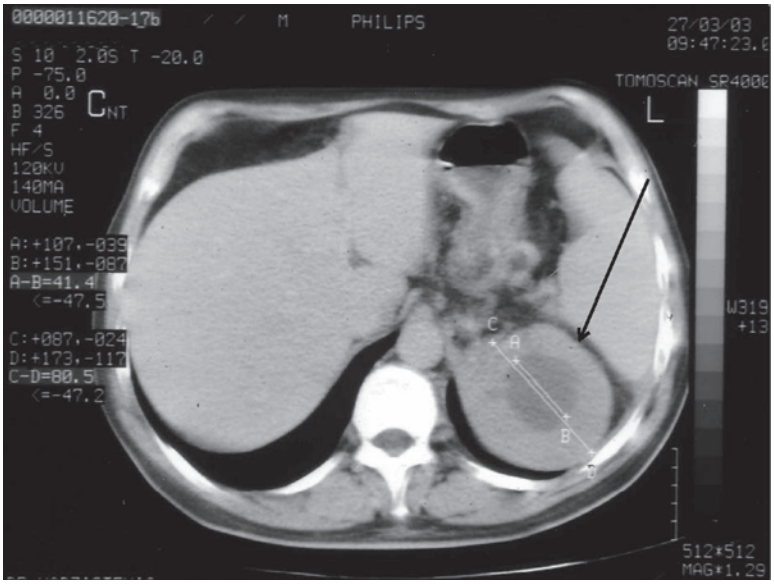

Fig. 1. Computed tomography (CT) of the abdomen showing the tumor mass (10 × 7.5 cm) in the region of left adrenal (indicated with an arrow).

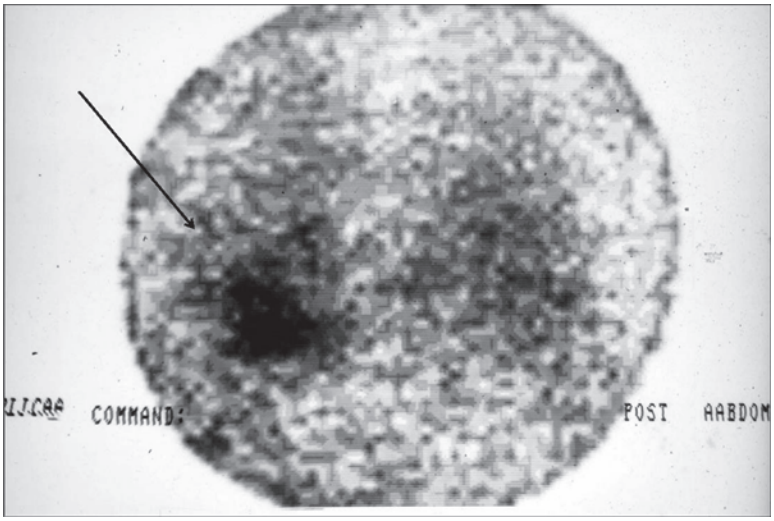

Fig. 2. [^{131}I]MIBG scintigraphy (72 h after applying 768 μCi [^{131}I]MIBG), posterior view, showing uptake in the region of left adrenal (indicated with an arrow).

to synthesize catecholamines. One possible explanation for elevated urinary dopamine level is that it may be the consequence of the increased dopamine release from the kidney due to compressed renal vessels from the large retroperitoneal mass *(12)*.

Laboratory tests revealed a leukemoid reaction. This finding is uncommon in malignant mesenchymal tumors with the exception of malignant lymphomas. There are reports of sarcomas (liposarcoma, fibrosarcoma, rabdomyosarcoma, leiomyosarcoma) associated with leukemoid reaction *(13)*. Roques et al. reported the first case of MFH associated with inflammatory reaction *(5)*. Several cytokines (G-CSF, IL-6, IL-7, IL-8, IFN) have been detected in the cells of IMFH with leukemoid reaction. In addition, elevated levels of cytokines were demonstrated in the sera of these patients *(6)*.

In conclusion, a positive [^{131}I]MIBG scan might not be as specific as thought for differentiating pheochromocytoma from other masses in the retroperitoneum. In cases of unexplained MIBG accumulation, the possibility of prolonged retention of the tracer due to abnormalities in its excretion should be considered.

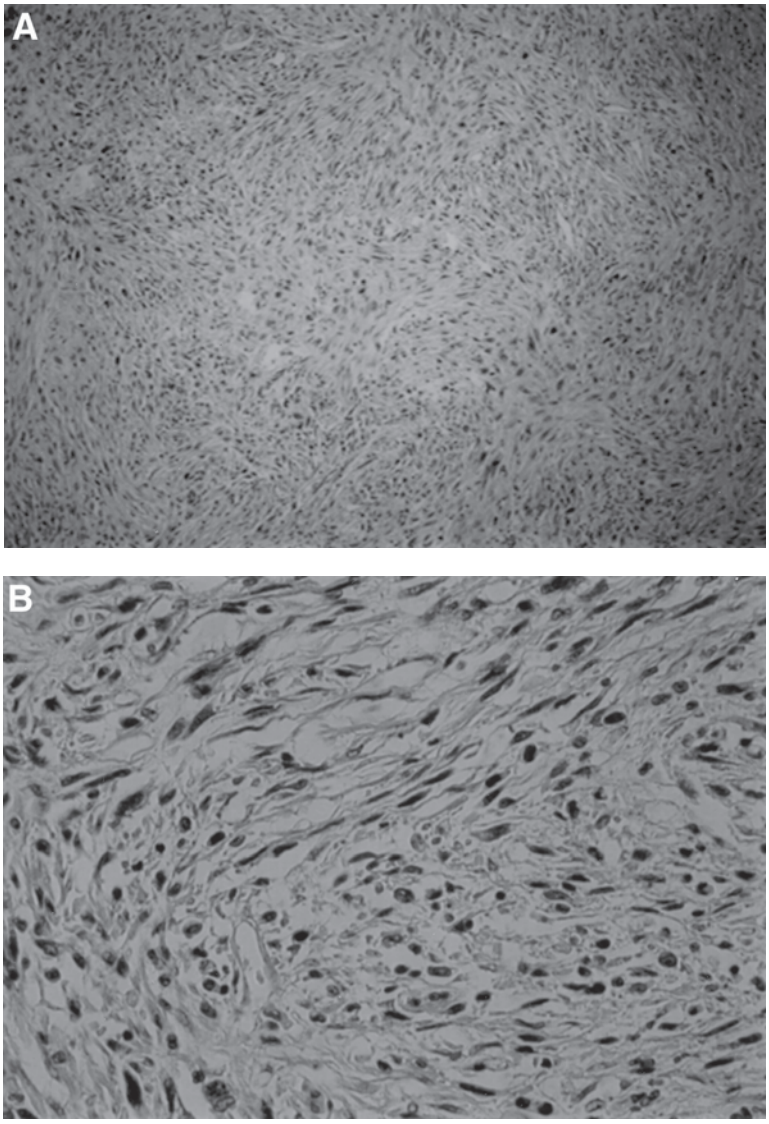

Fig. 3. Hematoxilin-eosin staining of the tumor showing the characteristic features of a malignant fibrous histiocytoma (**A**, magnification 100×; **B**, magnification 400×).

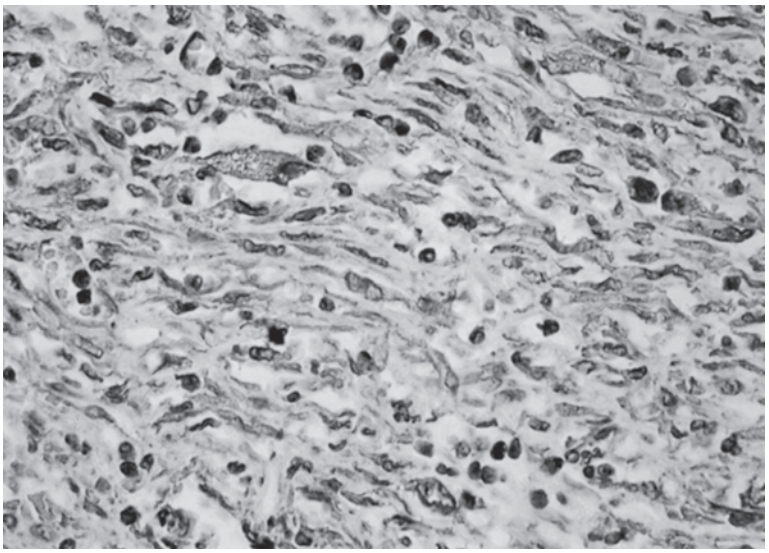

Fig. 4. Immunohistochemistry of the tumor (anti-vimentin antibodies). The tumor cells are strongly immunopositive for vimentin (magnification 400×).

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