MALIGNANT PHEOCHROMOCYTOMA
Report of four cases

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Objective :

Report clinical, diagnostic procedures and evolution characteristics of four (04) malignant pheochromocytoma cases encountered in our service so far.

OBSERVATION 1:

A female patient, 23 years old, with a family history of neurofibromatosis in her father and two brothers was sent for exploration of a right adrenal mass discovered at abdominal ultrasound performed during abdominal pain. Clinically, she presented typical cutaneous signs of type 1 neurofibromatosis (café au lait spots, freckling, neurofibromas). However, there was no hypertension nor adrenergic signs.

Abdominal computed tomography showed a huge heterogeneous right adrenal mass, measuring 50 mm, moderately enhanced after injection (fig 1).

Further exploration with I^{131}-MIBG scintigraphy showed an uptake of the right adrenal mass without other locations. Urinary metanephrines were normal.

The patient was operated on by laparoscopy. There was a rounded fibrous mass of 7 cm diameter, bleeding at the slightest contact.

Histopathological study concluded to a pheochromocytoma with an aggressive potential. PASS score **(Pheochromocytoma Adrenal Gland of the Scaled Score)** was greater than 4.

Evolution was devastating with occurence after three months of multiple secondary locations (liver, muscle, peritoneal, parietal, lung and bone marrow) shown at CT scan (Fig. 2,3), I^{131}-MIBG scintigraphy (Fig. 4) and bone scintigraphy (Fig. 5)

OBSERVATION 2:

A female patient aged 27, in whom the diagnosis of sporadic multiple endocrine neoplasia type 2(NEM2), combining a bilateral pheochromocytoma and medullary thyroid carcinoma was made at the age of six years. She underwent bilateral adrenalectomy and total thyroidectomy. Histopathological study concluded to bilateral pheochromocytoma and hyperplasia of C cells. She was in remission since

Twenty years later, adrenergic signs recurred. Biologically, metanephrines increased again. Abdominal computed tomography showed four abdominal lymph nodes, they were heterogeneous with areas of necrosis and highly vascularized on contrast enhanced CT. These lymph nodes were visualized at MIBG scintigraphy. The diagnosis of malignant pheochromocytoma was made.

OBSERVATION N°3:

A male patient, 26 years old, admitted for severe hypertension lasting for 03 years associated with adrenergic sings and orthostatic hypotension. Biologically, there was a rise of Metanephrines. On computed tomography there was a right side adrenal mass of 7cm.

The patient was operated. Histopathological study concluded to a 8 cm pheochromocytoma with vascular invasion but not capsular involvement.

Postoperative evaluation (CT scan) showed a residual tumor of 22x31 mm uptaking at MIBG scintigraphy.

Surgical resection of the process could not be performed due to locoregional invasion found during surgical procedure

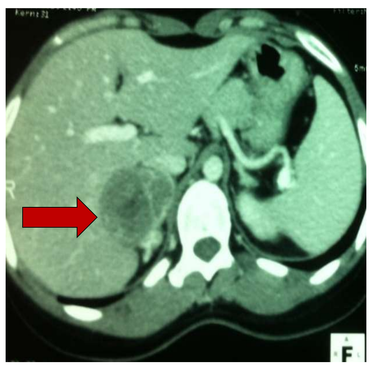
OBSERVATION N°4:

33 year old male patient, in whom a left large adrenal mass of 125 mm with central necrosis associated with a metastatic liver mass of 90 mm was discovered at abdominal ultrasound performed on the occasion of pain in the right hypochondrium

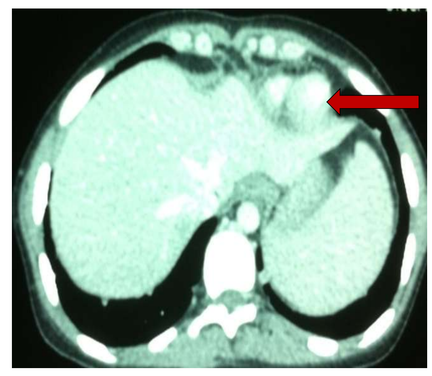
Clinically there was deterioration of general condition, adrenergic signs and resistant hypertension. Urinary metanephrines were very high. MIBG scintigraphy showed an heterogeneous hepatic uptake but not adrenal uptake (extensive necrosis). Diagnosis of malignant pheochromocytoma was made.

	Age at diagnosis	Gender	Circumstances of discovery	Size of the mass	Time between diagnosis and metastasis	Type of metastases	form
CASE 1	23years	F	Abdominal pain	50 mm	11 months	Lung, Bone, Liver, Parietal Peritoneal Muscles Lymph node Medullary	NF1
CASE 2	06 years	F	Hypertension Adrenergic signs	27 mm left 30 mm Right	20 years	lymph node	NEM2
CASE 3	23 years	M	Hypertension Adrenergic signs	70 mm	1 year	Renal infiltration, lymph node	sporadic
CASE 4	33 years	M	Abdominal and back pain, hypertension	125mm	At diagnosis	hepatic	sporadic

TABLE 1: Characteristics of our patients with Malignant Pheochromocytoma



(fig1)



(fig2)

Figure 1. Abdominal CT showing huge right adrenal mass
Figure 2 . computed tomography :hepatic metastasis

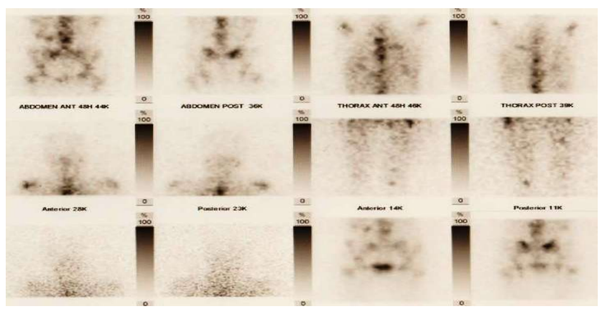


Figure 4. Metastasis uptake at -MIBG scintigraphy

Discussion:

The four cases of malignant pheochromocytoma represent 10% of all pheochromocytomas encountered in our department (41cases) which corresponds to literature data (Ajallé.al) (1)

Hypertension is the most frequently presenting symptom (90%) (Baguet and al. 2004) (2). It was found in three of our 04 cases.

Atypical signs: abdominal and back pain occurred more frequently in malignant pheochromocytomas. It was the presenting sign in two patients.

Tumors were large (higher than 5 cm) in three patients, this criterion is in favor of a greater risk of malignancy (Lenders JW and al) (3). Malignant pheochromocytoma can be sporadic or part of a familial syndrome: multiple endocrine neoplasia type 2 (MEN 2), type 1 neurofibromatosis (NF1), von Hippel-Lindau-(VHL) disease and mutations of nuclear succinate dehydrogenase gene (SDH)

Syndromic pheocromocytoma was found in two of our patients. The first presents an NF1. Pheochromocytoma is rare in this condition: 1% among which12% are malignant. The second patient presented a NEM 2A. Malignant form in this condition is rare (less than 5%). (Fishbein and Nathanson, and Jafri and Maher, 2012)

For the fourth case reported in 1993 we could not exclude SDH mutations as these mutations were discovered in 2000 (4).

Time for occurrence of metastases is very variable, as they were already present at diagnosis in one of our cases (No. 4), and occurred after 20 years in another case (No. 2)

Surgery is not always curative and anti-cancer therapies (chemotherapy, I131 MIBG metabolic radiotherapy ...), are not very effective. They can improve comfort and ensure a partial remission (Scholz . al)(5).

Conventional chemotherapy can also be used. It is based on the combination of cyclophosphamide, vincristine and dacarbazine (CVD) (Keiser et al and Hui Huang et al.) The first patient received I^{131}-MIBG metabolic radiotherapy and conventional radiotherapy with partial improvement.

Recent years have seen the advent of new treatments such as of tyrosine kinase inhibitors (Sun-Kyung Park), somatostatin analogs and alkylating agents (temozolomid). These drugs should be subjected to larger studies to prove their efficacy and safety.

CONCLUSION

Pheochromocytoma has an unpredictable course. There is not a benign pheochromocytoma, but pheochromocytoma with "non-aggressive potential," hence the need for lifelong monitoring of any pheochromocytoma.

Genetic counselling is necessary, given the relative frequency of familial forms

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