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Case Report

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ADRENAL OLIGOMETASTATIC MALIGNANT PHEOCHROMOCYTOMA

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ABSTRACT

Pheochromocytoma is a neuroendocrine tumor derived from the chromaffin cells of the adrenal medulla. Malignancy is defined by the presence of metastases in non-chromaffin tissue or by the appearance of recurrences. About 40% of cases are genetic. It is therefore important to look for symptoms that suggest a genetic predisposition syndrome, particularly the multiple endocrine neoplasia (MEN). The severity of this cancer is due to its rarity, a common cause of delayed diagnosis. Through the observation of our patient followed for malignant pheochromocytoma for 3 years and became oligometastatic, we would like to present the characteristics of this rare disease and to underline the interest of an optimal as well specific management of the tumor, the oligometastases, and associated complications, passing through experienced multidisciplinary teams.

KEYWORDS: Malignant pheochromocytoma, oligometastases, metabolic radiotherapy with MIBG.

INTRODUCTION

Pheochromocytoma is a tumor developed at the expense of chromaffin cells of the adrenal medulla producing excess catecholamines. The malignancy of these tumors comes fromtheir metastatic or recurrent character that occurs in less than 10% of cases. The research of a genetic context is systematic. The management of this disease has a double objective: to improve the survival and the quality of life of the patients,by controling the tumor and the secretions of catecholamines.

CASE

A 37-year-old patient, diabetic and hypertensive for 2 years on treatment, had paroxysmal attacks of left lower back pain for 3 years, associated with headaches, tachycardia and sweating. Having motivated the consultation revealing a hypertension + type 2 diabetes, with a metanephrine dosage elevated to 11 times normal, evoking a pheochromocytoma. A CT scan showed a tissue mass in the left adrenal compartment of 34 × 19.5 × 112mmwithout secondary lesion at a distance. Operated twice with a recurrence interval of 1 year. Currently, the patient presents another loco-regional recurrence as a 12 cm mass in its longest axis, associated with latero-aortic and retro-peritoneal lymphadenopathy, with the appearance of bone metastases at the sacroiliac, costal and level of the cervical spine. The patient was still followed for hypertension and diabetes.Finally a metabolic radiotherapy with MIBG (metaiodobenzylguanidine) was indicated for our patient.

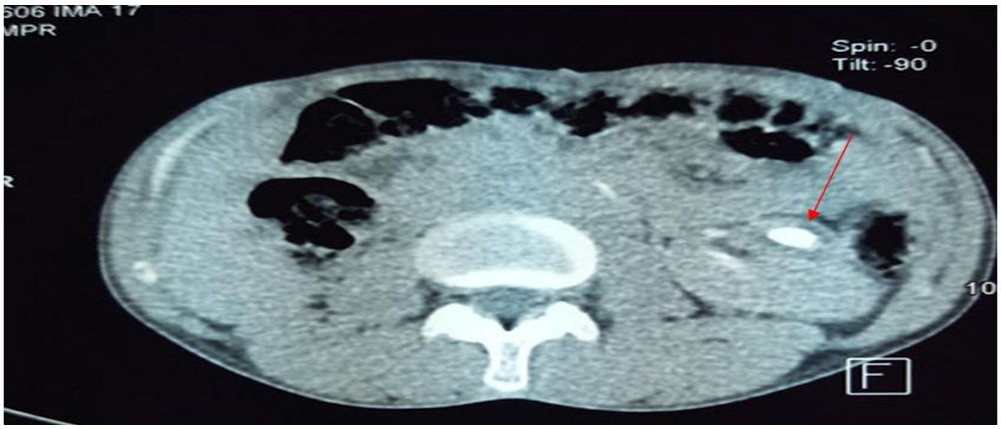

Figure: CT scan showing a locally infiltrating left adrenal gland mass.

DISCUSSION

Malignant pheochromocytoma is a tumor of the adrenal medulla which secretes excess catecholamines with the presence of metastasis in a non-chromaffin or recurrent tissue. Its annual incidence is from 2 to 8 per million adults. A peak in frequency is observed between 30 and 40 years of age. As for the prevalence of metastatic stages; it varies from 5 to 26%.[1]

The occurrence ofpheochromocytoma can be sporadic but can also be part of genetic diseases in 40%: MEN type 2 (10%), von Hippel-Lindau disease, mutation of the Succinate Dehydrogenase B subunit (SDHB), neurofibromatosis type 1, Sturge-Weber syndrome or tuberous sclerosis.[1-2] An oncogenetic consultation is therefore recommended in case of suspected genetic background or in case of bilateral malignant pheochromocytoma, and in young patients (under 45 years). The identification of the constitutional mutation on the SDHB gene is considered to be a risk factor for malignancy and is said to be associated with a poor prognosis.[3]

Before the biological confirmation by the elevation of the methoxylated derivatives of catecholamines in the serum or in the urine, thepheochromocytomais conventionally revealed by a resistant arterial hypertension, a high blood pressure lability or an evocative symptomatology (headache, palpitations, sweating...), a mass syndrome (cervical mass, hearing loss or deafness, tinnitus, paralysis of a cranial nerves for ENT forms), a cardiovascular complication (heart failure), or during the assessment of diabetes, an incidentaloma or a deterioration of the general condition. The diagnosis can also be revealed by a metastatic symptomatology which can occur in 5 years, even in more than 20 years.[5] and are most often pulmonary, hepatic and osseous. Brain metastases are exceptional.[4] Recurrences and the occurrence of bone metastases in our patient has proven the malignant nature of this tumor. Hence the importance of long-term monitoring of any patient operated for pheochromocytoma.

Imaging tests to locate tumors are usually done if there are abnormal screening results. These examinations must include a thoraco-abdomino-pelvic CT. MRI does not provide additional diagnostic elements compared to the CT scan, its sensitivity and specificity arelower: 78 and 87% respectively in tissue characterization.[6] The aim of these examinations is to detect metastases from a distance (liver, lungs, bones, peritoneum) as well as to detect any associated syndromic lesions (such as for example kidney cancer and / or pancreatic tumors in the context of the disease of von Hippel Lindau). Positron emission tomography (PET) is also useful in the extension assessment and makes it possible to calculate the ratio of the SUV max (maximum standard uptake value) of the tumor to that of the liver (SUV max tumor / SUV max liver).A report ≥1.45 is highly predictive of malignancy. It is currently recommended in the preoperative malignant pheochromocytoma extension assessment.[7] Another exam from the 1980s used in pheochromocytoma assessment is Meta-iodo-benzylguanidine scintigraphy marked with iodine 123 (123I-MIBG). Normal adrenal tissue rarely fixes MIBG, but 85% of pheochromocytomas fix this isotope. However, this examination has been supplanted by the PET.[6] The treatment is most often multidisciplinary. It is based on carcinological excision surgery which includes an adrenalectomy on the healthy margin (lymph node dissection is not systematic) and metastasectomy. It can be combined with chemoembolization, cryoablation or radiofrequency techniques for optimal excision of metastases.

Pharmacological control of hormonal symptoms: Treatment with an alpha-blocking vasodilator is recommended as first-line treatment in hypertension, with the treatment of constipation, the treatment of induced diabetes and hygienic-dietetic measures.

Chemotherapy is offered for symptomatic, clearly progressive patients. The most widely used chemotherapy protocol is a Cyclophosphamide-Vincristine-Dacarbazine (CVD) combination. The biological response rate varies from 0 to 78% and the tumor response from 0 to 50%. But the response, when present, would be short-lived (<2 years). No prospective study has confirmed these results.[9] Recent data has shown promising results with the chemotherapy agent temozolomide and the targeted therapy sunitinib with less toxicity and where the genetic background could predict the response (SDHB mutation).[10-11]

Stereotaxic external radiotherapy can be discussed as an adjuvant to R2 surgery or in a palliative analgesic / decompressive situation. The parameters that will be taken into account are the residual tumor volume, the regional risk, the expected morbidity, the secretory and genetic status.[12]

Metabolic radiotherapy with 131I-MIBG: an interesting therapeutic option in the management of oligometastatic disease, in particular offered to our patient. It gives an improvement in clinical signs in 75% of the cases, a decrease in hormonal activity in 50% and a significant tumor reduction varying from 24 to 45%.[2]

CONCLUSION

The oligometastatic pheochromocytoma is a rare entity requiring highly specific and multidisciplinary management. The diagnosis is clinically oriented and the most sensitive imaging is PET-FDG. Progress is being made and more is expected in the treatment of these cases: surgery, chemoembolization, radiofrequency of metastases, new chemotherapy molecules and targeted therapy, stereotaxic and metabolic radiotherapy with MIBG.

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