

Malignant pheochromocytoma - a challenging diagnosis

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Introduction:

Pheochromocytoma is a rare tumor arising from chromaffin cells located originally in the adrenal medulla. Malignant pheochromocytoma is an even more rare tumor, being accepted that about 10% of pheochromocytoma is malignant, and it is a difficult disease because it is diagnosed only in the presence of metastases, with no definitive histological or cytological criteria of malignancy. It typically metastasizes to local lymph nodes, bone (50%), liver (50%) and lung (30%) (1); the metastasis being defined as the presence of chromaffin tissue in nonchromaffin organs.

Case report:

History: A 38 years old woman, without pathological personal history, presented for hypertension (maximum of the systolic blood pressure=160 mmHg), palpitation and dyspnea. From her family antecedents it should be remembered: mammary cancer at a second degree relative and hypertension at a first degree relative.

Clinical examination: palpable adenopathies at the submandibular level, bilateral laterocervical and in the left axilla, with maximum diameter of 1 cm, mobile on all plans; blood pressure equal at both arms=110/60 mmHg without orthostasis, heart rate 70/min, with no other pathological modifications.

Laboratory test:

- Biological tests were normal;
- Hormonal profile - the only modifications were metanephrine raised 5.4 fold (486.8 pg/ml) and normetanephrine raised 1.35 fold (244.6 pg/ml), the other hormonal measurements being in normal limits: TSH=1,36 µUI/ml, iPTH=58,52 pg/ml, ACTH=10,1 pg/ml, cortisol=18,3 µg/ml (8 a.m.), with normal nycthemeral rhythm, prolactin=19,46 ng/ml, FSH 8,93 mUI/ml, LH=6,8 mUI/ml, estradiol=52,54 pg/ml (the 3th day of menstrual cycle), testosterone=23,6 ng/ml.

CT: tumor formation with central necrosis in the left adrenal gland



CT with contrast: iodophil formation with central necrosis in the left adrenal gland



CT: axillary adenopathies



CT: left mammary nodes



Imaging exams:

- Ultrasonography - normal thyroid gland, laterocervical and submandibular adenopathies and a node in left breast;
- Thoraco-abdomino-pelvic contrast CT: an iodophil formation of 29/26 mm, with central necrosis in the left adrenal, two pulmonary micronodules, bilateral multiple axillary adenopathies predominantly at the right axilla with maximum diameter 24 mm, left mammary nodes 24/16 mm, two hypodense and iodophil formations in the liver space of 24 mm and 38 mm; multiple abdomino-pelvic adenopathies with maximum diameter -14 mm
- Cerebral CT: no lesions or formations observed.

Evolution:

It was preceded left unilateral adrenalectomy and the histopathologic exam confirm the diagnosis of pheochromocytoma (tumor size 3 cm). Furthermore, two weeks postsurgery the metanephrine and normetanephrine are maintained elevated (metanephrine raised about 5 times and normetanephrine about 2 times).

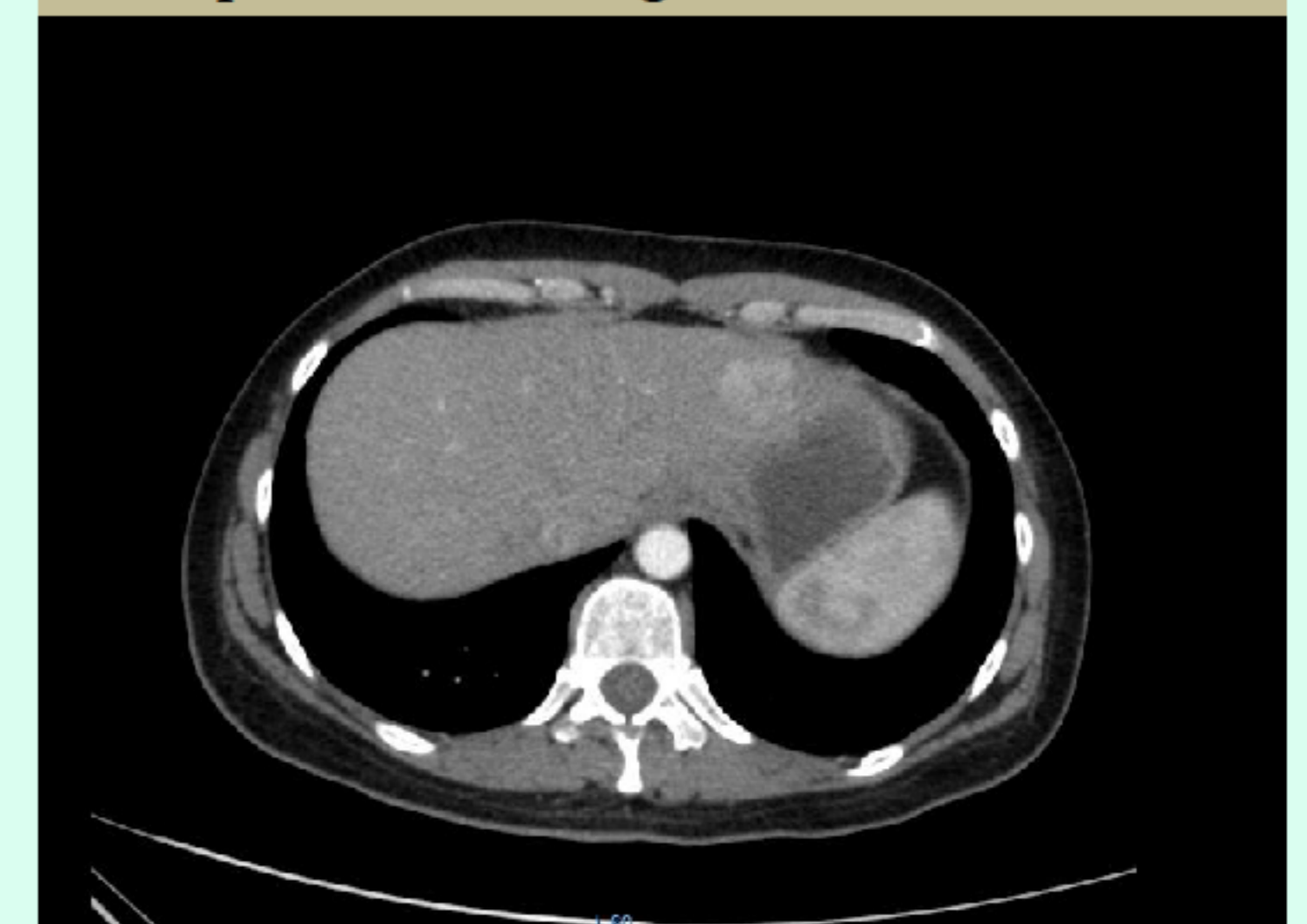
Discussion:

Malignant pheochromocytoma is a controversial diagnosis starting from its definition, malignancy being determined only in the presence of metastasis with no other criteria. In the literature are several markers suggested to correlate with the risk of malignancy like : tumor weight >80 g and high, tumor concentration of dopamine (2), tumor size >5 cm (3) , the presence of confluent tumor necrosis, extra-adrenal manifestations and a younger age (4). Also, several scoring system to predict the malignancy has been proposed like - The Pheochromocytomas of the Adrenal Gland Scaled Score (PASS) which has included invasion, histologic growth patterns, cytological features, mitotic activity, and other characteristics (5), but currently is no consensus on adoption of a formal scoring system. There are more other markers: biochemical markers(e.g. methoxytyramine, chromogranin A, neuron-specific enolase), imaging markers (e.g.123I metaiodobenzylguanidine scintigraphy (123I-MIBG), PET with 6-[18F]-fluoroDOPA ([18F]-DOPA), 111In-pentetreotide), histologic markers (e.g. Ki-67 proliferative index, hTERT mRNA, the heat shock protein HSP 90, vascular endothelial growth factor) studied in relationship with chromaffin tumors but with no conclusive data. Even if some of them appears to diagnose better the presence of metastases like 123I-MIBG, [18F]-DOPA their availability is not that accessible.

CT with contrast: iodophil formation in the liver space - eight segment



CT with contrast: iodophil formation in the liver space - second segment



Conclusions:

We present a case of a young woman with catecholamine hypersecretion and a mass in the left adrenal - a pheochromocytoma, with associated lymphadenopathies, liver formations and pulmonary micronodules- places where pheochromocytoma usually metastasizes, and with metanephrine and normetanephrine maintained elevated postsurgery, so most probably malignant pheochromocytoma. The final diagnosis could be established only after the demonstration of chromaffin cells in the nonchromaffin tissues. Although the clinical presentation and the laboratory findings were not that impressive, the malignant pheochromocytoma cannot be excluded regarding its definition, so other noninvasive, sensitive, specific and accessible criteria of diagnosis would be necessary.

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