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CASE REPORTS

Retroperitoneal Malignant Pheochromocytoma

Feocromocitoma maligno de presentación retroperitoneal

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ABSTRACT

Introduction: the most common and best-known neoplasm of the adrenal medulla is benign pheochromocytoma, which can be defined as a paraganglioma of the adrenal medulla, which may secrete catecholamine of the types of norepinephrine, epinephrine, or both.
Clinical case: a 36-year-old, white race, female patient with a health history, assessed for a non-irradiated lumbar pain, which was spontaneously relieved, a blood pressure of 170/100 mm Hg at admission, the ultrasound reported the presence of a retroperitoneal tumor, the surgical exeresis of the tumor was performed, during the trans-operative stage the patient suffered from hemodynamic instability, hypotension, tachycardia and cardio-respiratory arrest, which was managed to her recovery. The patient dies in the first 6 hours as a consequence of a postoperative shock.

Conclusions: malignant pheochromocytoma constitutes only 10 % of these types of neoplasm, being an infrequent tumor in our environment; its report was significant to be presented. The diagnosis was made by histological study, considering malignant pheochromocytoma. A clinical case of adrenal malignant pheochromocytoma was reported, with the intention of contributing to the acquisition of a better management in relation to this type of neoplasm.
MeSH: RETROPERITONEALNEOPLASMS/surgery; PHEOCHROMOCYTOMA/diagnosis; PARAGANGLIOMA; CHROMAFFIN CELLS/ultrastructure; INTRAOPERATIVE COMPLICATIONS.

RESUMEN

Introducción: la neoplasia más común y mejor conocida de la médula adrenal es el feocromocitoma benigno, que puede definirse como un paraganglioma de la médula suprarrenal, el cual puede secretar catecolaminas del tipo, norepinefrina, epinefrina o ambas.
Presentación de caso: paciente femenina de 36 años, de raza blanca, con antecedentes de salud, valorada por dolor lumbar no irradiado, que se aliviaba espontáneamente, con cifras tensionales al ingreso de 170/100 mm de Hg, la ecografía informa la presencia de tumor retroperitoneal, se realiza exéresis quirúrgica del tumor, durante el transoperatorio la paciente sufre inestabilidad hemodinámica, con hipotensión, taquicardia y parada cardiorrespiratoria, que logra recuperarse. La paciente fallece en las primeras seis horas del postoperatorio en un cuadro de shock.
Conclusiones: el feocromocitoma maligno constituye solo el 10 % de estas neoplasias, siendo una tumoración infrecuente en nuestro medio, motivo por el cual se consideró pertinente su presentación. El diagnóstico se realizó por estudio histológico, planteándose el feocromocitoma maligno. Se presentó un caso clínico de feocromocitoma maligno suprarrenal, pretendiendo con ello aportar un mayor conocimiento de esta neoplasia.
DeCS: NEOPLASIAS RETROPERITONEALES/cirugía; FEOCROMOCITOMA/diagnóstico; PARAGANGLIOMA; CÉLULAS CROMAFINES/ultraestructura; COMPLICACIONES PEROPERATORIAS.

INTRODUCTION

The most common neoplasm of the adrenal medulla is benign pheochromocytoma, defined as a paraganglioma of the adrenal medulla, which may secrete catecholamines of the type, norepinephrine, epinephrine, or both.[1]

Between 10 % and 20 % are diagnosed during childhood, with an average age of 11 years and predominance in males. When a child has high blood pressure, in 1.7 %, has a tumor that secretes catecholamine, hypertension is usually cured if the tumor is diagnosed and treated correctly, but if not, it can lead to death. Necroscopic series indicate that most pheochromocytomas are not diagnosed by the clinical practice, even in cases of fatal outcomes. [1, 2]

We report a case of malignant pheochromocytoma, studied at Abel Santamaría Cuadrado General Teaching Hospital, which evolved torpidly with pulmonary edema, coagulation disorders and shock, which caused the death of the patient. The aim of the study is to widen knowledge of the tumor throughout its clinical course and the different therapeutic actions.

CASE REPORT

A 36-year-old, white race female patient with no personal or family pathological history who had no toxic habits; she complained of having an oppressive, non-irradiated, intermittent low back pain, which was spontaneously relieved and exacerbated by postural changes. The physical examination showed high blood pressure figures, 150/100 as the only positive data.

Among the complementary images performed, the ultrasound showed a right adrenal tumor image, hyperecogenic, with ecolucent areas inside, measuring approximately, 10.3 x 6.8 mm, without other alterations, with diagnostic impression of retroperitoneal tumor.

With the diagnosis of retroperitoneal tumor, the surgical intervention was decided by exploratory laparotomy, which lasted for five hours and 15 minutes. Exceresis was performed on the retroperitoneal tumor projected below the inferior cava.

During the transoperative period, the patient presented hemodynamic instability, hypotension, and tachycardia, cardiorespiratory arrest with effective resuscitation maneuvers; she remained in shock and died in the immediate postoperative period.

The biopsy defines as macroscopic diagnosis: tissue mass of 90 x 60 mm, weight 800 grams, brown, irregular, soft consistency, with cystic cavity, occupied by necrotic tissue and blood.

Microscopic: surgical specimen labeled as a 90 x 60 mm retroperitoneal tumor, with abundant areas of necrosis, hemorrhage, polyhedral tumor cells with clear cytoplasm, vacuolated, eosinophils with nuclear atypia, which were arranged in solid, alveolar and trabecular patterns closely related to the vascular network in which tumor thrombi were located. There was recurrent atypical mitosis. The diagnosis of malignant pheochromocytoma was concluded.

In the necropsy study, the following chronopathology was established: direct cause of death: mixed shock; intermediate cause of death: transoperative status of removal of retroperitoneal tumor by malignant pheochromocytoma; basic cause of death: malignant pheochromocytoma; contributing cause: pulmonary thromboembolism of fine and medium bilateral branches.
Other diagnoses: distress lung (edema, intra-alveolar hemorrhage, interstitial, bibasal atelectasis); mild hepatic steatosis; biliary cholestasis; acute splenic congestion; shock kidneys (acute tubular necrosis and hemoglobinuric cylinders); focal areas of serous hemorrhage of the large intestine, diaphragm and renal capsule; along with acute gastritis.

DISCUSSION

Pheochromocytoma is a tumor of chromaffin tissue. This tissue, is formed by cellular migration from the neural crest, it forms the paraganglionic system, made up of the adrenal medulla, the carotid and aortic bodies, the **organ** of **Zuckerkandl** and remains of nodes located along the sympathetic ganglion chain.

Although extra-adrenal pheochromocytoma is the name given to the tumor of the chromaffin system other than the adrenal tissue and with catecholaminergic (functional) activity, there are schools that designate paraganglioma to those non-functional extra-adrenal tumors. It was also called 10 % tumor, therefore: 10-15 % are extradrenal (paraganglioma), another

10 % of pheochromocytomas are bilateral, especially those that appear in the context of family syndromes, 10 % are malignant (without specific biochemical or histological characteristics but with the capacity to invade and metastasize at a distance), 10 % are diagnosed in childhood; 10 % relapse after surgical removal; the same percentage is diagnosed following the discovery of an incidentaloma (due to improved imaging techniques) and account for 0.10 % of cases of hypertension.

The erroneousness of this rule has been proved. The prevalence of bilateral adrenal tumors is greater than 10 % in some familial syndromes, such as MEN-II and von Hippel-Lindau syndrome. The prevalence of extradrenal adrenal tumors may be as high as 20 % and up to a quarter or more are hereditary, although metastases may be rare for adrenal pheochromocytomas (up to 5 %), the prevalence of malignant disease is 33 % for extradrenal pheochromocytomas and even higher in patients with specific mutations such as those causing some forms of familial paraganglioma.[3,4]

The results of the analysis of the pheochromocytoma genome confirm a high heritability of this disease and discover new genes that may become therapeutic targets for the future. Between 35 and 40 % of them have a hereditary base secondary to a mutation of the germinal lines. [1, 3, 5]

It is estimated that 17-18 % of pheochromocytomas are extra-adrenal; they can be located in any structure containing chromaffin tissue, although 85 % are located below the diaphragm. The highest incidence appears between the second and third decades of life, with no clear predominance of gender, except those of bladder location, with slight female predominance. Adrenal tumors synthesize noradrenaline and adrenaline to a greater extent, despite the fact that the normal adrenal medulla contains 85 % adrenaline.

The level of catecholamine production and release depends on the enzyme endowment of the tumor. Symptoms and signs will mostly depend on the amount and type of catecholamines released into circulation. The clinic shows that it can be asymptomatic or present with sustained or paroxysmal blood hypertension, accompanied by the classic triad of headache, hyperhidrosis and tachycardia. The clinical manifestations are so varied that it is known as the "great simulator".[1,6,7]

High blood pressure would correspond to the vasoconstriction induced by noradrenaline through the stimulation of receptors α1. Paroxysmal hypertensive crises would be the consequence of a sudden and very high release of noradrenaline. Glucagon receptors have been found in these tumors, which would explain the induction of paroxysmal hypertensive crises, sometimes several hours after administration. In the rare tumors in which there is a predominance of adrenaline release, by stimulation of beta adrenergic receptors, blood hypotension occurs secondary to extensive peripheral vasodilatation.[7, 8]

A reduction in plasma volume due to sustained vasoconstriction and a possible loss of tone of the postural receptors could be implicated in the appearance of orthostatic hypotension. The excessive secretion of adrenaline would stimulate, through beta receptors, the hepatic production of glucose and inhibit, through alpha receptors, the secretion of insulin responsible for disorders in hydrocarbon metabolism, even causing diabetes mellitus. Likewise, adrenaline would originate, by beta adrenergic stimulation, tachycardia and other multiple metabolic manifestations. [8]

A genetic alteration has been found in which the short arm of chromosome 1 loses heterozygosis, which alters the suppressor gene involved in the tumor genesis of pheochromocytomas and abdominal paragangliomas. [2,4]

The diagnosis is based on clinical suspicion and confirmation is made by verifying increased excretion of catecholamines or their metabolites in 24-hour urine; it can be seen with increased levels of plasma catecholamines (**Vanillylmandelic** acid (VMA) and **metanephrine**). Tumor localization is mostly done by MIBG-I131, CT and MRI tracking [5, 6, 8, 9].

In this study, the definitive diagnosis is provided by Pathology study. Macroscopic pathology: the tumor measured 90 x 60 mm; this corresponds to the literature that refers to a variable size, where the smallest are the ones that cause the most clinical manifestations.

Pheochromocytoma is a partial or total encapsulated tumor, very vascularized, which with some frequency presents hemorrhagic areas. Large tumors show hemorrhagic necrosis and cystic degeneration. (Fig. 1)

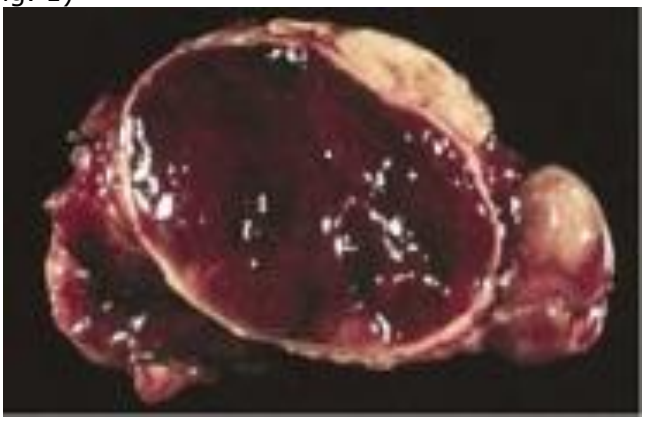

Fig. 1 Macroscopy: tumor with cystic and hemorrhagic degeneration.

Microscopic pathology: they are formed by a proliferation of neuroendocrine cells arranged in nests, separated by a delicate fibrovascular stroma. The tumor cells have a basophilic or eosinophilic cytoplasm; they are pleomorphic, of very variable size. (Fig. 2, 3)

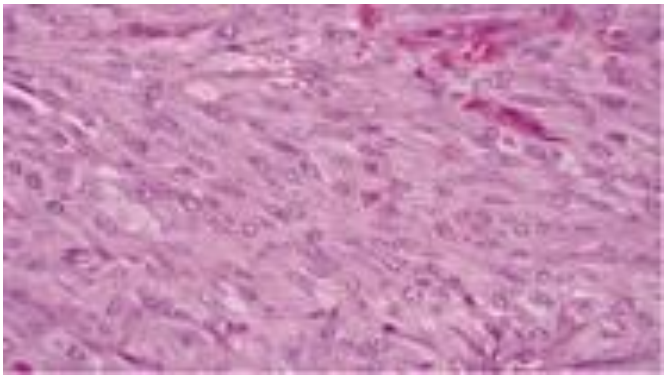

Fig 2. Microscopía: células de citoplasma basófilo con pleomorfismo nuclear.

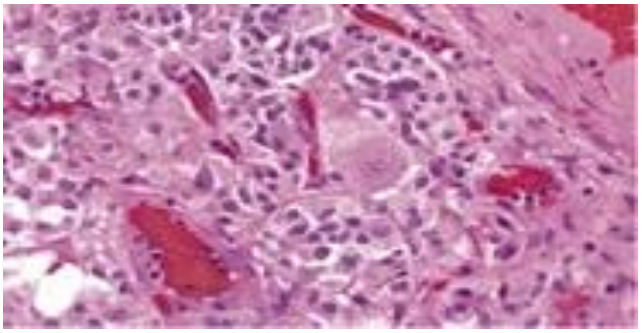

Fig. 3. Feocromocitoma que muestra necrosis hemorrágica y pleomorfismo nuclear.

Malignant tumors cannot be diagnosed with certainty if only histological criteria are taken into consideration. Strictly speaking, those with metastases in locations where chromaffin tissue is present may be considered malignant.[4,6,8,9] Metastases usually occur in the skeleton, liver, lung, lymph nodes and brain.

Extra-adrenal pheochromocytomas are located in areas where chromaffin tissue exists, usually around sympathetic nodes. In most cases they are intra-abdominal (Zuckerkandl organ and urinary bladder), but may also appear in the posterior mediastinum, pericardium and, rarely, in the cervical region.

When located in the Zuckerkandl organ, it is still very difficult to evaluate invasion of adjacent tissues due to the intimate relationships between this organ and the aortic artery and the vena cava.[10]

The treatment is surgical, with complete removal of the mass, as was done in the case presented, where the death occurred in the immediate postoperative under the action of catecholamine discharges, which favored an intense beta-adrenergic action, which led to pulmonary edema, coagulation disorders and shock.

The timely diagnosis, along with a consequent preoperative behavior, effective surgical resection with the use of drugs indicated for nosological disease, are the basic pillars in a competent medical practice.

Conflict of interest: The authors state that there is no conflict of interest.

Authors' contribution: The authors contributed equally to the design of the study.

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