INTERNATIONAL SEVEN JOURNAL
OF HEALTH RESEARCH
ISSN: 2764-9415

Adrenocortical epithelial neoplasia with intense cellular pleomorphism in a young patient: A case report

Neoplasia epitelial adrenocortical com intenso pleomorfismo celular em paciente jovem: Um relato de caso

DOI: 10.56238/isevjhv3n2-001
Receipt of originals: 02/14/2024
Publication acceptance: 03/06/2024

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Abstract

Adrenocortical epithelial neoplasms represent a diverse spectrum of tumors originating from the adrenal cortex such as adrenal cortical carcinomas (ACCs) and adrenal cortical adenomas (ACAs), which are rare but clinically significant tumors. The objective of this article is to report the clinical case of a 29-year-old female patient who was affected by an adrenocortical epithelial neoplasm with intense cellular pleomorphism. Surgical treatment was performed in the emergency room to resolve the initial condition, and the diagnosis was aided by imaging and anatomopathological methods.

Keywords: Adrenocortical, Cellular pleomorphism, Carcinoma.

INTRODUCTION

The adrenal gland can be thought of as two separate organs, the adrenal cortex and the adrenal medulla, each with a distinct structure, function, and embryological origin. Neoplasms arise from both components and typically present with different clinical symptoms. Tumors of

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the adrenal cortex include neoplasms of the adrenal cortex, such as adenomas and carcinomas of the adrenal cortex. Tumors of the medullary component typically present as pheochromocytomas, but in rare cases cases cases of adrenocortical carcinoma may occur[1].

Adrenocortical carcinoma (CAC) is a rare, heterogeneous neoplasm with a poor prognosis. According to the 2004 WHO classification, CAC variants include oncocytic CACs, myxoid CACs, and CACs with sarcomatous areas[2], and it is considered a rare heterogeneous malignancy with an incidence of 0.7-2.0 cases per million inhabitants per year3. Although the diagnosis of malignancy is easy in most cases, mainly due to the advanced stage of presentation, strictly intra-adrenal tumors should be evaluated for malignant potential[4].

Most patients present with steroid hormone excess, e.g., Cushing's syndrome or virilization, or abdominal mass effects, but an increasing proportion of patients with adrenocortical carcinoma (currently > 15%) are initially diagnosed incidentally. There is no consensus on diagnostic and therapeutic measures for adrenocortical carcinoma, but collaborative efforts such as international conferences and networks, including the European Network for the Study of Adrenal Tumors (ENSAT), have advanced substantially in the field.

Several multiparametric scoring systems, including the Hough scoring system, the Weiss scoring system, the Van Slooten scoring system, and the Weiss revisited index[5], and also recently, diagnostic algorithms such as the system and the simplified diagnostic algorithm have been generated. The latter takes into account the presence of a ruptured reticulin structure, which constitutes the first step in this diagnostic approach, as being the most sensitive feature of malignancy. Other parameters include mitotic count >5⁄50 HPF, presence of necrosis, and venous invasion[6].

The Weiss scoring system is the most popular among multi-parameter scoring systems, due to its reliability and relative simplicity. It includes nine parameters related to tumor structure (loss of clear cytoplasm, presence of diffuse architecture and necrosis), cytological characteristics (atypia, mitotic count, atypical mitotic figures) and invasive properties (sinusoidal, venous and capsular invasion)[6]. However, the Weiss system suffers from particular limitations, including (1) lack of reproducibility of multiple criteria, (2) "borderline" tumors with a Weiss score of 2 or 3, (3-4) oncocytic and myxoid variants of adrenocortical tumors, and (5) pediatric adrenocortical neoplasms[4,7].

Currently, there is also the histopathological criteria proposed by Weiss and modified by Aubert S. for tumors of the adrenal cortex that are based on five parameters: 1. Mitotic activity (>5 mitoses/ 50 CGA); 2. Figures of atypical mitoses; 3. Cytoplasmic characteristics (>75% of

non-clear cell pattern); 4. Necrosis; 5. Venous/capsular invasion. A score greater than or equal to 3 (i.e., the presence of 3 or more of these criteria) is related to malignant behavior; Therefore, the present case suggests malignancy4.

In patients with suspected adrenocortical carcinoma, a complete endocrine and imaging evaluation is recommended to guide the surgical approach aimed at complete tumor resection. Most patients benefit from adjunctive treatment with mitotane. In metastatic disease, mitotane is the cornerstone of initial treatment, and cytotoxic drugs should be added in case of progression[3].

METHODS

The present study was based on information obtained from physical and electronic medical records that recorded the attendance, conducts, laboratory and imaging tests pertinent. In parallel, a brief literature review was conducted in databases such as PubMed and Lilacs. This study was prepared following the precepts of the National Council for Ethics in Research (CONEP).

CASE REPORT

In 2018, a 26-year-old female patient, with no history of previous diseases, went to the emergency room of a city in the interior of São Paulo due to severe abdominal pain, stab type, with radiation to the back, more intense on the left side, associated with nausea and vomiting at the peak of pain and sweating. He was referred to the city's specialized service, where an ultrasound was performed, which showed significant bleeding in the adrenal region, and emergency adrenalectomy surgery was chosen.

The removed tumor was very voluminous, friable and irregular with extensive foci of necrosis, measuring 15.0 x 8.0 x 5.0 cm and weighing 219 grams, and a fragment was removed for biopsy and immunohistochemistry. After hospitalization, the patient continued to be followed up on an outpatient basis and was referred to the oncology service for treatment with oral chemotherapy using mitotane.

The macroscopy of the anatomopathological report was observed predominantly of adipose tissue surrounded by blood clots (hematoma). On the cuts, a whitish solid tumor, with a soft consistency, is observed in the midst of the blood clots, and there are also fragments of adrenal glands closely associated with this tumor.

The microscopy of the anatomopathological report revealed an adrenocortical epithelial neoplasm with intense cellular pleomorphism and extensive necrosis and hemorrhage, suggesting a case of malignancy, according to Weiss's criteria.

In addition, a new examination of slides and evaluations of the histological and immunohistochemical findings was requested to define the biological behavior of this neoplasm (benign vs. malignant) and through the application of the Weiss criteria modified by Aubert, it was reaffirmed that it was an adrenocortical epithelial neoplasm with intense cellular pleomorphism, in which at least 3 of these predictive criteria of malignant behavior are present: Mitotic index greater than 5 mitoses/50 fields of high magnification (in this case, 11 mitoses/50 CGA) + Presence of atypical mitoses + Presence of necrosis. In conclusion, this is a neoplasm to be considered as predictably malignant

The immunohistochemical study revealed positive expression for alpha-inhibin and negative expression for calretinin, chromogranin A and cytokeratins of 40, 48, 50 and 50.6 kDa and reaffirmed that it was an adrenocortical epithelial neoplasm with intense cellular pleomorphism and foci of necrosis.

After 1 year and a half of follow-up and treatment, ultrasonography revealed the presence of nodular rhetorperitoneal lesions, which later confirmed the suspicion of recurrence by means of a positron emission tomography scan, which showed tumor recurrence and the presence of metastatic foci with hypermetabolic lesions in the right lung, liver, lymph node, retroperitoneal, peritoneal and right diaphragmatic cortex. Thus, chemotherapy and routine CT scans were started again to monitor the evolution of the condition.

However, at the end of 2021, due to the ineffectiveness of the use of chemotherapy, palliative treatment was chosen. On June 29, 2022, the patient underwent pulmonary embolism and hypoglycemia, and died.

DISCUSSION

Myxoid extracellular matrix is a histological feature that can be found in both physiological and pathological conditions, *non-neoplastic* (e.g., myxedema) as well as *neoplastic*, as in this case, due to the fact that the tumor in question is of epithelial origin. This is important so that, in the presence of an extracellular matrix such as this one, the tumors in question can never be ruled out2.

The reported age range of MNA (46 cases) is 16 to 82 years, with a mean and median of 51 and 51.5 years, respectively. In general, cases in women slightly outnumber those in men

(26:20). Hormonal hypersecretion often occurs in these tumors; Only 13 of the 42 cases did not function (eight adenomas, one borderline and four carcinomas), while five patients had biochemical evidence of hormone production (two adenomas, one borderline and two carcinomas)[2].

The diagnostic suspicion usually occurs due to hormonal excess and, occasionally, palpable abdominal mass. Children and adolescents typically present with signs and symptoms of excessive androgen production, virilization, which is the most common hormonal disorder, or excess cortisol, Cushing's syndrome, or both, and are considered mixed tumors[8].

In Brazil, in the South and Southeast regions, the incidence of CSR is 10 to 15 times higher than the global incidence, reaching 4.2 cases per million inhabitants9. Thus, a thorough investigation of the subject is necessary, with the objective of discovering the reason for this exacerbated incidence of cases of this disease in these regions of Brazil.

Although surgical resection is the only therapy with curative potential for CAC. There are also treatments that are indicated exclusively when there is confirmation of tumor malignancy and aim to reduce the chances of disease recurrence. These adjuvant therapeutic options are based on the use of mitotane and/or radiotherapy[10].

Mitotane promotes a 38% reduction in recurrences and a 31% reduction in mortality in patients affected by the cancer in question. This occurs because it has an apoptotic effect on CAC cells through an intracellular oxidative stress that is generated by this drug. In cases of disseminated disease, it is used as a first-line drug, and can be used either as monotherapy or associated with other chemotherapy drugs, such as etoposide, doxorubicin and cisplatin[10].

To accelerate mitotane deposition in adipose tissue, it is mixed with medium-chain triglycerides and other fatty foods routinely ingested in the patient's diet (milk, chocolate, yogurt)[11].

Despite the proven beneficial effects of mitotane, there are still adverse effects in its users, which include: gastrointestinal symptoms (nausea, vomiting and diarrhea), weight loss, asthenia, neurological symptoms (lethargy, confusion, drowsiness, vertigo and dizziness). Also noteworthy are some metabolic and endocrine effects, such as adrenal insufficiency, hypercholesterolemia and hypertriglyceridemia, hypothyroidism and hypogonadism (the latter mainly in males)[12].

It is known that the signs and symptoms in adult women who have secretory tumors and evolve with virilization include: oligomenorrhea, hirsutism, acne, increased muscle mass, temporal baldness, increased libido and clitoromegaly[14]. Thus, in view of the picture presented

by the patient in the case, where there were no such complaints and presentations, the only clinical findings that led to the diagnosis of the pathology involve abdominal pain, with irradiation to the back, associated with nausea and vomiting at the peak of pain and sweating.

This fact corroborates the increase in the physician's expertise, so that in the face of similar conditions, he knows that there may be situations in which the clinical picture of adrenocortical carcinoma does not show an abundance of specific characteristics. Because of this, the examiner should be wise about requesting complementary tests in order to reach the final diagnosis.

Conflicts of interest
The authors declare that there is no potential conflict of interest that could compromise the impartiality of this scientific work.

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