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Adrenocortical carcinoma: Retrospective analysis of the last 22 years

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KEYWORDS
Adrenocortical carcinoma;
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Abstract
Background: Adrenocortical carcinoma (ACC) is a rare disease with a poor prognosis. The clinical experience acquired, even from a small number of cases, has improved understanding of this condition. The purpose of this study is to characterize patients with ACC followed up at a Portuguese reference center over the past 22 years.
Methods: Retrospective analysis of clinical records of patients with histopathological diagnosis of ACC followed up from 1992 to 2014.
Results: The study sample consisted of 22 patients, 20 of them female. Eleven patients were in stage II, four in stage III, and five in stage IV; 13 patients had functioning lesions. Adrenalectomy was performed in 20 patients, with complete tumor resection in 90% of the cases. During follow-up, eight patients experienced recurrence of local disease, and 12 distant metastases. Fourteen patients received mitotane, 35.7% ($n = 5$) as adjuvant therapy and 64.3% ($n = 9$) after recurrence; therapeutic plasma mitotane levels were achieved in 70% of patients. Stage III patients who received adjuvant therapy had longer survival time (13.5 vs. 2.5 months). Two patients were given chemotherapy associated to mitotane. Median survival was 11 months (0–257 months); it was slightly longer in younger patients or patients with non-functioning tumors. Six patients are still alive, four of them with no evidence of disease.
Conclusion: Despite the overall poor prognosis, some patients with ACC may have a long survival time. Although complete tumor removal remains the only potentially curative treatment, diagnosis at a younger age, presence of non-functioning tumors, and mitotane treatment also seemed to be associated to longer survival in our patients.

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PALABRAS CLAVE
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Carcinoma de la corteza suprarrenal: análisis retrospectivo de los últimos 22 años

Resumen
Antecedentes: El carcinoma de la corteza suprarrenal (ACC) es una enfermedad rara, con mal pronóstico. La experiencia clínica, incluso cuando se obtiene a partir de un número limitado de casos, ha mejorado el conocimiento sobre esta entidad. Este estudio tiene como objetivo caracterizar los pacientes con ACC seguidos en un centro de referencia portugués durante los últimos 22 años.
Métodos: Análisis retrospectivo de la historia clínica de los pacientes con diagnóstico histopatológico de ACC seguidos entre 1992 y 2014.
Resultados: Se incluyeron 22 pacientes, 20 de ellos mujeres. Once pacientes se encontraban en estadio II, 4 en estadio III y 5 en estadio IV, mientras que 13 pacientes mostraron lesiones funcionales. La adrenalectomía se realizó en 20 pacientes, con resección completa del tumor en el 90% de los casos. Durante el seguimiento 8 pacientes presentaron recurrencia de la enfermedad local y 12 metástasis a distancia. Catorce pacientes recibieron tratamiento con mitotano: adyuvante en el 35,7% (n = 5) o después de la recidiva de 64,3% (n = 9), alcanzándose niveles plasmáticos terapéuticos en el 70% de los casos tratados. Los pacientes en estadio III que recibieron tratamiento adyuvante presentaron mayor supervivencia (13,5 frente a 2,5 meses). Dos pacientes fueron sometidos a quimioterapia asociada con mitotano. La mediana de supervivencia fue de 11 meses (0-257 meses), y resultó ligeramente mayor en los pacientes más jóvenes o con tumores no funcionantes. Seis pacientes continúan vivos, 4 de ellos sin evidencia de enfermedad.
Conclusión: A pesar del mal pronóstico global, algunos pacientes con ACC pueden presentar una larga supervivencia. Aunque la eliminación completa del tumor sigue siendo el único tratamiento potencialmente curativo, en nuestros pacientes el diagnóstico a una edad más joven, la presencia de tumores no funcionantes y el tratamiento con mitotano también parecen asociarse con una mayor supervivencia.

Introduction

The adrenocortical carcinoma (ACC) is a rare disease, with an annual incidence of about 0.7–2 cases per million population.[1,2] It mainly affects women aged 40–50 years; most of ACC are sporadic, although there are also some congenital and familial forms of this disease.[3,4] ACC are larger than benign adrenal masses and measure about 10–12 cm. ACC accounts for 2% of adrenal tumors that measure 4 cm or less, 6% of tumors that measure from 4.1 to 6 cm, and 25% of those tumors greater than 6 cm.[5] According to their functional type ACC may be classified as hormone secreting tumors or non-functioning tumors. Hormone-secreting ACC appear with manifestations of virilization, feminization or Cushing syndrome; on the other hand, non-functioning ACCs are usually diagnosed incidentally.[6,7] Regarding its prognosis, unfortunately this tumor represents one of the most aggressive malignant endocrine neoplasia. In fact, the first reports of this disease date back to 1958 and referred that untreated patients have a lifespan of only 3 months.[8]

Although the interest in this disease has increased exponentially over the past few years, its rarity has limited a large-scale analysis of all possible factors with prognostic effects. Our current knowledge has been mainly obtained from clinical experience obtained from series of patients with ACC, even including a limited number of cases. The majority of published studies did not present data on long-term follow-up, which also limited insight about its evolution, including the rate of cure or late recurrence of the disease.

In this study the authors aim to present their experience in the diagnosis, therapeutic management and clinical outcome of patients with ACC followed in a Portuguese reference center over the last 22 years.

Methods

Twenty-two patients with ACC were diagnosed and monitored at the Endocrinology, Diabetes and Metabolism Department of Coimbra Hospital and University Centre from 1992 to 2014. The authors performed a retrospective analysis, through the review of individual medical records, of clinical features, diagnostic approach, therapeutic regimens and evolution of these patients.

Definitions

The diagnosis and therapeutic approach of ACC patients were based on the guidelines of our own institution, and more recently the implementation of the guidelines of ENSAT (European Network for the Study of the Adrenal Tumours) Group.[9]

ACC was considered as functioning when the patients presented clinical manifestations caused by hormonal