Adrenocortical Carcinoma

Review of the Pathologic Features, Production of Adrenal Steroids, and Molecular Pathogenesis

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KEYWORDS

• Adrenocortical carcinoma • Weiss criteria • Molecular pathology • Steroidogenesis • Immunohistochemistry

KEY POINTS

- Adrenocortical carcinoma (ACC) is a rare malignant neoplasm with an aggressive biological behavior.
- The Weiss criteria of adrenocortical malignancy are known as the most reliable tool for histopathological scoring system.
- Genomic features of adrenocortical carcinoma have been recently reported and may be used for the diagnosis of ACC.
- ACC cases may be hormonally functional, and immunohistochemical analysis of steroidogenic enzymes is utilized for the analysis of intratumoral production of corticosteroids.

INTRODUCTION

Adrenocortical carcinoma (ACC) is a rare malignant neoplasm arising from adrenocortical parenchymal cells. ACC is also known to have unique features compared with other tumors. In particular, ACC often secretes several types of steroid hormones with a pattern of disorganized steroidogenesis. This article summarizes the clinical,

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histopathological, and biological features of ACC that are relevant to its pathogenesis, diagnosis and prognosis.

CLINICAL AND HISTOPATHOLOGICAL FEATURES OF ADRENOCORTICAL CARCINOMA

The incidence of ACC is estimated to be approximately 0.7 to 2 cases per 1 million population, accounting for 0.05% to 2% of all malignant tumors.[1] The age distribution of ACC is bimodal; the first peak is in early infancy under the age of 5 years, mainly derived from hereditary syndromes such as the Li-Fraumeni and Beckwith-Wiedemann syndromes.[2] The second peak is the fourth to fifth decades of life. The frequency in both genders is similar, but some reports indicate a slightly higher incidence in women.[2] The average overall survival in ACC cases was reported to be 14.5 months, with a 5-year mortality rate of approximately 75% to 90%.[3,4] Presently, only 30% of all ACCs are potentially curable at early stages after diagnosis. Metastases of ACC have been detected in the liver (48%–85%), lung (30%–60%), lymph nodes (7%–20%), and bones (7%–13%).[5,6] Clinical staging of ACC is usually based on the presence or absence of invasion or distant metastases.[7] Tumor size and weight are also reliable clinical parameters of staging ACC. Appropriate cut-off value of tumor weight (50 g) and tumor size (6.5 cm) indicates the high sensitivity (91%) and specificity (100%) in distinguishing ACC from adrenocortical adenoma (ACA).[8]

The histological diagnosis of ACC is pivotal in order to establish the final diagnosis. The Weiss criteria of adrenocortical malignancy comprise the most reliable histopathological scoring system differentiating ACC from ACA (**Table 1**).[9–11] ACC can be diagnosed by the presence of at least 3 of the 9 Weiss criteria. Three relate to cytological features (nuclear grade, mitoses and atypical mitoses); three refer to tumor structure (clear cells, diffuse architecture, and confluent necrosis), and three relate to invasion (venous invasion, sinusoidal invasion, and capsular infiltration). Most ACC cases are associated with relatively high scores in the Weiss criteria and do not pose major diagnostic challenges or problems for surgical pathologists involved in the diagnosis of resected adrenal neoplasms. However, occasionally some cases such as pediatric tumors or adrenocortical oncocytomas do pose diagnostic challenges if the final diagnosis is based solely on the Weiss criteria. In addition, as in any of the histopathological scoring

Table 1
Summary of Weiss criteria

	Scoring Points	
Criteria	**0**	**1**
Nuclear grade (Fuhrmann nuclear grade system)	I/II	III/IV
Mitoses	<6/10 HPF	≥6/10 HPF
Atypical mitoses	–	+
Clear cell component	<25%	≥25%
Diffuse architecture	<1/3	≥1/3
Confluent necrosis	–	+
Venous invasion	–	+
Sinusoidal invasion	–	+
Capsular infiltration	–	+

Three or more of the following 3 criteria indicate malignancy. Nuclear grade assessed by Fuhrmann nuclear grade, and grade III and/or IV indicates malignancy in adrenal tumors.

Abbreviation: HPF, high power fields.

Data from Refs. [9–11]