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Endocrine manifestations of renal tumors; current knowledge

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ABSTRACT

Renal cell carcinoma (RCC) can lead to various paraneoplastic syndromes, both endocrine and non-endocrine. Endocrine manifestations include hypercalcemia, hypertension, polycythemia, galactorrhea, Cushing's syndrome, and alterations in glucose metabolism. These syndromes are not necessarily indicative of metastatic disease or poor prognosis but can present as paraneoplastic manifestations of primary or recurrent RCC. Understanding these manifestations is crucial for diagnosis and treatment, as they may be the initial signs of the disease.

Keywords: Kidney cancers, Renal cell carcinoma, Paraneoplastic syndrome, Hypercalcemia, Clear cell renal cell carcinoma, Renal tumor

Implication for health policy/practice/research/medical education:
Kidney cancers can lead to endocrine manifestations such as paraneoplastic syndromes. These syndromes include hypercalcemia, erythrocytosis, hypertension, and Cushing's syndrome.

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Introduction

Renal tumors can be classified into benign and malignant types. Kidney cancers can have various pathologic features, including clear cell renal cell carcinoma (RCC) as the most common type (in approximately 90% of all kidney cancers), papillary RCC, chromophobe RCC, and collecting duct carcinoma (1,2). Other less common types include renal medullary carcinoma, translocation RCC, and oncocytoma. Each type has distinct characteristics and may require different treatment approaches (1-3). Within RCC, there are several subtypes, including clear cell RCC, papillary RCC, chromophobe RCC, and other rare subtypes. Each of these subtypes has unique histologic and molecular characteristics (1,3,4). Clear cell RCC is the most common subtype and is characterized by clear or pale cytoplasm due to the accumulation of glycogen and lipids (5). Papillary RCC is characterized by tumor cells arranged in papillary structures, while chromophobe RCC is composed of large cells with prominent cell membranes and distinct cell borders (5). Other less common types of kidney cancer include transitional cell carcinoma, which originates from the renal pelvis, and Wilms tumor, which is a type of renal cancer that primarily affects children. In addition to these primary types of kidney cancer, there are also various histologic and molecular variations within each subtype that can impact the behavior and prognosis of the disease. These tumors can exhibit endocrine manifestations due to the production of hormones or hormone-like substances. These manifestations may include paraneoplastic syndromes, hormonal disorders, and other related symptoms (1,2,6). This mini-review paper aims to summarize the endocrine manifestations associated with renal tumors.

Search strategy

For this study, we searched PubMed, Web of Science, EBSCO, Scopus, Google Scholar, Directory of Open Access Journals (DOAJ) and Embase, using different

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keywords including kidney cancers, renal cell carcinoma, paraneoplastic syndrome, hypercalcemia, clear cell renal cell carcinoma and renal tumor.

Endocrine features of renal cell carcinoma

Renal cell carcinoma can have various endocrine manifestations due to its effects on hormone production and metabolism (1-3). RCC can lead to the overproduction of erythropoietin, which results in polycythemia (7). In some cases, it can produce parathyroid hormone-related protein that leads to hypercalcemia (8). In rare cases, RCC can produce adrenocorticotropic hormone, a hormone that stimulates the production of cortisol by the adrenal glands. This condition results in Cushing's syndrome (9). Additionally, kidney cancers can produce insulin-like growth factor 1, a peptide that promotes cell growth and division, which can lead to acromegaly (10). RCC can also produce renin or renin-like substances, causing secondary hypertension (11). Previous studies showed that RCC can also produce estrogen or androgen, causing feminization or masculinization, respectively. Moreover, these tumors may provoke a febrile response due to the release of inflammatory cytokines (1-3,11,12). Additionally, unintentional weight loss can occur in patients with renal tumors due to the metabolic effects of the tumor or associated systemic symptoms. These patients may experience fatigue as a result of anemia, metabolic disturbances, or the overall burden of the disease (14). Other uncommon manifestations included galactorrhea and alterations in glucose metabolism (15). These endocrine abnormalities are not necessarily indicative of metastatic disease or poor prognosis, but can present as initial signs of primary or recurrent RCC (15,16). In rare cases, anemia, neuromyopathies, vasculopathy, nephropathy, coagulopathy and elevated prostaglandins were reported (17). Paraneoplastic glomerulopathies, such as membranous nephropathy, have also been reported with RCC, though less commonly than with other solid tumors (18).

Prognosis of patients with paraneoplastic syndrome in RCC

The prognosis for patients with paraneoplastic syndromes in RCC varies based on the specific syndrome and its impact on the disease (19). The study by Sun et al to analyze the non-metastatic RCC individuals undergoing surgery showed that the presence of paraneoplastic syndromes was associated with older age, higher comorbidity, advanced tumor stage, and aggressive tumor histology (20). While patients with paraneoplastic syndromes had worse estimated recurrence-free survival, cancer-specific survival, and overall survival rates, adjusting for known prognostic factors showed that the presence of paraneoplastic syndromes was not strongly independently related with recurrence or death (20). Another study reported that the prevalence of paraneoplastic syndromes in RCC patients was 24.4%, with symptomatic patients having more syndromes and higher stages of RCC (20). Other studies also showed elevated ESR was the most common parameter, and symptomatic patients had a higher prevalence of paraneoplastic syndromes and more advanced RCC staging (20-22). Among various paraneoplastic syndromes, Stauffer's syndrome was significantly associated with a poor outcome in RCC patients (21,22). Persistent leukocytosis, though rare, was also noted as a feature of paraneoplastic syndromes. Moreover, the presence of paraneoplastic signs and symptoms was correlated with poor survival in previous studies (23-25).

Conclusion

Renal cell carcinoma can lead to a wide range of paraneoplastic syndromes, both endocrine and non-endocrine in nature. Understanding these manifestations is crucial for early diagnosis and treatment, as they may be the initial presentation of the malignancy.

Authors' contribution

Conceptualization: Ali Thoulfikar A. Imeer.
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Visualization: Ali Thoulfikar A. Imeer
Writing-original draft: Ali Thoulfikar A. Imeer.
Writing-review and editing: All authors.

Conflicts of interest

The authors declare that they have no competing interests.

Ethical issues

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the authors utilized Perplexity to refine grammar points and language style in writing. Subsequently, the authors thoroughly reviewed and edited the content as necessary, assuming full responsibility for the publication's content.

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