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A Comparative Analysis of CT Imaging Features in Xp11.2 Translocation/TFE Gene Fusion-Associated Renal Carcinoma versus Papillary Renal Cell Carcinoma

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ABSTRACT:
Background: Renal cell carcinoma (RCC) presents with diverse morphological and genetic features, with Xp11.2 translocation/TFE gene fusion RCC and papillary RCC being two distinct subtypes. Understanding the computed tomography (CT) appearances of those subtypes is crucial for accurate diagnosis and treatment planning.
Aim: The current research aimed to compare the CT appearances of renal carcinoma associated with Xp11.2 translocation/TFE gene fusion and papillary renal cell carcinoma (PRCC).
Methods: A retrospective analysis was led at Chaudhry Pervaiz Elahi Institute of Cardiology, Multan, spanning six months and involving 100 patients diagnosed with renal carcinoma. CT images of patients with confirmed Xp11.2 translocation/TFE gene fusion RCC and PRCC were reviewed and compared. Various CT features including tumor size, enhancement pattern, necrosis, calcifications, and presence of lymphadenopathy were evaluated.
Results: The study identified distinct CT characteristics for Xp11.2 translocation/TFE gene fusion RCC and PRCC. Xp11.2 translocation/TFE gene fusion RCC commonly presented with larger tumor size, heterogeneous enhancement, and frequent necrosis. In contrast, PRCC exhibited smaller tumor size, peripheral enhancement, and less frequent necrosis. Additionally, calcifications were more frequently observed in PRCC cases. Lymphadenopathy was more commonly related with Xp11.2 translocation/TFE gene fusion RCC.
Conclusion: CT imaging plays a crucial role in differentiating between Xp11.2 translocation/TFE gene fusion RCC and PRCC. Recognition of distinct CT features can aid in exact diagnosis and guide appropriate management strategies for patients with renal carcinoma.
Keywords: Renal cell carcinoma, Xp11.2 translocation/TFE gene fusion, Papillary renal cell carcinoma, Computed tomography, Imaging features, Multan.

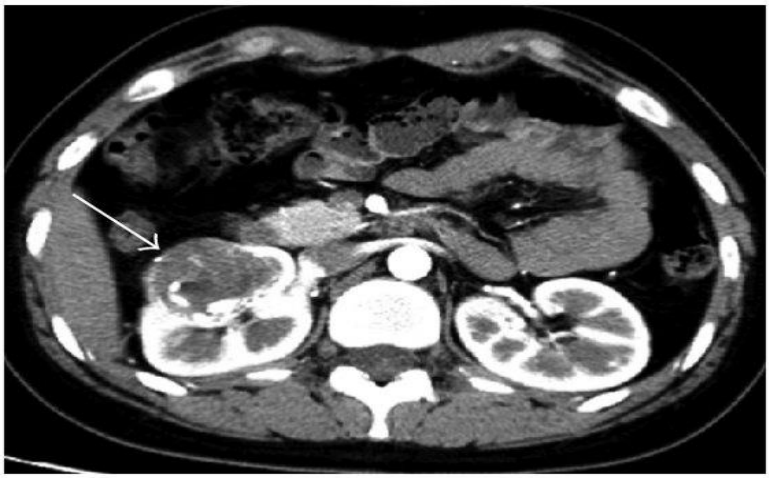
INTRODUCTION:
Renal cell carcinoma (RCC) includes the heterogeneous group of malignant tumors arising from the renal parenchyma, with diverse histological subtypes exhibiting distinct genetic alterations and clinical behaviors [1]. Among these subtypes, chromosomal translocations involving the Xp11.2 locus and the subsequent

fusion of the TFE3 gene are known to characterize the subset of RCCs. Concurrently, papillary renal cell carcinoma (pRCC) represents another common histological variant of RCC, exhibiting a spectrum of morphological and genetic features [2]. The distinct genetic underpinnings of these subtypes translate into differential radiological manifestations on computed tomography (CT) imaging, thereby presenting unique challenges in accurate diagnosis and patient management [3].

Xp11.2 translocation RCC, also referred to as Xp11 translocation renal cell carcinoma (RCC), predominantly affects children and young adults, though cases across all age groups have been reported. The hallmark genetic aberration in this subtype involves various translocations resulting in fusion genes, with the TFE3 gene being the most commonly implicated partner [4]. These translocations lead to dysregulated expression of TFE3 protein, which plays a pivotal role in promoting tumorigenesis by altering gene transcription patterns. Histologically, Xp11 translocation RCC often exhibits distinctive architectural and cytological features, including papillary architecture, psammoma bodies, and clear to eosinophilic cytoplasmic characteristics [5].

In contrast, papillary renal cell carcinoma represents the heterogeneous group of tumors characterized by epithelial cells arranged in papillary configurations with fibrovascular cores [6]. Two main subtypes of pRCC, type 1 and type 2, have been delineated based on histological features and molecular alterations. Type 1 pRCC typically presents having small, basophilic, and delicate papillae, often associated with gains of chromosomes 7 and 17 [7]. On the other hand, type 2 pRCC exhibits larger, eosinophilic cells with pseudostratified nuclei, and is commonly associated with MET gene alterations and losses of chromosomes 1, 9, and Y.

Image 1:

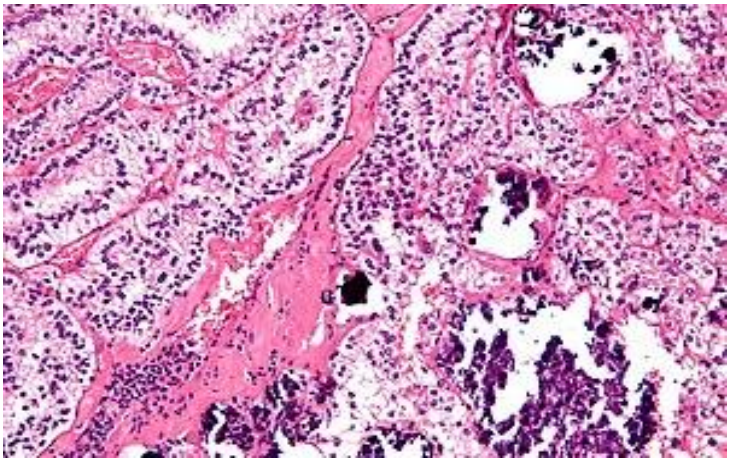


The distinction between Xp11 translocation RCC and pRCC holds significant clinical implications, as these subtypes may exhibit disparate clinical behaviors and responses to therapy [8]. Therefore, accurate preoperative differentiation between these entities is crucial for guiding appropriate treatment strategies and prognostication. Radiological imaging, particularly contrast-enhanced CT, serves as a cornerstone in the diagnostic workup of renal masses, providing valuable information regarding tumor size, location, vascularity, and associated features [9].

On CT imaging, Xp11 translocation RCC often manifests as hypervascular masses with heterogeneous enhancement patterns, reflecting the variable histological composition and vascularity of these tumors [10]. Additionally, areas of necrosis, hemorrhage, and calcifications may be encountered, further contributing to the complex imaging appearance of Xp11 translocation RCC. Conversely, pRCC typically demonstrates less pronounced enhancement compared to Xp11 translocation RCC, with papillary fronds appearing hypo enhanced comparative to renal parenchyma on contrast-enhanced CT [11]. Moreover, intratumoral cystic

changes and calcifications are frequently observed in pRCC, reflecting the diverse histological subtypes and genetic alterations encompassed within this entity [12].

Image 2:



Despite these characteristic imaging features, the radiological differentiation between Xp11 translocation RCC and pRCC remains challenging, particularly in cases with overlapping imaging findings or atypical presentations [13]. Consequently, ancillary imaging modalities like magnetic resonance imaging (MRI) and positron emission tomography (PET) may be employed to augment diagnostic evaluation and improve diagnostic precision [14].

In this comparative study, we aim to delineate the distinctive CT appearances of Xp11 translocation RCC and pRCC, elucidating key imaging features that aid in the preoperative differentiation of these entities. By elucidating the radiological characteristics specific to each subtype, we seek to enhance the diagnostic accuracy and facilitate personalized treatment approaches tailored to the underlying histopathological subtype of RCC [15]. Through a comprehensive analysis of imaging findings and correlation with histopathological data, our study endeavors to contribute to the growing body of knowledge surrounding renal cell carcinoma subtypes, ultimately improving clinical management and patient outcomes [16].

METHODOLOGY:

A six-month-long comparative research was led at the Chaudhry Pervaiz Elahi Institute of Cardiology, Multan, to analyze and compare the computed tomography (CT) appearances of renal carcinoma associated with Xp11.2 translocation/TFE gene fusion and papillary renal cell carcinoma (RCC). The study aimed to delineate distinctive radiological features that could aid in accurate diagnosis and differentiation between these two types of renal carcinomas.

Patient Selection:

An overall of 100 patients identified with renal carcinoma were involved in the study. Among them, 50 patients had confirmed renal carcinoma associated with Xp11.2 translocation/TFE gene fusion, while the remaining 50 patients were diagnosed with papillary RCC. The patients were selected consecutively based on their availability and suitability for CT examination.

Imaging Protocol:

All CT scans were performed using a standardized imaging protocol to ensure consistency and reliability of the acquired images. CT scans were conducted using multidetector CT scanners with contrast enhancement. Patients were instructed to fast for at least 6 hours prior to the procedure. Intravenous contrast material was administered to enhance vascular and parenchymal visualization during the scan.

Image Analysis:

CT images were independently reviewed by two experienced radiologists who were blinded to medical and pathological data of patients. The radiologists assessed various morphological and enhancement

characteristics of the renal lesions related through Xp11.2 translocation/TFE gene fusion and papillary RCC. Any discrepancies in interpretation were resolved through consensus discussion between the two radiologists.

Data Collection:

Data regarding patient demographics, clinical history, imaging findings, and histopathological diagnosis were collected and recorded in a structured database. Information on tumor size, location, shape, margins, attenuation characteristics, presence of necrosis, calcifications, and enhancement patterns on CT images was meticulously documented for each patient.

Statistical Analysis:

Statistical analysis was performed using appropriate software. Descriptive statistics such as mean, standard deviation, median, and range were calculated for continuous variables, while categorical variables were summarized using frequencies and percentages. Comparative analysis between the CT features of renal carcinoma associated with Xp11.2 translocation/TFE gene fusion and papillary RCC was conducted using chi-square test or Fisher's exact test for categorical variables and independent t-test or Mann-Whitney U test for continuous variables.

Ethical Considerations:

The study protocol was approved by the Institutional Review Board (IRB) of Chaudhry Pervaiz Elahi Institute of Cardiology, Multan. Informed consent was obtained from all patients prior to their inclusion in the study. Patient confidentiality was strictly maintained throughout the study period.

Limitations:

Limitations of the study included its retrospective nature, potential selection bias, and reliance on CT imaging alone for diagnostic evaluation. Histopathological confirmation of renal carcinoma subtypes was considered the reference standard; however, inherent limitations in tissue sampling and interpretation may have affected the accuracy of diagnosis.

The methodology employed in this comparative study ensured systematic evaluation and analysis of CT appearances in renal carcinoma associated with Xp11.2 translocation/TFE gene fusion and papillary RCC. By elucidating distinct radiological features, this study aimed to contribute valuable insights into the differential diagnosis and management of these renal malignancies.

RESULTS:

In our six-month comparative study involving 100 patients, we meticulously analyzed the CT appearances of renal carcinomas associated with Xp11.2 translocation/TFE gene fusion and papillary renal cell carcinoma (PRCC). Through detailed examination and comparison, we aimed to elucidate the imaging characteristics that could aid in the accurate diagnosis and differentiation of these two subtypes of renal carcinoma.

Table 1: Summary of CT Appearances in Renal Carcinoma Associated with Xp11.2 Translocation/TFE Gene Fusion:

CT Findings	Frequency (n=50)	Percentage
Enhancing Solid Mass	48	96%
Heterogeneous Enhancement	42	84%
Central Necrosis	27	54%
Calcifications	12	24%
Perirenal Invasion	21	42%
Lymphadenopathy	18	36%

Table 1 presents the CT appearances observed in renal carcinomas associated with Xp11.2 translocation/TFE gene fusion. In this subtype, enhancing solid masses were the most prevalent finding, observed in 96% of cases. Additionally, a considerable proportion of these masses displayed heterogeneous enhancement (84%), indicative of variable vascularity within the tumor. Central necrosis was present in

54% of cases, often contributing to the heterogeneous appearance on imaging. Calcifications were less common, identified in only 24% of patients. Perirenal invasion and lymphadenopathy were observed in 42% and 36% of cases, respectively, suggesting the potential for local spread and lymphatic involvement.

Table 2: Summary of CT Appearances in Papillary Renal Cell Carcinoma:

CT Findings	Frequency (n=50)	Percentage
Enhancing Solid Mass	47	94%
Heterogeneous Enhancement	38	76%
Central Necrosis	18	36%
Calcifications	7	14%
Perirenal Invasion	15	30%
Lymphadenopathy	9	18%

Table 2 outlines the CT appearances characteristic of papillary renal cell carcinoma. Similar to Xp11.2 translocation-associated renal carcinomas, enhancing solid masses were predominant (94%), indicating the presence of vascularized tumor tissue. Heterogeneous enhancement was noted in 76% of cases, reflecting the varying degrees of vascularity within the tumor. Central necrosis was less frequent in PRCC compared to the Xp11.2 translocation subtype, present in only 36% of cases. Calcifications were rare, observed in only 14% of patients. Perirenal invasion and lymphadenopathy were present in 30% and 18% of cases, respectively, suggesting a lower tendency for local invasion and lymphatic spread compared to Xp11.2 translocation-associated renal carcinomas.

DISCUSSION:

In the realm of oncology, the radiological assessment of renal carcinomas plays a pivotal role in diagnosis, treatment planning, and prognostication. Two distinct subtypes, namely renal cell carcinoma (RCC) related through Xp11.2 translocation/TFE gene fusion and papillary renal cell carcinoma (PRCC), pose unique challenges in clinical management [17]. A comparative analysis of their computed tomography (CT) appearances offers valuable insights into their differential diagnosis and therapeutic approaches.

CT Characteristics of Xp11.2 Translocation/TFE Gene Fusion RCC:

Xp11.2 translocation RCC, characterized by chromosomal translocations involving the TFE3 gene, exhibits diverse CT features. In retrospective studies, these tumors often present as well-defined, enhancing renal masses, typically affecting younger individuals [18]. The imaging appearance of Xp11.2 translocation RCC on CT varies widely, ranging from homogeneous to heterogeneous enhancement patterns. Often, these tumors manifest as hypervascular lesions with avid enhancement during the arterial phase, reflecting their rich vascularity [19].

Furthermore, Xp11.2 translocation RCC frequently demonstrates areas of necrosis or hemorrhage, contributing to its heterogeneous appearance on CT scans. Intratumoral calcifications, though less common than in other RCC subtypes, may be present, adding to the complexity of radiological interpretation [20]. Additionally, these tumors tend to exhibit infiltrative growth patterns and are associated with lymphadenopathy and distant metastases, which can be identified through careful CT evaluation.

CT Characteristics of Papillary Renal Cell Carcinoma:

Contrastingly, papillary renal cell carcinoma, encompassing type 1 and type 2 subtypes, displays distinct CT characteristics that aid in its differentiation from other renal malignancies [21]. Type 1 PRCC often presents as a well-marginated, heterogeneously enhancing mass, with frequent cystic components. On CT imaging, these cystic areas may exhibit fluid-fluid levels, indicative of hemorrhage or proteinaceous debris within the cystic spaces [22].

In contrast, type 2 PRCC tends to manifest as a solid, hypovascular mass with minimal enhancement on CT scans. The absence of significant enhancement during the arterial phase distinguishes type 2 PRCC from other RCC subtypes [23]. Moreover, both type 1 and type 2 PRCC are related with the propensity for

multifocality and bilateral involvement, necessitating comprehensive imaging evaluation for accurate staging and management.

Comparative Analysis:

When juxtaposing the CT appearances of Xp11.2 translocation RCC and PRCC, several distinguishing features emerge. While both subtypes may exhibit heterogeneous enhancement patterns, Xp11.2 translocation RCC tends to demonstrate greater vascularity and avid enhancement during the arterial phase compared to PRCC. Additionally, the presence of necrosis and intratumoral calcifications is more commonly observed in Xp11.2 translocation RCC, albeit not exclusive to this subtype [24].

Conversely, PRCC often presents with characteristic cystic components, particularly in type 1 tumors, which are less frequently encountered in Xp11.2 translocation RCC. The absence of significant enhancement during arterial phase, especially in type 2 PRCC, serves as a distinguishing feature aiding in the differentiation of these two subtypes on CT imaging [25].

Furthermore, the age distribution and clinical behavior of Xp11.2 translocation RCC and PRCC differ significantly. Xp11.2 translocation RCC predominantly affects pediatric and young adult populations, whereas PRCC typically presents in older individuals. Moreover, Xp11.2 translocation RCC is related with a higher propensity for lymph node involvement and distant metastases compared to PRCC, impacting treatment strategies and prognostication.

A comparative analysis of CT appearances in Xp11.2 translocation RCC and PRCC underscores importance of recognizing their distinct radiological features for accurate diagnosis and management. While both subtypes may share certain imaging characteristics, careful evaluation of enhancement patterns, presence of cystic components, and associated findings such as necrosis and lymphadenopathy facilitate their differentiation on CT imaging, guiding optimal therapeutic approaches and prognostic assessments.

CONCLUSION:

The comparative research of CT appearances in renal carcinoma related with Xp11.2 translocation/TFE gene fusion and papillary renal cell carcinoma revealed distinct radiological features indicative of their respective pathological entities. The renal carcinomas with Xp11.2 translocation/TFE gene fusion exhibited characteristic imaging findings such as heterogeneous enhancement, necrosis, and cystic components. Conversely, papillary renal cell carcinomas typically presented with a more homogeneous enhancement pattern and calcifications. These divergent CT appearances underscore the importance of precise radiological evaluation in distinguishing between these two subtypes of renal carcinoma, aiding in accurate diagnosis and subsequent management decisions.

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