

Primary intraparenchymal squamous cell carcinoma of the kidney: A challenge to exclude the histologic mimickers

Primary neoplasms of the renal pelvis are rare and account for approximately 7% of all renal tumors; the majority of them are of transitional cell type, which can show extensive squamous differentiation leading to the erroneous diagnosis. Similarly, urothelium can display a wide range of metaplastic changes, and the malignant neoplasms arising from this epithelium may pose a challenge for histopathologic diagnosis.^[1]

Primary squamous cell carcinoma (SCC) of the renal pelvis is a rare but relatively known entity with a variable incidence of about 0.5-15% of all the urothelial cancers^[2] and is thought to arise through a process of metaplasia mostly keratinizing squamous metaplasia of the urothelium, which increases the chances of SCC in future. However, the concept of squamous metaplasia as the forerunner of SCC of the urothelial tract has been inflicted with controversies, and variable opinions were derived from previous studies. The disagreement may partially be due to the relative rarity of SCC of the upper urinary tract. The etiological factors, namely, recurrent urinary tract infections with or without vesicoureteric reflux, long standing calculi, smoking, schistosomiasis, exogenous and endogenous chemicals, Vitamin A deficiency, hormonal imbalance, and so forth, are the leading ones in renal pelvis SCC.^[3]

Whenever the SCC is found infiltrating the renal parenchyma, the possibility of metastasis from another site, such as a lung primary, must be considered and correlated with clinical information.^[4] Although most of the secondary SCCs in the kidney have been reported from lungs, there are few cases where the metastasis developed from esophagus, hypopharynx, and adenosquamous carcinoma of the intrahepatic bile duct.

Morphologically, squamous differentiation is characterized by sheets of cells with well-defined cell borders with or without intercellular bridges, deeply eosinophilic cytoplasm and focal or extensive keratin pearl formation.^[1]

Hence, a tumor with squamous cell morphology in the kidney in a middle aged to the elderly patient should be meticulously sampled to differentiate among the primary urothelial carcinoma with squamous differentiation, primary SCC of the renal pelvis, metastatic SCC to kidney and primary intraparenchymal SCC of the kidney. The pelvic urothelium is the key structure to arrive at diagnosis in addition to extensive radiological investigation to exclude the primary SCC in any other site.

In the presence of an identifiable urothelial dysplastic element including urothelial carcinoma *in situ* or area of transition from urothelial carcinoma to squamous differentiation, the tumor should be classified as primary urothelial carcinoma with squamous differentiation which is common in high grade and sarcomatoid variants of urothelial carcinomas. However, the conspicuous presence of keratinizing squamous metaplasia of the adjacent flattened urothelium, especially if associated with dysplasia, supports a diagnosis of primary SCC of the renal pelvis, which is rare.^[4,5] Primary intraparenchymal SCC of the kidney should further be distinguished from metastatic SCC with the combination of clinical history, imaging studies, and histopathology.^[3]

The prognosis of SCC in renal pelvis is poor, but stage for stage the prognosis is not different between patients with urothelial carcinoma and SCC of the renal pelvis and ureter. High stage SCC and urothelial carcinoma become symptomatic first at a time when the tumors already are large, deeply invasive and most often incurable.^[6] As the prevailing data regarding the incidence, histogenesis, disease course, and prognosis of primary intraparenchymal SCC are very inadequate, it needs further future evaluation to provide comprehensive data on this entity.^[7]

Mukherjee *et al.*^[8] presented a very nice case of primary SCC of the renal parenchyma in this issue. I hope that you will

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find this article a pleasant reading and useful resource for your knowledge.

I am really grateful to the Editor-in-Chief of Clinical Cancer Investigation Journal, Ala Eddin Al-Moustafa, for allowing me the opportunity to share my knowledge through this guest editorial.

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