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A Review Of The Case Reports On Metastatic Renal Cell Cancer In The Absence Of Tumour In Primary Organ

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Abstract

Summary. The aim of this review was to search for case reports concerning the presentation, diagnosis, and management of metastatic RCC in the absence of a primary tumour in the primary organ, i.e., kidneys. The most common presentation involves lymph nodes, with varying clinical manifestations such as pain, haematuria, confusion, mass, lymph node enlargement, or biochemical changes like hypercalcemia. Case reports illustrate clear cell RCC as the most common histopathology, often presenting as lymph node masses. Immunohistochemical staining is typically positive for vimentin, cytokeratin, and CD 10. The prognosis for mRCC CUP with Immunotherapy and Tyrosine Kinase Inhibitors (TKIs) has shown promising responses with or without surgery, better than metastatic RCC. The decision for treatment needs an individualized approach as recommended by the specific CUP MDT arranged.

Keywords. Metastatic Renal cell cancer (mRCC), Cancer of unknown primary (CUP), Renal cell carcinoma

Introduction:

Carcinoma of unknown primary origin (CUP) refers to metastatic cancer where the primary site remains unidentified despite standard investigations. It represents approximately 3% of diagnosed human cancers ¹.

Diagnostic and management challenges arise due to its aggressive spread and unpredictable metastatic pattern ². CUP is characterized by theories suggesting either undetectable primary lesions or regression of primary

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tumours ³. NICE categorizes metastatic cancers into Malignancy of Uncertain Primary Origin/site/organ (MUO), Provisional Carcinoma of Undetermined Primary Organ/origin/site (Provisional CUP), and Confirmed Carcinoma of Unknown Primary Origin (Confirmed CUP). The objective of this review is critical appraisal and thorough evaluation of cases of interest, examining their presentation, diagnostic processes, assessments, treatment

approaches, and ultimate outcomes as reported in various case studies.

A literature search from 2013 to Jan 2024 was conducted on PubMed and Google Scholar using keywords related to metastatic renal cell cancers with an unknown primary organ. Nine relevant case reports were identified and included in the review. Data were extracted and presented in a Table.

Table. case reports and outcome

Cases reported	Symptoms and signs	Findings/pathologies	Immunohistochemical staining	Surgery performed	Adjuvant treatment	outcome	Learning outcomes/learned
Shields and Kalebasty, 2020	No symptoms/ Absence of hematuria, pain, or any other urinary symptoms.	A left retroperitoneal lymph node measuring 1.8 cm	PAX 8,(CK), AE1, and AE3.	RPLND	no	No recurrence	Retroperitoneal lymph node dissection helps in metastatic CUP RCC
Kumar et al., 2014	Elevated calcium levels, cognitive confusion.	bone lesions in the left side scapula bone. Right side 7 th rib , the fifth rib on the left side, and the left (SCJ)sternoclavicular joint .left pulmonary nodules	Detection of cam5.2, vimentin, and cd10 with positive staining.	No surgery	Sunitinib and Zolendronic acid	Regression of pulmonary lesions and bone metastasis	Adjuvant therapy beneficial in mCUP RCC treatment
Thamcharoen and Chaiwiriya Wong , 2013	Abdominal and chest Hilar lymphadenopathy	Slight reticular densities at the apex of the right lung, mass on the left side of the neck, and at the renal level.	CD10, Vimentin and RCC	No surgery	Sunitinib	Stable disease	Immunohistochemical staining
Choi et al., 2012	Gradual emergence of a mass in the right supraclavicular region.	right supraclavicular LN enlargement	Expressing positivity for pan-cytokeratin, Vimentin, and CD10.	No surgery	Radiotherapy with adjuvant sunitinib	Regression of the lesions	Radiotherapy and Adjuvant therapy
Wayne et al., 2010	Appearance of mass subcutaneous	Pancreatic body mass	CD10,AE1/AE3, PNRA, Vimentin	Surgical excision, 1- superficial parotidectomy, 2- central pancreatectomy	No	Surgically excised metachronous oligometastatic	Surgical excision of single lesion (metastatic)
Hlaing et al., 2022	Bronchitis	T8, T7, T11 and L1 lesions	Expression of cytokeratin's (AE1/AE3), CD10, and nuclear staining for PAX8, , negative staining for CK7, P40, and TTF.	palliative radiation therapy	no	X	Radiotherapy + Immunohistochemical staining of biopsy tissue is helpful

Fayaz MS et al.,2017	neck mass (Left side) increasing Progressively.	4.7 × 3 × 3.3 cm (left Supraclavicular , left submandibular gland was observed.	Cytokeratin (CAM 5.2) and CD10, strong positivity, robust positive expression for PAX8 and vimentin.	No surgery	pazopanib	no progression of the disease	Prognostic and diagnostic Genomic profiling, immunohistochemical staining help in diagnosis.
Bimbatti et al.,2023	Pain abdomen	liver lesions, including a substantial tumour measuring 13 cm , lymph nodes in proximity to the pancreas and hepatic/liver hilum, the largest of which had a short axis of 3.5 cm.	PAX8.affirmative staining for PAX 8, MNF-116, and CD10	No surgery	Axitinib 10 mg /day, And Pembrolizumab 200 mg every 3 weeks	6 months CT. reduction of more than 30%	Tyrosine Kinase Inhibitors + immunotherapy, first-line treatment.
Abian N.,et al 2024	Lumbar pain	vertebral mass	clear cytoplasm, oval nuclei. Immunohistochemical (IHC) analysis positive reactivity for PAX8, EMA, CAIX, CD10, and CK	corpectomy and pedicle resection along with tumor removal	Sunitinib50 mg	Follow up CT scan3 months no sign of renal tumour, disease progression	Surgery + sunitinib option in CUP-mRCC in solitary bone lesion

Table 1 shows the diversity of presentation of different reported cases, histological findings for immunohistochemical staining and outlines the outcomes that are with or without surgery for the lesion. Clinical presentations varied, mostly including lymph node masses ⁴, bone lesions ⁵, and liver involvement. Investigations involved CT scans, PET imaging, and serum marker tests. Histological examinations confirmed mostly clear cell RCC through immunohistochemical staining. Treatments ranged from surgery to targeted therapies, with positive outcomes observed in terms of regression or stable disease. The cases highlighting the importance of personalized treatment strategies based on individual patient characteristics and disease biology. Management includes surgery, targeted therapies, immunotherapy, and radiation therapy, depending on the extent of disease and patient factors. Immunohistochemical staining play crucial roles in diagnosis and treatment planning. An important finding is that the response to treatment shows either regression or stable disease in case of metastatic RCC Carcinoma of

Unknown primary. While an analysis based on the SEER database shows he median survival for patients with lung, bone, liver, or brain metastasis was 7 months, 7 months, 4 months, and 5 months, respectively ⁶.In conclusion, this review of reported cases underscores the diverse clinical presentations and treatment modalities in metastatic clear cell renal cell carcinoma (mCUP RCC). Immunohistochemical staining played a crucial role in confirming diagnoses and guiding treatment decisions. Surgical interventions such as retroperitoneal lymph node dissection and excision of metastatic lesions demonstrated favourable outcomes, while adjuvant therapies, including targeted agents and immunotherapy, showed promising results in controlling disease progression. These findings emphasize the importance of a multidisciplinary approach, incorporating both surgical and medical interventions, in the management of mCUP RCC, and highlight the significance of immunohistochemical staining in diagnosis and treatment planning.

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