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Commentary

Adapted and Remodelled-ELOC Mutated Renal Cell Carcinoma

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ELOC mutated renal cell carcinoma configures as a variant of renal cell carcinoma which histologically simulates clear cell renal cell carcinoma and clear cell papillary renal cell tumour. ELOC mutated renal cell carcinoma is constituted of aggregates of clear cells permeated with voluminous, clear cytoplasm. Tumour parenchyma is traversed by thick bands of fibromuscular tissue wherein the fibromuscular septa may induce a multi-lobular neoplastic appearance.

ELOC mutated renal cell carcinoma is additionally designated as transcription elongation factor B (TCEB1) mutated renal cell carcinoma or monosomy 8 renal cell carcinoma.

Previously denominated as TCEB1 mutated renal cell carcinoma and renal cell carcinoma with TCEB1 mutation, neoplasm requires demarcation from TFEB renal cell carcinoma or renal tumour with t(6;11) translocation. Neoplasm is non concordant with renal angiomyoadenomatous tumour.

The exceptionally discerned tumefaction commonly incriminates subjects between 32 years to 77 years.

ELOC mutated renal cell carcinoma manifests as a solitary tumefaction incriminating renal parenchyma. Generally, neoplasm is confined to renal cortex [1,2].

The low grade tumefaction is accompanied by bi-allelic inactivation or mutation of TCEB1 gene which appears concurrent with monosomy 8. Loss of heterozygosity at chromosome 8q21 may occur. Additionally, lack of VHL genetic mutations with hyper-methylation or loss of heterozygosity at chromosome 3p may be delineated [1,2].

Tumefaction enunciates TCEB1 gene situated upon chromosome 8q21.11 which encodes 112-residue protein elongin C subunit 1 of transcription factor B (SIII) complex. Transcription elongation factor B-polypeptide 1 (TCEB1) emerges as a segment of a complex which adheres to genomic product of VHL gene, consequently functioning as a tumour suppressor [2,3].

Notwithstanding, elongin C configuring a segment of VHL complex engenders proteosomic degradation or ubiquitination of hydroxylated hypoxia inducible factor (HIF) [2,3].

Subsequently, decimated elongin C engenders stabilization of HIF1α along with accumulation and activation of hypoxia inducible growth factors which enhance neoplastic development. Additionally, downregulation of diverse genes incriminated within ubiquitination complex such as POLR2E, POLR2C, CDK7, TCEA1 and TCEB2 may ensue. Elevated POL II transcription in concurrence with elongation past template and encoding of arresting genetic sites may be encountered. Neoplasm exhibits hotspot genetic mutations confined to TCEB1 gene along with loss of chromosome 8 and loss of heterozygosity at position 8q or monosomy 8. Genomic mutations within TCEB may appear non concurrent to VHL anomalies.

ELOC mutated renal cell carcinoma exhibits genetic mutations within TCEB1, Tyr79, Ala100, Ala 106 or Ser23 [2,3].

Copy number analysis expounds loss of heterozygosity of chromosome 8 along with copy neutral loss of heterozygosity.

Also, RNA expression analysis exemplifies mRNA downregulation within POLR2E, POLR2C, CDK7, TCEA1 and TCEB2 genes.

Majority of neoplasms are discovered incidentally and configure stage T1a. Exceptionally, advanced grade tumours of stage T3a may be expounded [2,3].

Grossly, neoplasm is uni-focal, nodular or lobulated, well circumscribed and partially encapsulated. Tumour magnitude varies from 1.6 centimetres to 3.5 centimetres. Cut surface appears cystic, pale or tan and is traversed by fibro-muscular bands [3,4].

Upon low power examination, the multi-nodular neoplasm is constituted of clear cells. Tumour parenchyma is traversed by bands of thick fibrous tissue or fibromuscular tissue [3,4].

Neoplasm enunciates variable architecture comprised of solid, alveolar or nested tumour configuration. An intermingling of diverse patterns may be discerned. Occasionally, neoplasm may delineate cystic or tubulo-papillary articulations [3,4].

Tumour cells are incorporated with voluminous, preponderantly clear cytoplasm and demonstrate conspicuous cellular membranes with inconspicuous nucleoli. Neoplasm is comprised of clear cells pervaded with abundant apical cytoplasm, basal nuclei and nucleoli with nucleolar grade II. Occasionally, luminal nuclei may be observed. Tumour parenchyma is traversed by distinct fibromuscular bands.

Circumscribing stroma is devoid of an intense infiltrate of inflammatory cells. Tumour necrosis, lymphatic invasion or vascular invasion is absent [3,4].

Molecular variants	Mutated genes	Genetic location	Chaperone genes
TFE3 rearranged RCC	Transcription factor binding to IGHM enhancer 3 (TFE3)	Xp11.23	ASPL, PRCC, SFPQ, CLTC, PARP14, RBM10, NONO, MED15
TFEB altered RCC	Transcription factor EB (TFEB)	6p21	MALAT1, CLTC, KHDRBS2, CADM2
ELOC mutated RCC	Elongin C	8q21.11	None
Fumarate hydratase deficient RCC	Fumarate hydratase (FH) gene	1q43	None
Succinate dehydrogenase deficient RCC	Succinate dehydrogenase (SDH)	SDHA: 5p15 SDHB: 1p35-p36.1 SDHC: 1q21 SDHD:11q23	None
ALK rearranged RCC	Anaplastic lymphoma kinase (ALK)	2p23	VCL, TPM3, EML4, STRN, HOOK1
SMARCB1 deficient RCC	Subfamily B member 1 (SMARCB1)	22q11.2	None

Table: *Molecular characterization of renal cell carcinoma [3].*

RCC: Renal Cell Carcinoma.

Neoplastic cells appear immune reactive to carbonic anhydrase IX (CAIX), CK7, CD10, succinate dehydrogenase subunit B (SDHB) or hypoxia inducible factor 1 α (HIF1α).

Tumour cells appear immune non reactive to transcription factor E3 (TFE3), high molecular weight cytokeratin (HMWCK), α methylacyl CoA racemase (AMACR), CK34βE12, human melanoma black antigen 45 (HMB45), Melan A or Cathepsin K [4,5].

ELOC mutated renal cell carcinoma requires segregation from neoplasms such as clear cell renal cell carcinoma, clear cell tubulo-papillary renal cell carcinoma, renal cell carcinoma with angioleiomyomatous stroma, tuberous sclerosis complex associated renal cell carcinoma or MiT family translocation renal cell carcinoma [4,5].

ELOC mutated renal cell carcinoma is optimally treated by surgical manoeuvers as partial nephrectomy or radical nephrectomy.

Prognostic outcomes are superior. Tumour reoccurrence or distant metastasis remains undocumented [4,5].

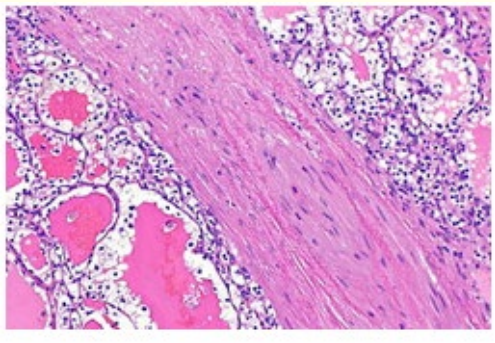

Figure 1: *ELOC mutated renal cell carcinoma demonstrating nests of tumour cells imbued with voluminous clear cytoplasm, regular nuclei and inconspicuous nucleoli. Tumour expanse is traversed by thick, fibromuscular bands. Surrounding stroma is devoid of an inflammatory exudate [6].*

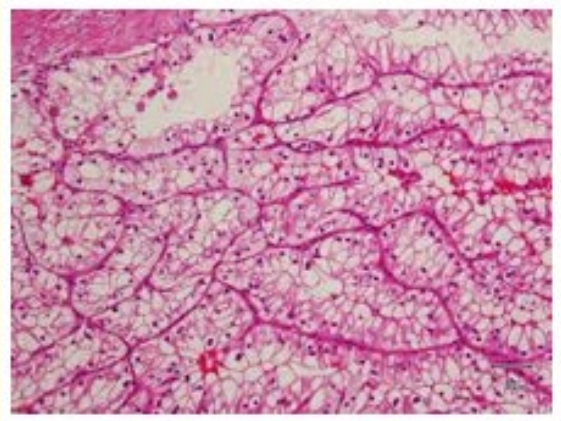

Figure 2: *ELOC mutated renal cell carcinoma delineating solid areas of tumour cells pervaded with abundant clear cytoplasm, uniform nuclei and inconspicuous nucleoli. Intervening stroma is scanty and non inflamed [7].*

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6. Image 1 Courtesy: Libre pathology.

7. Image 2 Courtesy: Europe PMC.

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