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Kidney Cancer. 2017 Nov 27;1(2):143-149. doi: 10.3233/KCA-170013.

1. ## Tissue Expression of Erythropoietin Predicts Survival Rates in Clear Cell Renal Cell Carcinoma.

Ferreira DB[1], da Costa WH[1], Clavijo DA[2], Decia R[2], Cunha IW[3,4], **Schultz L**[4], Rocha RM[4], Guimarães GC[5], Zequi SC[1,3].

Author information

Abstract

OBJECTIVE: To evaluate immunohistochemical erythropoietin (EPO) expression in clear cell renal cell carcinoma (ccRCC), its association with major clinicopathological variables and its prognostic impact.

METHODS: A total of 220 patients with renal cell carcinoma (RCC) surgically treated between 1989 and 2009 were evaluated in this multi-institutional study. All the cases were reviewed by a single pathologist and the immunohistochemical reactivity to EPO was analysed using tissue microarray.

RESULTS: A total of 176 patients with ccRCC were considered, with an average of 48 months of follow-up. Of the tumours evaluated, 47 (26.7%) were negative for EPO expression, and 129 (73.3%) were positive. EPO expression was associated with incidental tumour (p=0.016), tumour size (p=0.015), Karnofsky Performance Score (KPS) (p=0.016), blood transfusion (p=0.009) and adrenal involvement (p=0.038). The median ages of the patients with positive and negative EPO expression were 56.2 years and 66.6 years. Immunohistochemical EPO expression affected overall survival (OS) and disease-specific survival (DSS) rates. The DSS rates of the patients whose tissue was positive and negative for EPO expression were 85.3% and 76.1%, respectively (p=0.044). In a multivariate analysis, the absence of EPO expression proved to be a bad prognostic factor and negatively affected the OS (p<0.001) and DSS (p<0.001) rates.

CONCLUSION: The absence of tumour EPO expression is an independent predictive factor with a negative effect on survival rates. The use of EPO as possible marker in the

management of ccRCC patients requires further studies and a better understanding of the role of EPO in tumour biology.

KEYWORDS: Biomarkers; EPO; oncology; prognosis; renal cell carcinoma

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Free PMC Article

Hum Pathol. 2019 Jan;83:159-165. doi: 10.1016/j.humpath.2018.08.021. Epub 2018 Sep 1.

2. ## Histologic findings associated with false-positive multiparametric magnetic resonance imaging performed for prostate cancer detection.

Gordetsky JB[1], Ullman D[2], **Schultz L**[3], Porter KK[4], Del Carmen Rodriguez Pena M[2], Calderone CE[5], Nix JW[5], Ullman M[6], Bae S[7], Rais-Bahrami S[8].

Author information

Abstract

Magnetic resonance imaging (MRI)/ultrasound fusion-targeted biopsy (TB) has been shown to more accurately identify higher-grade prostate cancers compared with standard-of-care systematic sextant prostate biopsy (SB). However, occasional false-positive imaging findings occur. We investigated the histologic findings associated with false-positive prostate MRI findings. A retrospective review was performed on our surgical pathology database from 2014 to 2017 selecting patients with no cancer detected on TB with concurrent SB after at least 1 prior benign SB session. Histologic features evaluated included percentage of core involvement by chronic inflammation, percentage of core composed of stroma, percentage of glands involved by atrophy, and presence of the following features: acute or granulomatous inflammation, stromal nodular hyperplasia, adenosis, squamous metaplasia, basal cell hyperplasia, and presence of skeletal muscle. Histologic findings were compared between TB and concurrent SB. We identified 544 patients who underwent TB. Of these, 41 patients, including 62 targeted lesions, met criteria. Compared with SB tissue, the mean percentage of stroma was increased in TB (P=.02). Basal cell hyperplasia was also found to be more common on TB (P=.02). Both high percentage of stroma (P=.046) and presence of basal cell hyperplasia (P=.038) were independent predictors on multivariate analysis. The combination of high chronic inflammation, high stroma, acute inflammation, and basal cell hyperplasia was associated with TB (P=.001). Atrophic glands and chronic inflammation showed a positive correlation (r=0.67, P=.003), which was especially seen in high prostate imaging

reporting and data system lesions. Specific benign histologic entities are associated with false-positive findings on prostate MRI.

KEYWORDS: Cancer; False-positive imaging; Histology; Multiparametric MRI; Pathology; Prostate biopsy; Prostatitis

Comment in

Re: Histologic Findings Associated with False Positive Multiparametric Magnetic Resonance Imaging Performed for Prostate Cancer Detection. [J Urol. 2019]

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ELSEVIER FULL-TEXT ARTICLE

Hum Pathol. 2018 Jun;76:68-75. doi: 10.1016/j.humpath.2018.03.005. Epub 2018 Mar 16.

3. ## Defining the optimal method for reporting prostate cancer grade and tumor extent on magnetic resonance/ultrasound fusion-targeted biopsies.

Gordetsky JB[1], **Schultz L**[2], Porter KK[3], Nix JW[4], Thomas JV[3], Del Carmen Rodriguez Pena M[5], Rais-Bahrami S[6].

Author information

Abstract

Magnetic resonance (MR)/ultrasound fusion-targeted biopsy (TB) routinely samples multiple cores from each MR lesion of interest. Pathologists can evaluate the extent of cancer involvement and grade using an individual core (IC) or aggregate (AG) method, which could potentially lead to differences in reporting. We reviewed patients who underwent TB followed by radical prostatectomy (RP). TB cores were evaluated for grade and tumor extent by 2 methods. In the IC method, the grade for each TB lesion was based on the core with the highest Gleason score. Tumor extent for each TB was based on the core with the highest percent of tumor involvement. In the AG method, the tumor from all cores within each TB lesion was aggregated to determine the final composite grade and percentage of tumor involvement. Each method was compared with MR lesional volume, MR lesional density (lesion volume/prostate volume), and RP. Fifty-five patients underwent TB followed by RP. Extent of tumor by the AG method showed a better correlation with target lesion volume (r= 0.27,P= .022) and lesional density (r = 0.32, P = .008) than did the IC method (r= 0.19 [P = .103] andr= 0.22 [P = .062]), respectively. Extent of tumor on TB was associated with extraprostatic extension on RP by the AG method (P= .04), but not by the IC method. This

association was significantly higher in patients with a grade group (GG) of 3 or higher (P= .03). A change in cancer grade occurred in 3 patients when comparing methods (2 downgraded GG3 to GG2, 1 downgraded GG4 to GG3 by the AG method). For multiple cores obtained via TB, the AG method better correlates with target lesion volume, lesional density, and extraprostatic extension.

KEYWORDS: Cancer grading; Cancer staging; Multiparametric MR; Pathology; Prostate cancer; Radical prostatectomy

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Publication type, MeSH terms, Substances

Am J Surg Pathol. 2018 Mar;42(3):279-292. doi: 10.1097/PAS.0000000000001000.

4. # Reappraisal of Morphologic Differences Between Renal Medullary Carcinoma, Collecting Duct Carcinoma, and Fumarate Hydratase-deficient Renal Cell Carcinoma.

Ohe C[1], Smith SC[2], Sirohi D[1], Divatia M[3], de Peralta-Venturina M[1], Paner GP[4], Agaimy A[5], Amin MB[6], Argani P[7], Chen YB[8], Cheng L[9], Colecchia M[10], Compérat E[11], Werneck da Cunha I[12], Epstein JI[7], Gill AJ[13], Hes O[14], Hirsch MS[15], Jochum W[16], Kunju LP[17], Maclean F[18], Magi-Galluzzi C[19], McKenney JK[19], Mehra R[17], Nesi G[20], Osunkoya AO[21], Picken MM[22], Rao P[23], Reuter VE[8], de Oliveira Salles PG[24], **Schultz L**[25], Tickoo SK[8], Tomlins SA[17], Trpkov K[26], Amin MB[1,27].

Author information

Abstract

Renal medullary carcinomas (RMCs) and collecting duct carcinomas (CDCs) are rare subsets of lethal high-stage, high-grade distal nephron-related adenocarcinomas with a predilection for the renal medullary region. Recent findings have established an emerging group of fumarate hydratase (FH)-deficient tumors related to hereditary leiomyomatosis and renal cell carcinoma (HLRCC-RCCs) syndrome within this morphologic spectrum. Recently developed, reliable ancillary testing has enabled consistent separation between these tumor types. Here, we present the clinicopathologic features and differences in the morphologic

patterns between RMC, CDC, and FH-deficient RCC in consequence of these recent developments. This study included a total of 100 cases classified using contemporary criteria and ancillary tests. Thirty-three RMCs (SMARCB1/INI1-deficient, hemoglobinopathy), 38 CDCs (SMARCB1/INI1-retained), and 29 RCCs defined by the FH-deficient phenotype (FH/2SC or FH/2SC with FH mutation, regardless of HLRCC syndromic stigmata/history) were selected. The spectrum of morphologic patterns was critically evaluated, and the differences between the morphologic patterns present in the 3 groups were analyzed statistically. Twenty-five percent of cases initially diagnosed as CDC were reclassified as FH-deficient RCC on the basis of our contemporary diagnostic approach. Among the different overlapping morphologic patterns, sieve-like/cribriform and reticular/yolk sac tumor-like patterns favored RMCs, whereas intracystic papillary and tubulocystic patterns favored FH-deficient RCC. The tubulopapillary pattern favored both CDCs and FH-deficient RCCs, and the multinodular infiltrating papillary pattern favored CDCs. Infiltrating glandular and solid sheets/cords/nested patterns were not statistically different among the 3 groups. Viral inclusion-like macronucleoli, considered as a hallmark of HLRCC-RCCs, were observed significantly more frequently in FH-deficient RCCs. Despite the overlapping morphology found among these clinically aggressive infiltrating high-grade adenocarcinomas of the kidney, reproducible differences in morphology emerged between these categories after rigorous characterization. Finally, we recommend that definitive diagnosis of CDC should only be made if RMC and FH-deficient RCC are excluded.

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Wolters Kluwer

Publication types, MeSH terms, Substances

Urol Case Rep. 2017 Dec 9;17:7-9. doi: 10.1016/j.eucr.2017.12.003. eCollection 2018 Mar.

5. **Bilateral renal involvement by solitary fibrous tumor - Report of a case in the post-WHO/2016 era.**

Bezerra ES[1,2,3], Andrighetto OP[3], Costa MVS[1,2], Chiarelli LO[1,2], Moleiro W[4], **Schultz L**[4].

Author information

KEYWORDS: Bilateral renal tumor; Hemangiopericytoma; NAB2-STAT6; Nomenclature; Renal

metastasis; Solitary fibrous tumor

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Publication type

6. Oral Surg Oral Med Oral Pathol Oral Radiol. 2017 Apr;123(4):e117-e122. doi: 10.1016/j.oooo.2016.10.017. Epub 2016 Nov 1.

Cribriform adenocarcinoma of the soft palate with multiple lymph node metastasis and long-term follow-up.

Mariano FV[1], Varanda RF[2], **Schultz L**[3], Correa MB[4], de Almeida OP[2], Altemani A[5], Lopes MA[2].

Author information

Abstract

INTRODUCTION: Cribriform adenocarcinoma of the tongue and minor salivary glands (CATMSG) is a recently described entity, with most cases previously published as polymorphous low-grade adenocarcinoma (PLGA). Typical cases share some main characteristics, such as oral sites (mainly tongue), regional lymph node metastasis, and morphology resembling solid and follicular variants of papillary thyroid carcinoma.

OBJECTIVE: To present a CATMSG and emphasize the importance of reclassifying PLGAs with unusual behavior.

CASE REPORT: A 78-year-old male presented with an ulcerated mass in the soft palate treated as PLGA. The patient developed 5 regional metastases over 11 years of follow-up, all diagnosed as PLGA. He died due to the disease, and because of the very aggressive behavior of PLGA, all histopathologic slides were revised and the tumor was reclassified as CATMSG.

CONCLUSION: This report emphasizes the importance of reevaluating aggressive PLGA and contributes to a better understanding of CATMSG.

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Publication type, MeSH terms

Urol Oncol. 2016 Nov;34(11):484.e9-484.e17. doi: 10.1016/j.urolonc.2016.05.031. Epub 2016 Jul 1.

7. # Ulceration in bladder cancer associates with extravesical disease, independent of cell cycle, or hypoxia pathways status: Integrating gross morphology and expression profiles in cystectomies.

Schultz L[1], Spagnul SJT[1], Damm GR[1], da Cunha IW[2], Bezerra SM[3], da Costa WH[4], Guimaraes GC[5], Zequi SD[5], Soares FA[2].

Author information

Abstract

OBJECTIVE: Ulceration is common in bladder tumors, but its prognostic role, although intuitive, is not established. We aim to explore the presence of gross ulceration and its relationship with other morphological and biological features classically associated with extravesical disease, in patients submitted to radical cystectomy.

METHODS: Tumor size and morphology were noted on 101 cystectomy patients (2000-2010). Papillary, exophytic, and vegetant tumors were grouped as "papillary" and solid/nodular, ulcerated and infiltrative as "nonpapillary." Ulceration was noted grossly in every case as a binary parameter, regardless of morphology. Immunohistochemistry was performed for hypoxia (hypoxia-inducible factor-1α and vascular endothelial growth factor), and cell cycle proteins (pRb, p53, and cyclin D1).

RESULTS: Mean age was 66.7 year, male:female ratio was 2:1, 20 patients received bacillus Calmette-Guerin and 10 neoadjuvant chemotherapy. Upstaging rate was 56.4%. Ulcerated lesions presented mostly as nonpapillary and nonorgan confined (nOC), whereas nonulcerated tumors were often papillary and organ confined (OC). Tumor size was smaller in nonpapillary tumors (P = 0.002), but did not associate with altered hypoxia or cell cycle expressions. pRb and cyclin D1 loss and p53 overexpression were more frequent in ulcerated and non-OC tumors as did the phenotype vascular endothelial growth factor-negative/hypoxia-inducible factor-1α-low (P<0.001). On a multivariate model, ulceration was

an independent predictor of non-OC and extravesical disease.

CONCLUSION: Patients with ulcerated tumors were often staged with extravesical disease, independent of other morphologic and biological features known to affect prognosis. Prospective studies are needed to confirm the predictive value of tumor ulceration at cystoscopy, which could improve patient stratification for neoadjuvant chemotherapy.

KEYWORDS: Bladder cancer; Cell cycle; Hypoxia; Morphology; Ulceration; pappilary

PMID: 27377810 DOI: 10.1016/j.urolonc.2016.05.031

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