Nové a nastupující typy renálního karcinomu

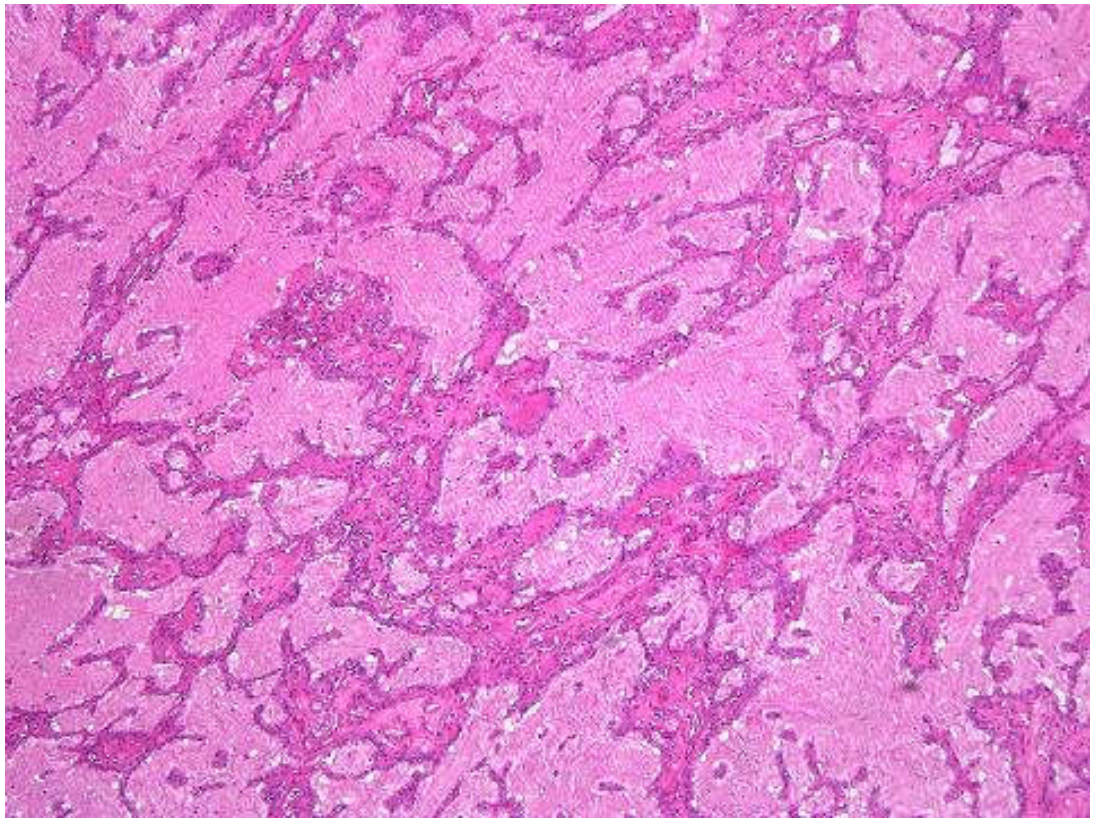
Ondřej Hes
ŠÚP FN a LF Plzeň, Bioptická laboratoř Plzeň
Senec 28.6.2019

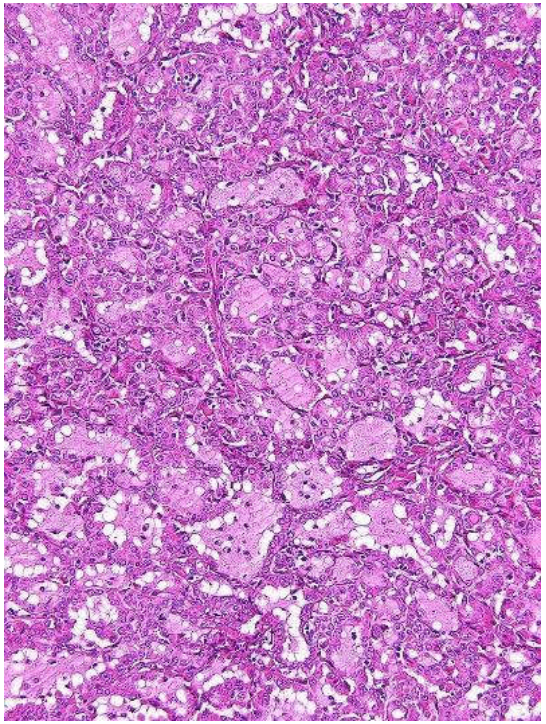
ALK-RCC

(Chromosomal rearrangements involving the *anaplastic lymphoma kinase gene (ALK*) at 2p23)

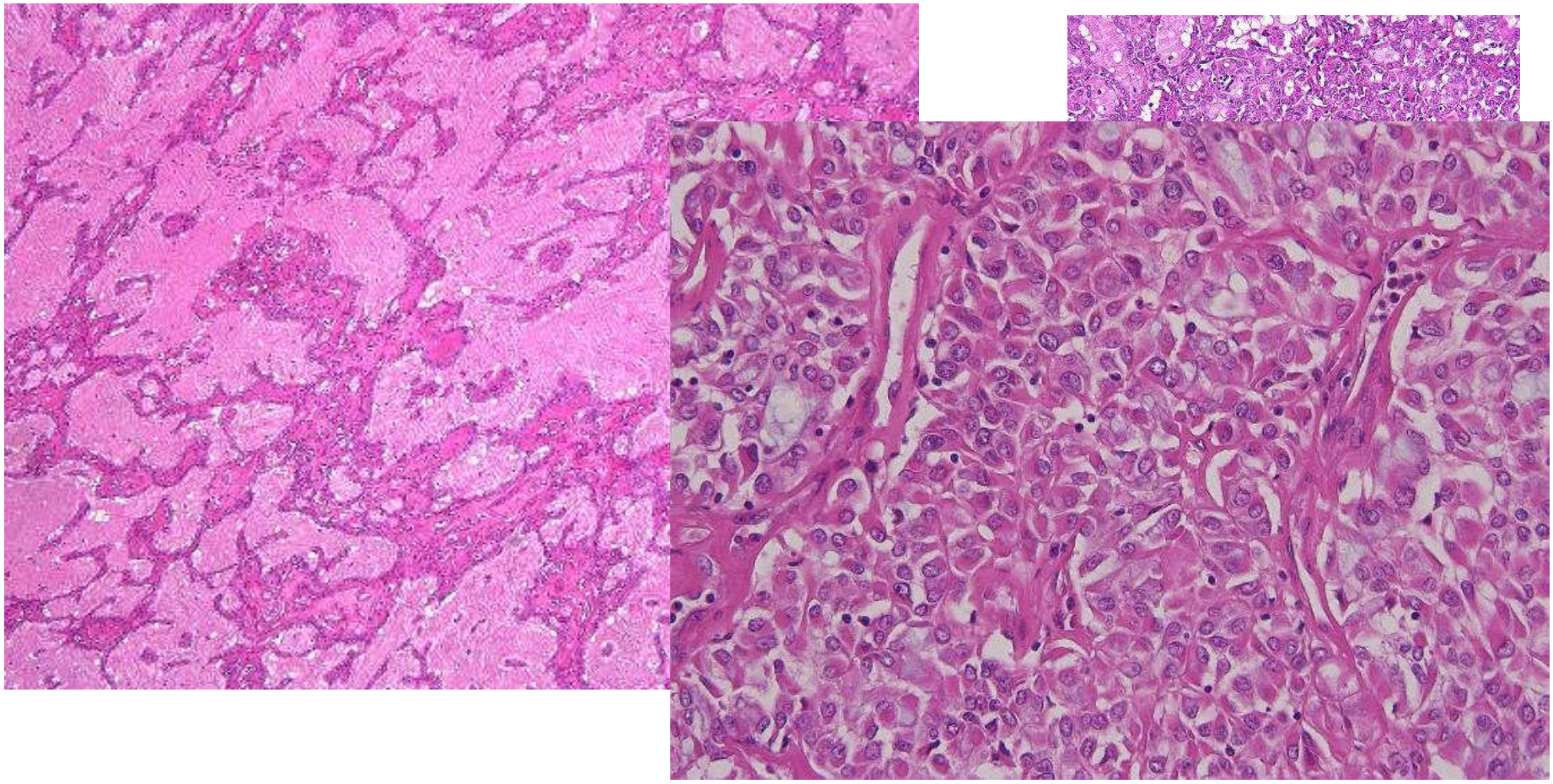
- „ALK-rearranged“ renální tumor je geneticky distinktní tumor
- Různí partneři: *STRN, KIF5B (CLIP1, KIF5B, KIAA1217*)
- Morphologie: „signet-ring“ buňky, myxoidní pozadí, solidní architektura a rhabdoidní buňky
- Metanefrický adenom nebo MTS-RCC ??!!.
- Immunohistochemie: ALK protein
- FISH *ALK* genu/NGS-Archer

ALK translocation RCC-papilární léze s mucinem

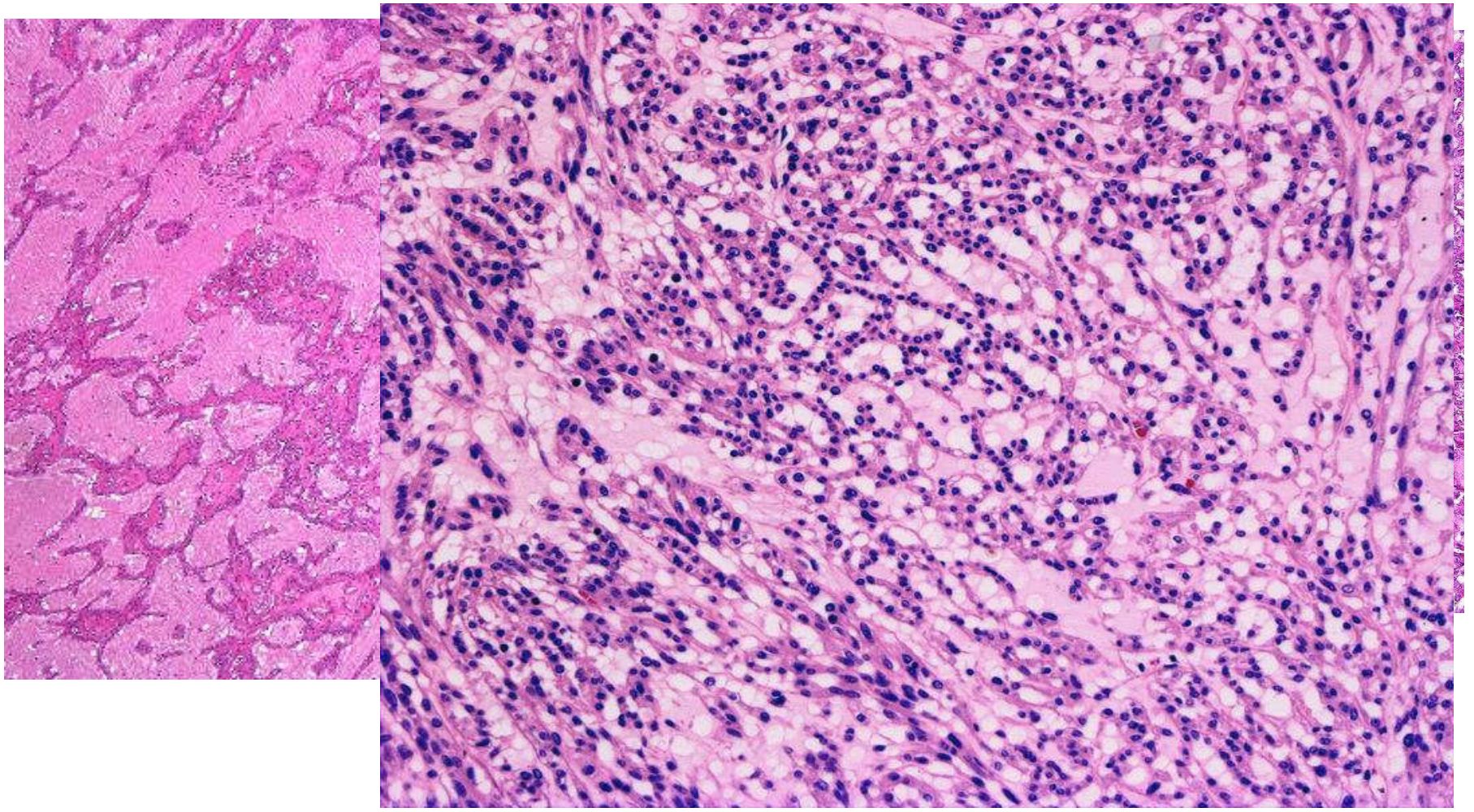




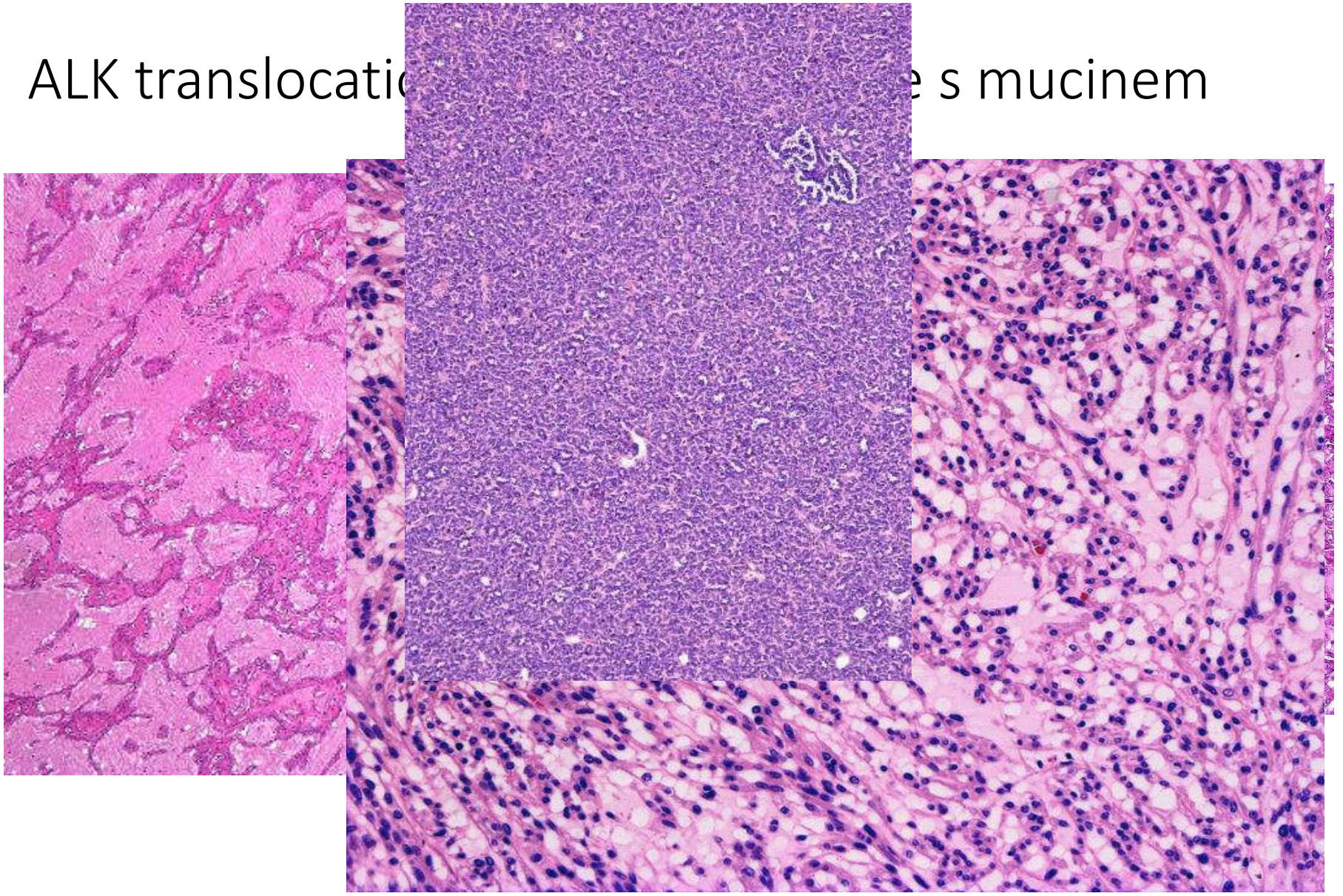
ALK translocation RCC-papilární léze s mucinem



ALK translocation RCC-papilární léze s mucinem



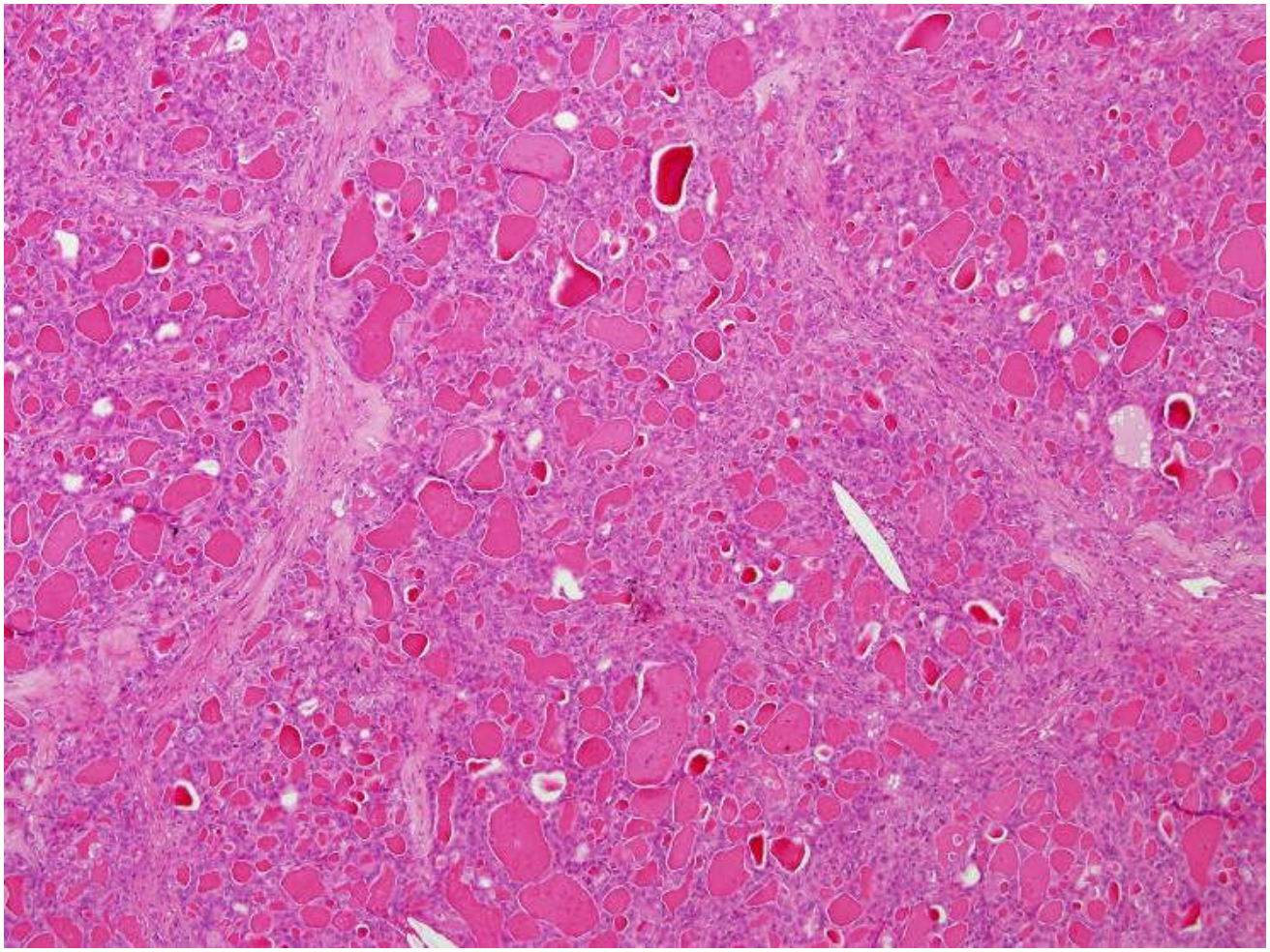
ALK translocati e s mucinem



Thyroid-like follicular tumor/karcinom ledviny

- 4 případy (2019) s meta do uzliny, 1 s meta do plic
- Věk 29 - 83 let
- Častěji u žen (F:M=8:5)
- Spojení s leukemií, nefrolithiasou, end-stage kidney

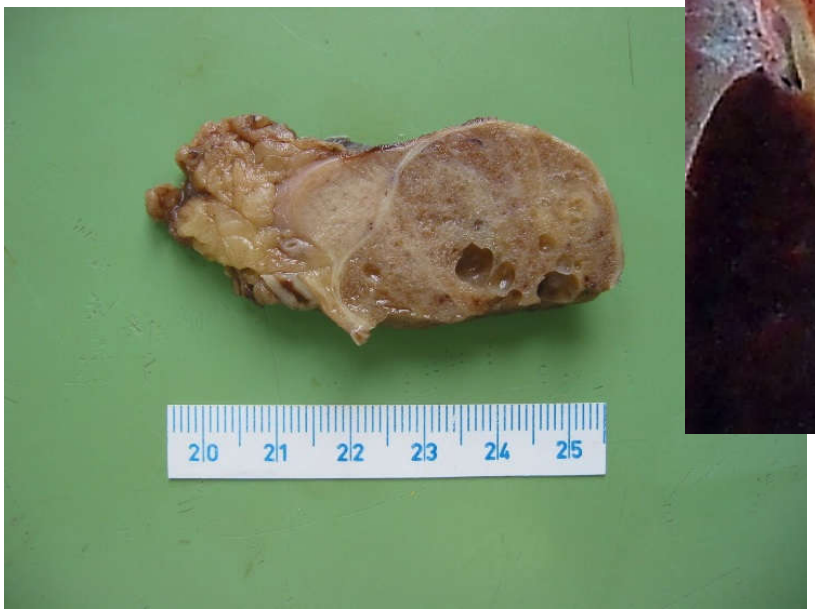
Thyroid-like follicular tumor/carcinoma of the kidney

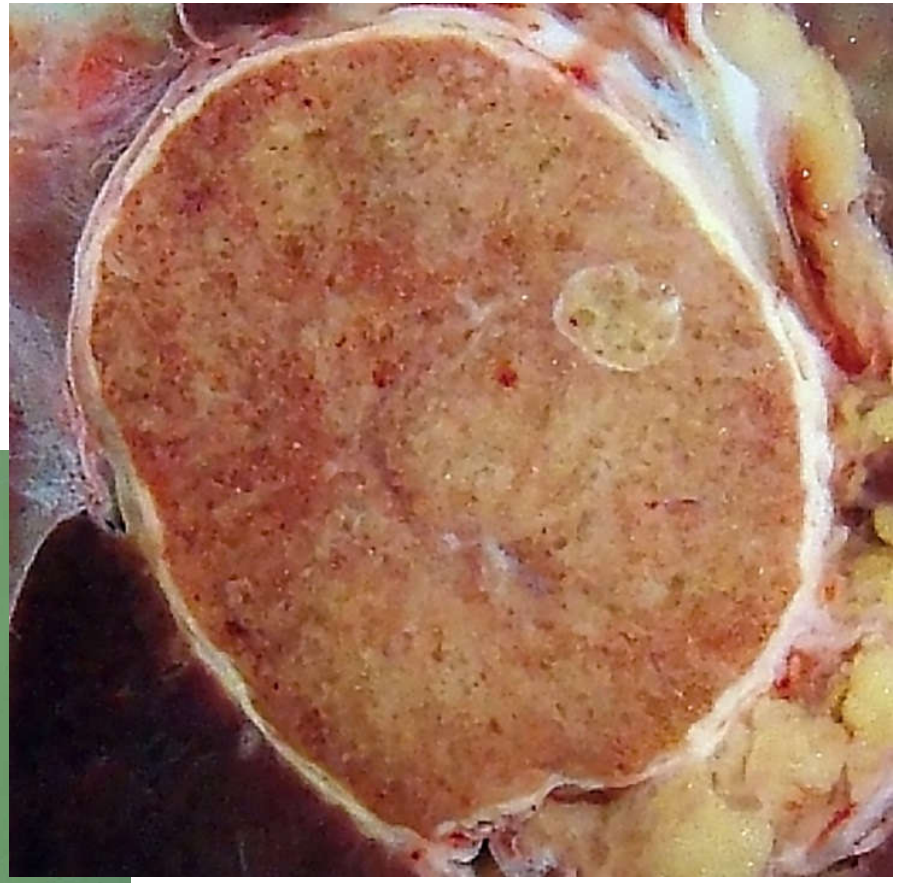


Diferenciální diagnóza

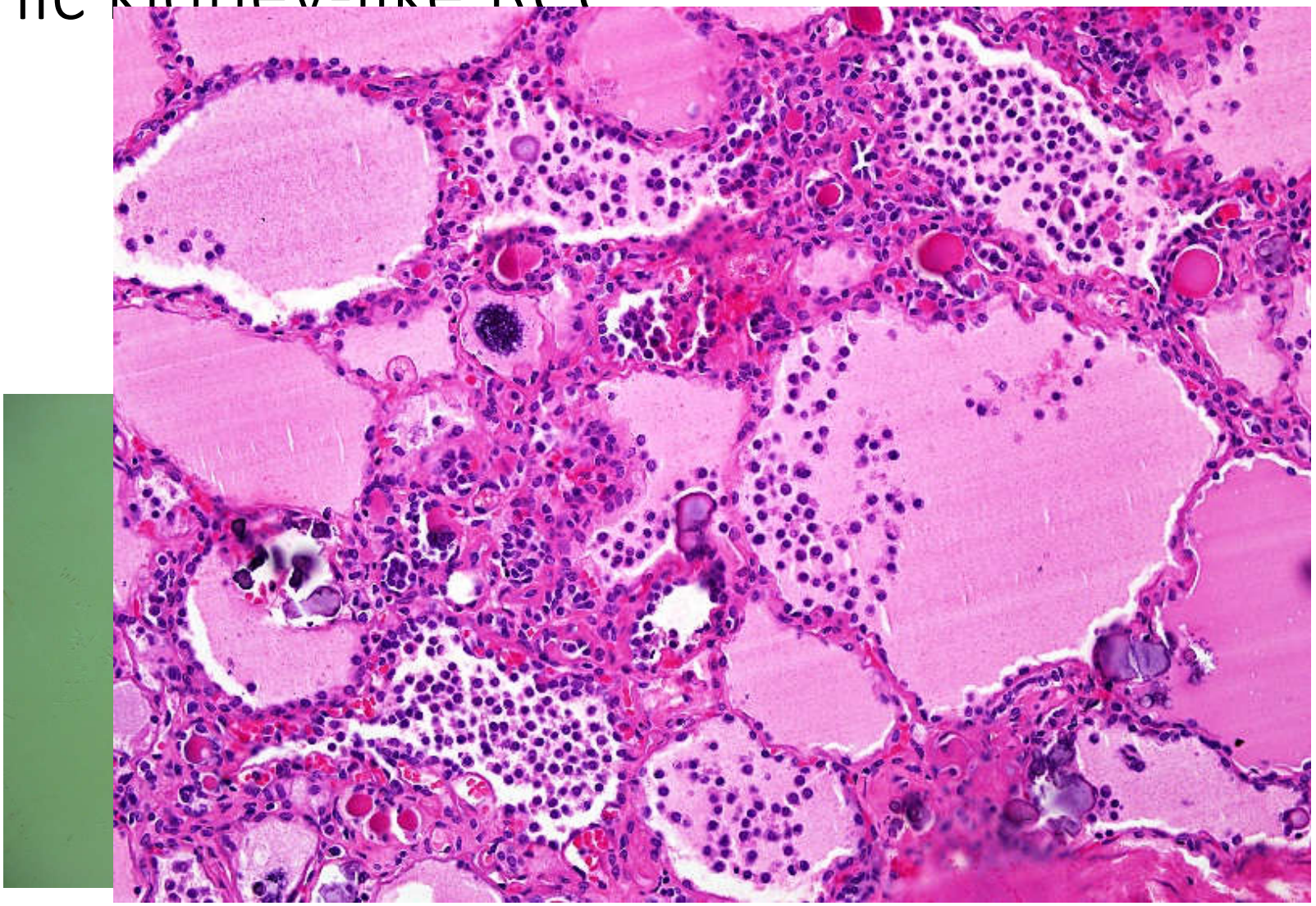
- Meta tyroidálního karcinomu (!!): IHC- thyreoglobulin, TTF1
- Papilární RCC
- Primární nebo sekundární teratom: sampling (!), gain 12p
- A…..atrophic-kidney like tumor

Atrophic kidney-like RCC





Atrophic kidney-like RCC



Annals of Diagnostic Pathology 18 (2014) 82–88

Contents lists available at ScienceDirect

Annals of Diagnostic Pathology

Distinctive renal cell tumor simulating atrophic kidney with 2 types of microcalcifications. Report of 3 cases☆,☆☆

Ondrej Hes, MD, PhD [a,b], Tulio Geraldo de Souza, MD [c], Kristyna Pivovarcikova, MUC [a], Petr Grossmann, PhD [a], Petr Martinek, MSc [a], Naoto Kuroda, MD [d], Denisa Kacerovska, MD, PhD [a], Marian Svajdler, MD [e], Lubomir Straka, MD [f], Fredrik Petersson, MD, PhD [g], Milan Hora, MD, PhD [b,h], Michal Michal, MD [a,*]

[a] Department of Pathology, Faculty of Medicine in Plzeň, Charles University in Prague, Pilsen, Czech Republic
[b] Biomedical Centre, Faculty of Medicine in Plzeň, Charles University in Prague, Pilsen, Czech Republic
[c] Department of Pathology, Hospital Aliança, Salvador, Bahia, Brazil
[d] Department of Pathology, Red Cross Hospital Kochi, Kochi, Japan
[e] Department of Pathology, Pasteur University Hospital Kosice, Kosice, Slovak Republic
[f] Klinicka Patologia Presov, Presov, Slovak Republic
[g] Department of Pathology, National University Health System, Singapore, Singapore
[h] Department of Urology, Faculty of Medicine in Plzeň, Charles University in Prague, Pilsen, Czech Republic

ARTICLE INFO

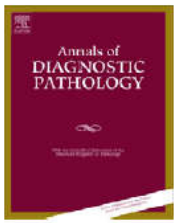
Keywords:
Kidney

ABSTRACT

We report 3 cases of primary renal cell tumor simulating atrophic kidney with distinct gross, morphologic, immunohistochemical, and molecular genetic features. The tumors were retrieved out of more than 17 000

Annals of Diagnostic Pathology 18 (2014) 82–88

Contents lists available at ScienceDirect



ORIGINAL ARTICLE

"Atrophic Kidney"–like Lesion

Clinicopathologic Series of 8 Cases Supporting a Benign Entity Distinct From Thyroid-like Follicular Carcinoma

Leal Herlitz, MD, Ondrej Hes, MD, PhD,† Michal Michal, MD,† Maria Tretiakova, MD, PhD,‡ Miguel Reyes-Múgica, MD,§ Jane K. Nguyen, MD, PhD,* Megan L. Troxell, MD, PhD,‖ Christopher G. Przybycin, MD,* Cristina Magi-Galluzzi, MD, PhD,* and Jesse K. McKenney, MD**

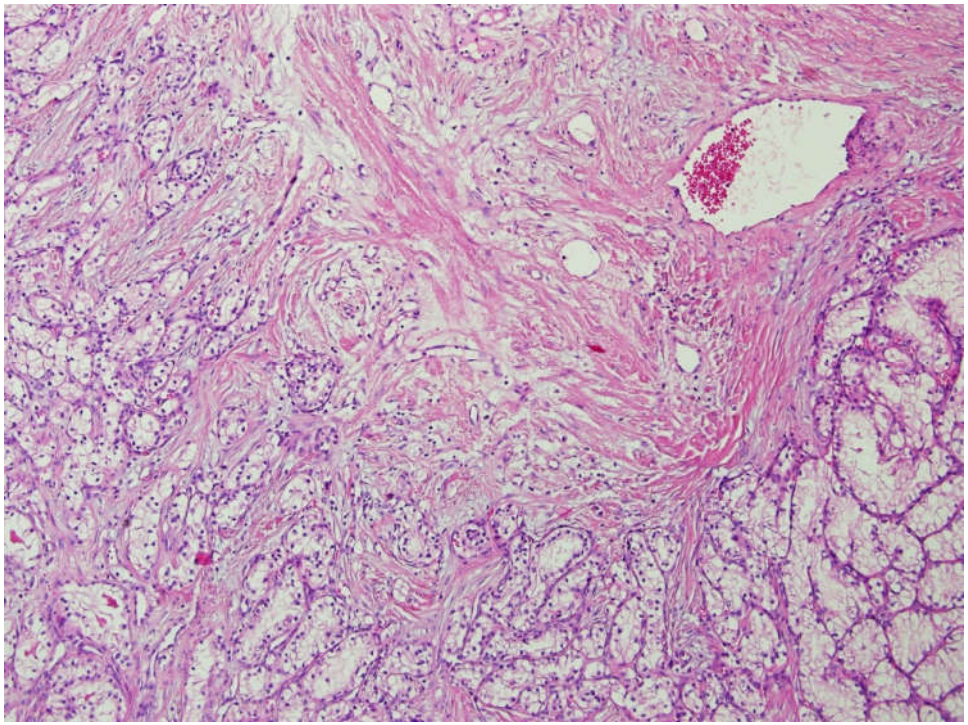
Abstract: Renal mass lesions with a follicular architecture resembling atrophic kidney have been described, but their distinction from thyroid-like follicular carcinoma of the kidney remains controversial. We collected 8 cases of this purported "atrophic kidney"–like lesion to fully describe their clinical and histologic spectrum, their possible etiology, and to discuss their distinction from other renal neoplasms. Eight total cases were identified with patient ages ranging from 9 to 48 years (mean: 29 y; median: 28.5 y). Four patients were female and 4 were male. The tumors were unifocal and size ranged from 1.6 to 4.9 cm (mean: 3.4 cm; median: 3.4 cm). All 8 tumors had a remarkably similar histology. Each was enveloped by a smooth muscle rich capsule and had an overall low power "follicular" architecture. The luminal spaces of the "follicles" (or cysts) contained eosinophilic secretions and the lining epithelium was often flattened and atrophic, but some had more rounded cells with a distinctive hobnail arrangement. Many cysts contained discohesive round cells floating within the eosinophilic material, and some contained small intraluminal tufts with features of markedly atrophic glomeruli. Periodic acid-Schiff stains highlighted basement membrane material extending into these glomerular-like tufts, and some contained small distinct capillaries surrounded by endothelial glomeruli were also present. The 2 tumors from the oldest 2 patients (48 and 39 y) had a more striking degree of stromal hyalinization. Immunohistochemically, the cyst lining cells had a predominant WT-positive/PAX-8 negative/CK7-negative phenotype, while tubules were typically WT-1 negative/PAX-8 positive/CK7-positive. Upon comparison to a control group of 10 kidneys containing incidental non–mass-forming glomerulocystic change, the morphologic features and immunophenotype were identical. To date, no patient has had any recurrence or aggressive clinical behavior based on follow status in 7 of 8 cases (follow-up range: 9 to 168 mo; median: 24 mo; mean: 40 mo). In summary, we describe the clinicopathologic features of 8 unique, benign "atrophic kidney"–like lesions that may simply represent a non-neoplastic form of organizing tubular atrophy and glomerulocystic change, and emphasize their distinction from thyroid-like follicular carcinoma of the kidney.

Key Words: atrophic kidney–like tumor, atrophy, thyroid-like follicular carcinoma, glomerulocystic

(*Am J Surg Pathol* 2018;42:1585–1595)

In 2014, Hes and colleagues described a series of 3 unique encapsulated renal masses as "renal cell tumor simulat-

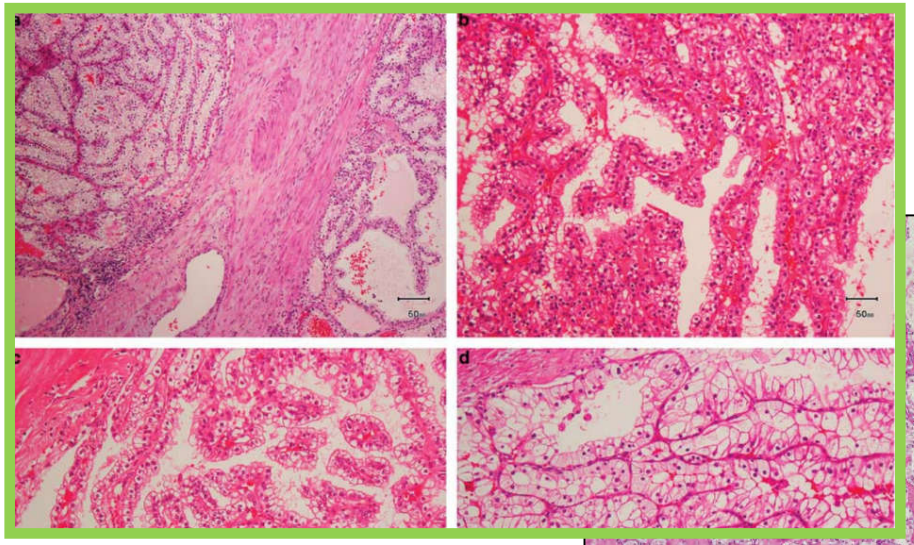
Renal cell carcinoma with prominent leiomyomatous stroma



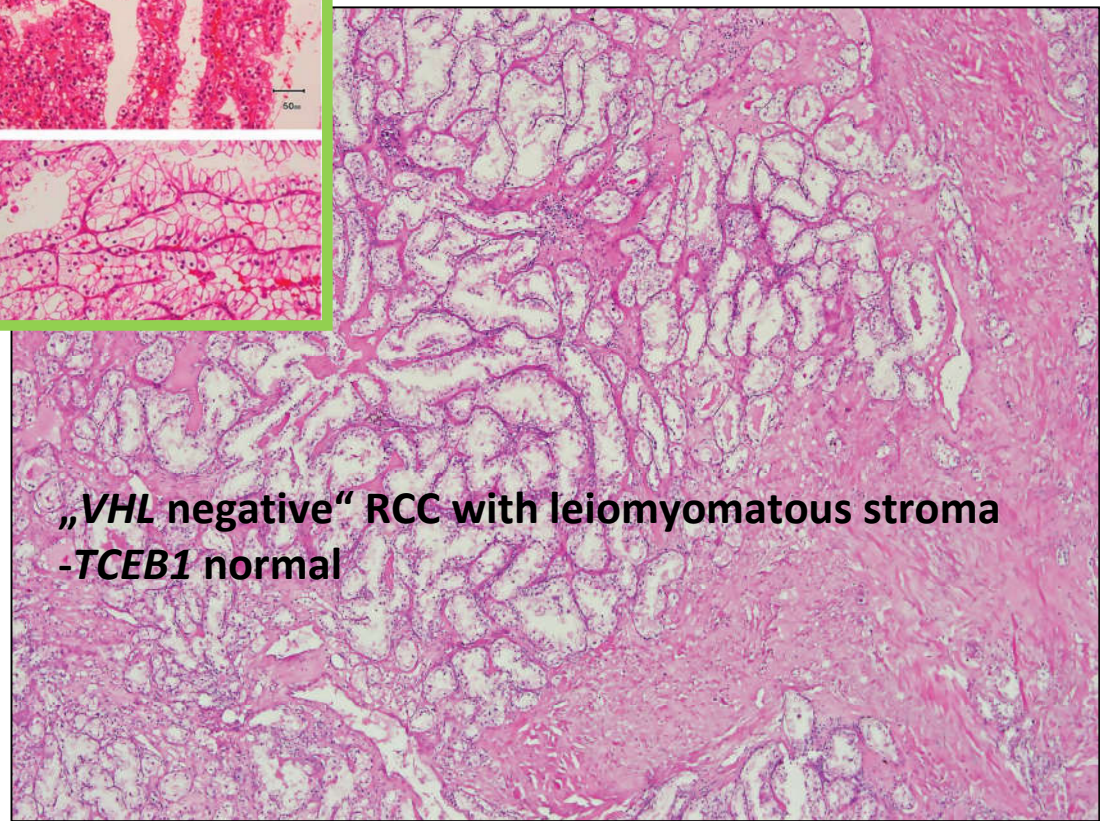
Renal cell carcinoma with leiomyomatous stroma

- Většinou náhodné nálezy, žádná specifická prezentace
- Zatím bez metastáz (ALE!!)
- Studie zvažují spojení s TS
- Jiné zvažují vztah k CCPRCC

Hakimi et al. TCEB1-mutated renal cell carcinoma: a distinct genomic and morphological subtype. *Modern Pathol 2015*



TCEB1-mutated RCC

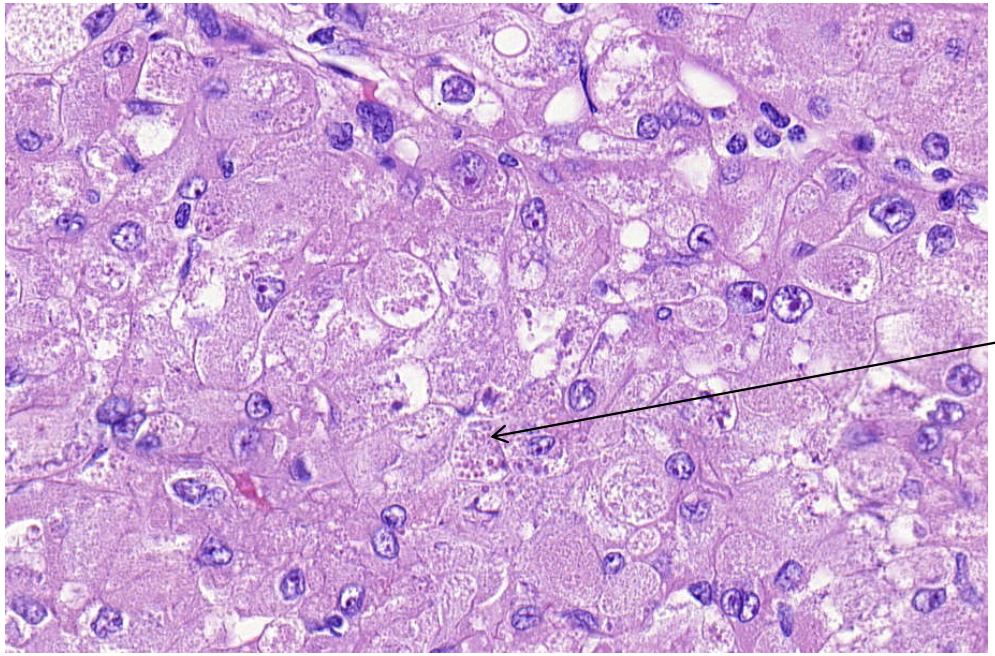


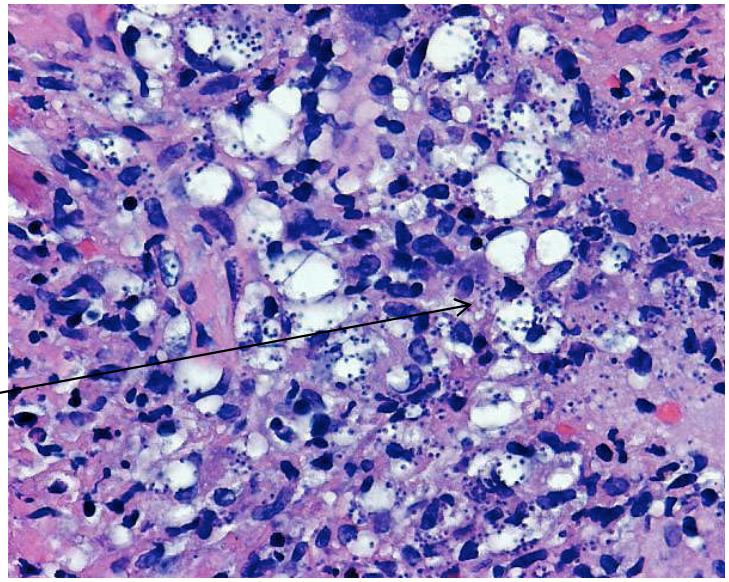
„*VHL* negative“ RCC with leiomyomatous stroma
-*TCEB1* normal

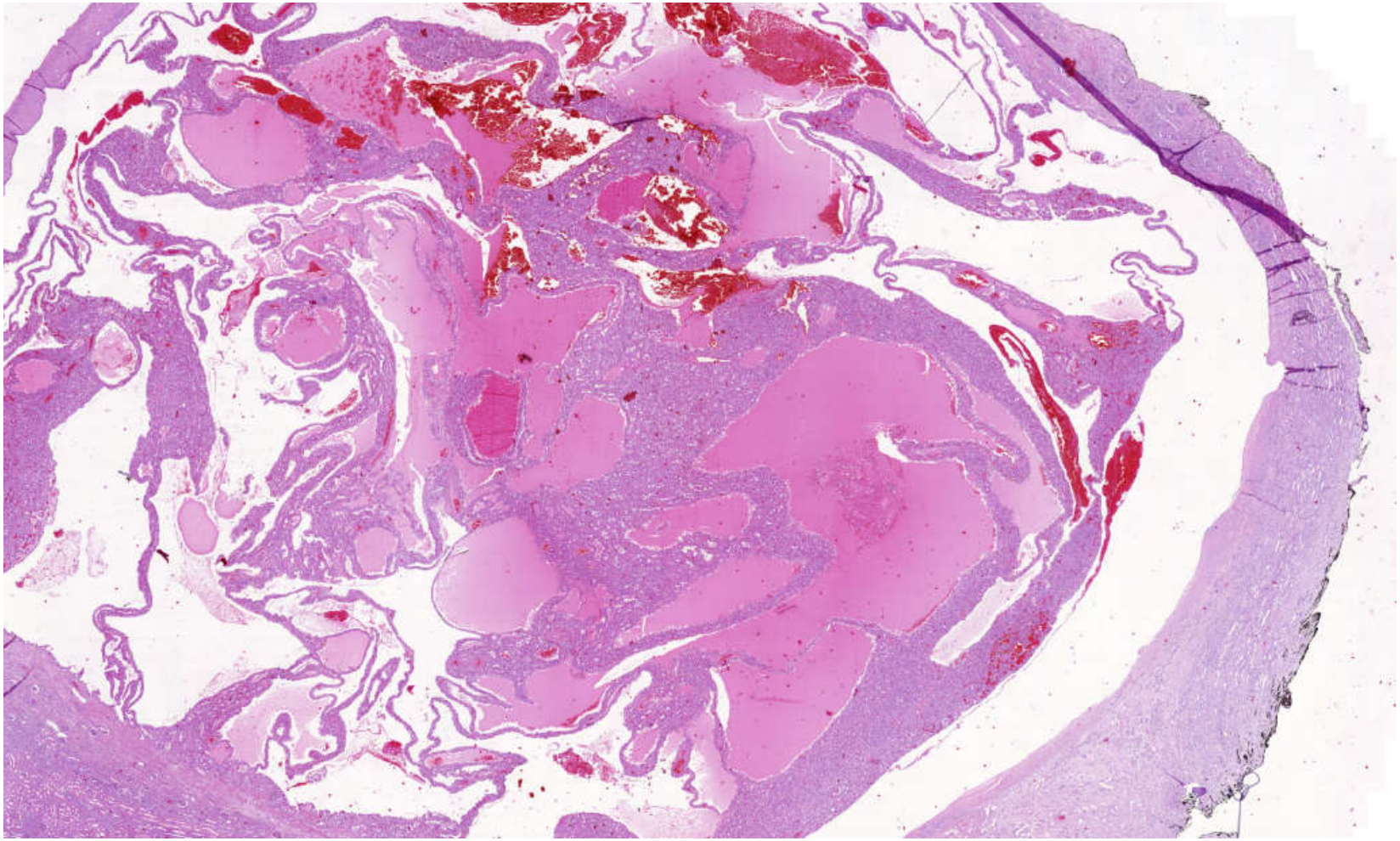
Takže zatím……..

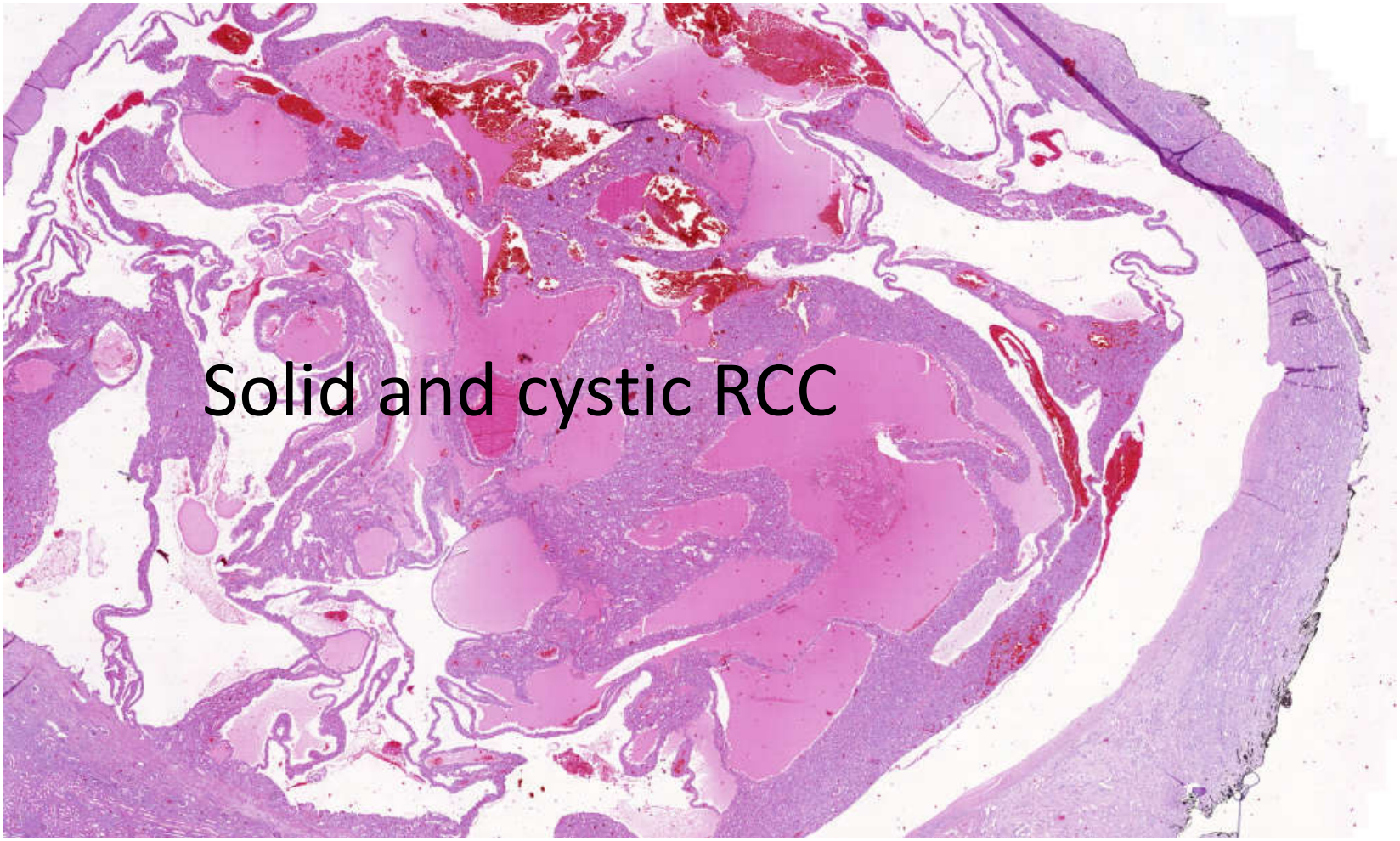
- Většina jsou CCRCC se stromatem (*VHL* abnormality)
- …některé jsou *TCEB1* mutované RCC
- …některé jsou *VHL a TCEB1* normální, bez mutací v „angio“ genech……. (Peterson Appl Imm Mol Morphol 2018)

Leishmania-like RCC AND Leishmaniosis








Solid and cystic RCC

Tuberous Sclerosis–associated Renal Cell Carcinoma

A Clinicopathologic Study of 57 Separate Carcinomas in 18 Patients

Juan Guo, MD, PhD, Maria S. Tretiakova, MD, PhD,† Megan L. Troxell, MD, PhD,‡ Adeboye O. Osunkoya, MD,§ Oluwole Fadare, MD,‖ Ankur R. Sangoi, MD,¶ Steven S. Shen, MD, PhD,# Antonio Lopez-Beltran, MD, PhD,** Rohit Mehra, MD,†† Amer Heider, MD,†† John P. Higgins, MD,‡‡ Lara R. Harik, MD,§§ Xavier Leroy, MD,‖‖ Anthony J. Gill, MD,¶¶ Kiril Trpkov, MD,## Steven C. Campbell, MD, PhD,*** Christopher Przybycin, MD,**** Cristina Magi-Galluzzi, MD, PhD,**** and Jesse K. McKenney, MD*****

Abstract: Tuberous sclerosis complex (TSC) is an autosomal dominant disorder with characteristic tumors involving multiple organ systems. Whereas renal angiomyolipoma (AML) is common in TSC, renal cell carcinoma (RCC) is rarely reported. Fifty-seven RCCs from 13 female and 5 male TSC patients were reviewed. Age at surgery ranged from 7 to 65 years (mean: 42 y). Nine patients (50%) had multiple synchronous and/or metachronous RCCs (range of 2 to 20 RCCs) and 5 had bilateral RCCs (28%). Seventeen patients (94%) had histologically confirmed concurrent renal AMLs, including 15 with multiple AMLs (88%) and 9 (50%) with AMLs with epithelial cysts. None of the 15 patients with available clinical follow-up information had evidence of distant metastatic disease from 6 to 198 months after their initial surgery (mean: 52 mo). The 57 RCCs exhibited 3 major distinct morphologies: (1) 17 RCCs (30%) had features similar to tumors previously described as "renal angiomyoadenomatous tumor" or "RCC with smooth muscle stroma"; (2) 34 RCCs (59%) showed features similar to chromophobe RCC; and (3) 6 RCCs (11%) showed a granular eosinophilic-macrocystic morphology. Distinct histologic changes were also commonly present in the background kidney parenchyma and included cysts or renal tubules lined by epithelial cells with prominent eosinophilic cytoplasm, nucleomegaly, and nucleoli. Immunohistochemically, all RCCs tested showed strong nuclear reactivity for PAX8 and HMB45 negativity. Compared with sporadic RCCs, TSC-associated RCCs have unique clinicopathologic features including female predominance, younger age at diagnosis, multiplicity, association with AMLs, 3 recurring histologic patterns, and an indolent clinical course. Awareness of the morphologic and clinicopathologic spectrum of RCC in this setting will allow surgical pathologists to better recognize clinically unsuspected TSC patients.

Key Words: tuberous sclerosis, renal cell carcinoma, angiomyolipoma, renal angiomyoadenomatous tumor, CA9, CK7, CD117, HMB45, PAX8

(*Am J Surg Pathol* 2014;38:1457–1467)

From the *Cleveland Clinic, Robert J. Tomsich Pathology & Labo-

Eosinophilic, Solid, and Cystic Renal Cell Carcinoma

Clinicopathologic Study of 16 Unique, Sporadic Neoplasms Occurring in Women

Kiril Trpkov, MD, FRCPC, Ondrej Hes, MD, PhD,† Michael Bonert, MD,* Jose I. Lopez, MD, PhD,‡ Stephen M. Bonsib, MD,§ Gabriella Nesi, MD,‖ Eva Comperat, MD,¶ Mathilde Sibony, MD,# Daniel M. Berney, MD,** Petr Martinek, MSc,† Stela Bulimbasic, MD,†† Saul Suster, MD,‡‡ Ankur Sangoi, MD,§§ Asli Yilmaz, MD,* John P. Higgins, MD,‖‖ Ming Zhou, MD, PhD,¶¶ Anthony J. Gill, MD, PhD,## Christopher G. Przybycin, MD,*** Cristina Magi-Galluzzi, MD, PhD,*** and Jesse K. McKenney, MD****

Abstract: A unique renal neoplasm characterized by eosinophilic cytoplasm and solid and cystic growth was recently reported in patients with tuberous sclerosis complex (TSC). We searched multiple institutional archives and consult files in an attempt to identify a sporadic counterpart. We identified 16 morphologically identical cases, all in women, without clinical features of TSC. The median age was 57 years (range, 31 to 75 y). Macroscopically, tumors were tan and had a solid and macrocystic (12) or only solid appearance (4). Average tumor size was 50 mm (median, 38.5 mm; range, 15 to 135 mm). Microscopically, the tumors showed solid areas admixed with variably sized macrocysts and microcysts that were lined by cells with a pronounced hobnail arrangement. The cells had voluminous eosinophilic cytoplasm with prominent granular cytoplasmic stippling and round to oval nuclei with prominent nucleoli. Scattered histiocytes and lymphocytes were invariably present. Thirteen of 16 patients were stage pT1; 2 were pT2, and 1 was pT3a. The cells demonstrated a distinct immunoprofile: nuclear PAX8 expression, predominant CK20-positive/CK7-negative phenotype, patchy AMACR staining, but no CD117 reactivity. Thirteen of 14 patients with follow-up were alive and without disease progression after 2 to 138 months (mean: 53 mo; median: 37.5 mo); 1 patient died of other causes. Although similar to a subset of renal cell carcinomas (RCCs) seen in TSC, we propose that sporadic "eosinophilic, solid, and cystic RCC," which occurs predominantly in female individuals and is characterized by distinct morphologic features, predominant CK20-positive/CK7-negative immunophenotype, and indolent behavior, represents a novel subtype of RCC.

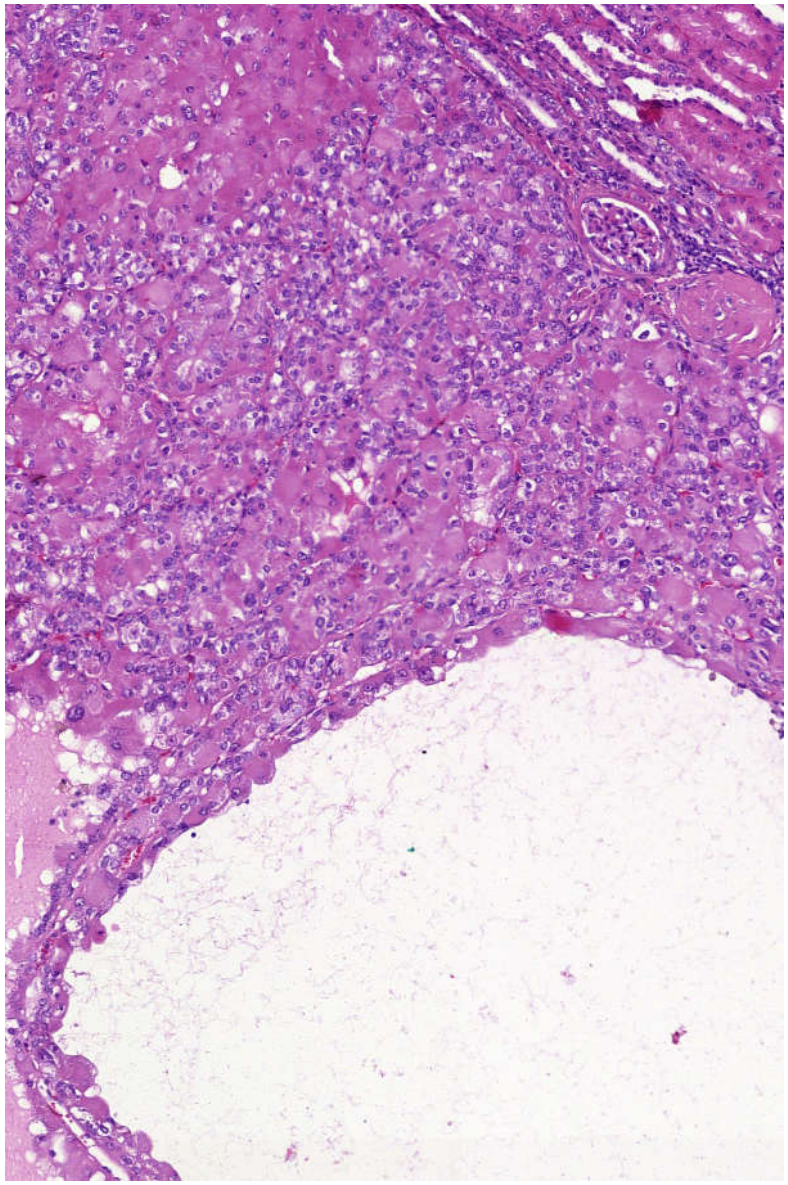
Key Words: eosinophilic tumor, renal cell carcinoma, tuberous sclerosis, CK20, unclassified oncocytic tumor, unclassified renal cell carcinoma

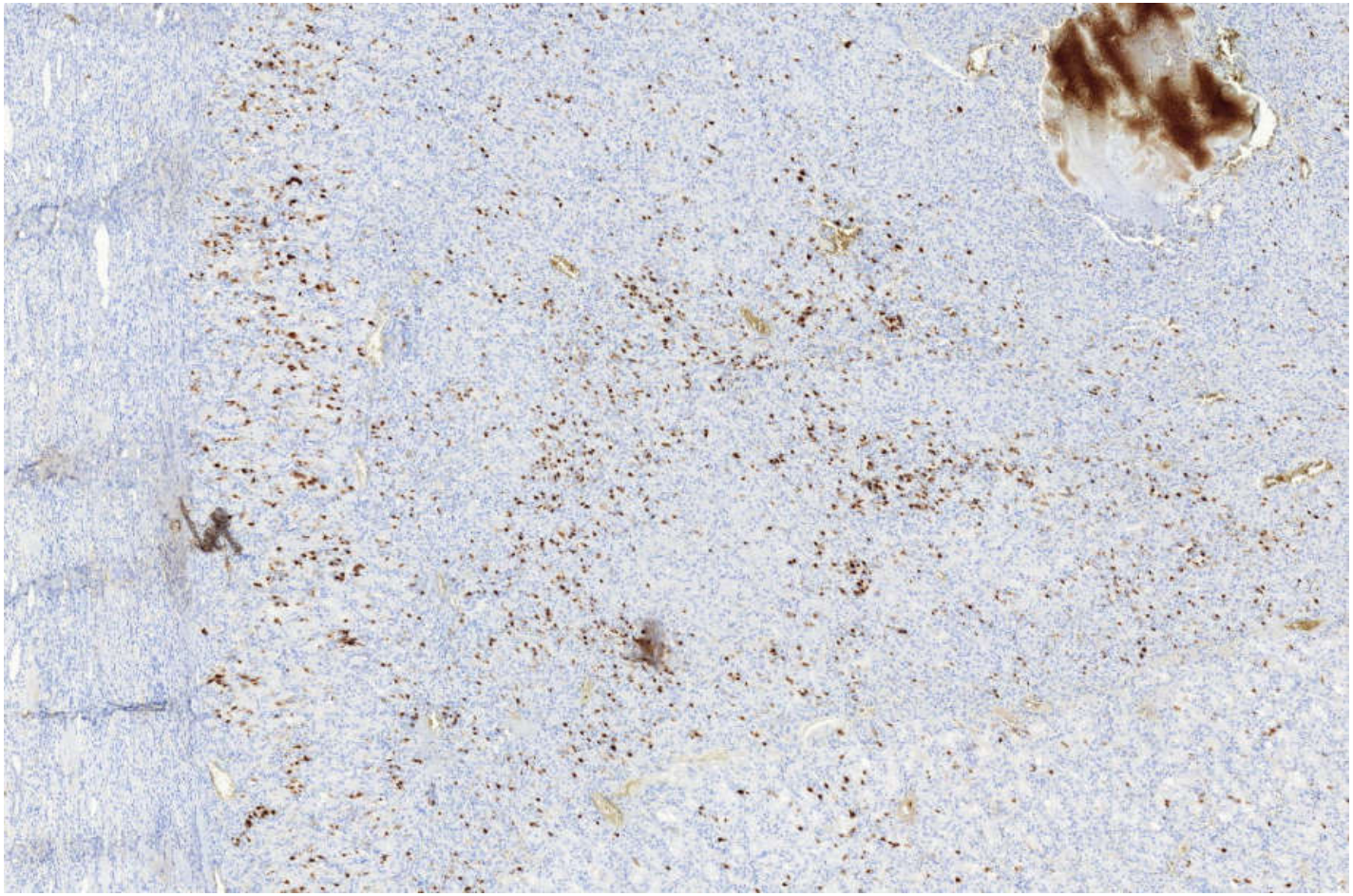
(*Am J Surg Pathol* 2016;40:60–71)

From the *Calgary Laboratory Services and University of Calgary, Calgary, AB, Canada; †Department of Pathology, Charles University, Pilsen, Czech Republic; ‡Cruces University Hospital, Bio-Cruces Institute, University of the Basque Country (UPV/EHU), Barakaldo, Bizkaia, Spain; §Nephropath, Little Rock, AR; ‡‡Medical College Wisconsin, Milwaukee, WI; §§El Camino Hos-

Solid and cystic RCC- souhrn

- Sporadické případy: většinou ženy
- Velikost 1.5-13.5 cm, pT1
- Neagresivní: **ALE**
- ISUP grade **3**
- **Spojení s TS** (Guo 2014, Yang 2014)





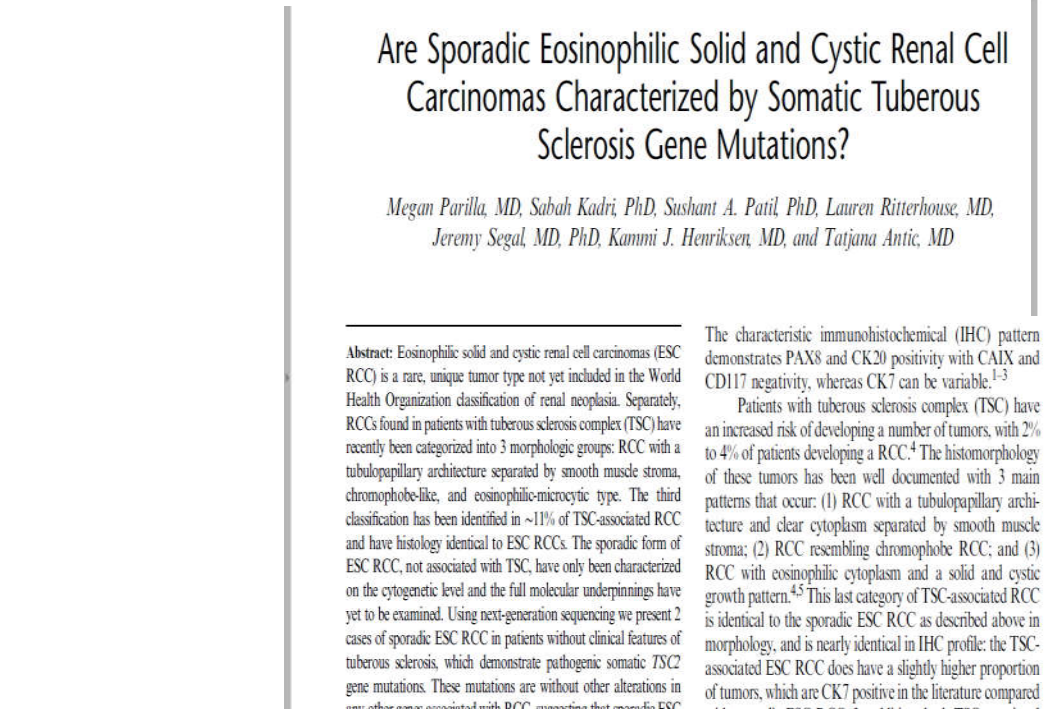
Immunohistochemie a genetika

- PAX 8, **CK 20+**
- Vimentin, AMACR, CD10 +-
- CK 7, CANH 9, CD117, HMB45-

- LOH: 16p, Xq, 11p
- Gain: 1p, 7p-q, 10q, 13q, 16p-q
- Loss: 19p, 11q, Xp, Xq

•+

Am J Surg Pathol 2018



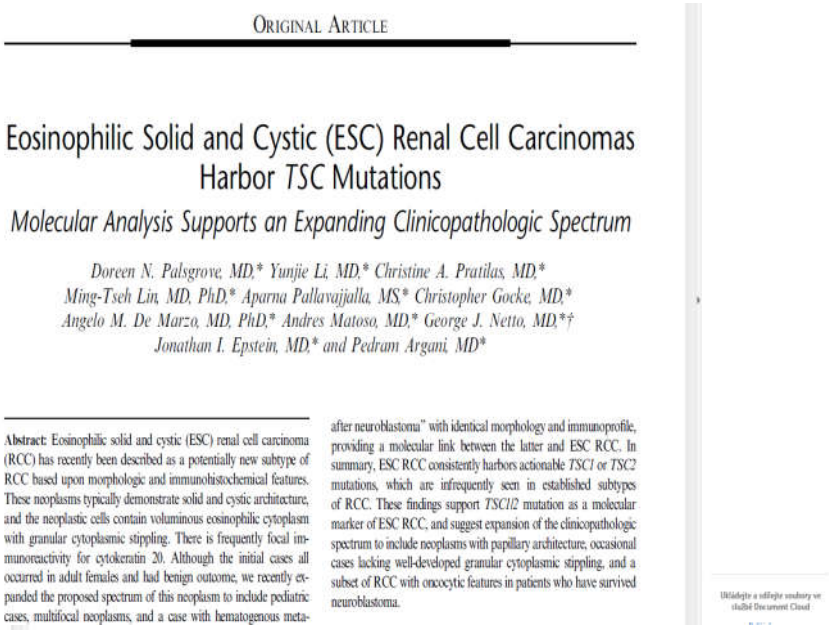
Are Sporadic Eosinophilic Solid and Cystic Renal Cell Carcinomas Characterized by Somatic Tuberous Sclerosis Gene Mutations?

Megan Parilla, MD, Sabah Kadri, PhD, Sushant A. Patil, PhD, Lauren Ritterhouse, MD, Jeremy Segal, MD, PhD, Kammi J. Henriksen, MD, and Tatjana Antic, MD

Abstract: Eosinophilic solid and cystic renal cell carcinomas (ESC RCC) is a rare, unique tumor type not yet included in the World Health Organization classification of renal neoplasia. Separately, RCCs found in patients with tuberous sclerosis complex (TSC) have recently been categorized into 3 morphologic groups: RCC with a tubulopapillary architecture separated by smooth muscle stroma, chromophobe-like, and eosinophilic-microcytic type. The third classification has been identified in ~11% of TSC-associated RCC and have histology identical to ESC RCCs. The sporadic form of ESC RCC, not associated with TSC, have only been characterized on the cytogenetic level and the full molecular underpinnings have yet to be examined. Using next-generation sequencing we present 2 cases of sporadic ESC RCC in patients without clinical features of tuberous sclerosis, which demonstrate pathogenic somatic *TSC2* gene mutations. These mutations are without other alterations in

The characteristic immunohistochemical (IHC) pattern demonstrates PAX8 and CK20 positivity with CAIX and CD117 negativity, whereas CK7 can be variable.[1-3]

Patients with tuberous sclerosis complex (TSC) have an increased risk of developing a number of tumors, with 2% to 4% of patients developing a RCC.[4] The histomorphology of these tumors has been well documented with 3 main patterns that occur: (1) RCC with a tubulopapillary architecture and clear cytoplasm separated by smooth muscle stroma; (2) RCC resembling chromophobe RCC; and (3) RCC with eosinophilic cytoplasm and a solid and cystic growth pattern.[4,5] This last category of TSC-associated RCC is identical to the sporadic ESC RCC as described above in morphology, and is nearly identical in IHC profile: the TSC-associated ESC RCC does have a slightly higher proportion of tumors, which are CK7 positive in the literature compared



ORIGINAL ARTICLE

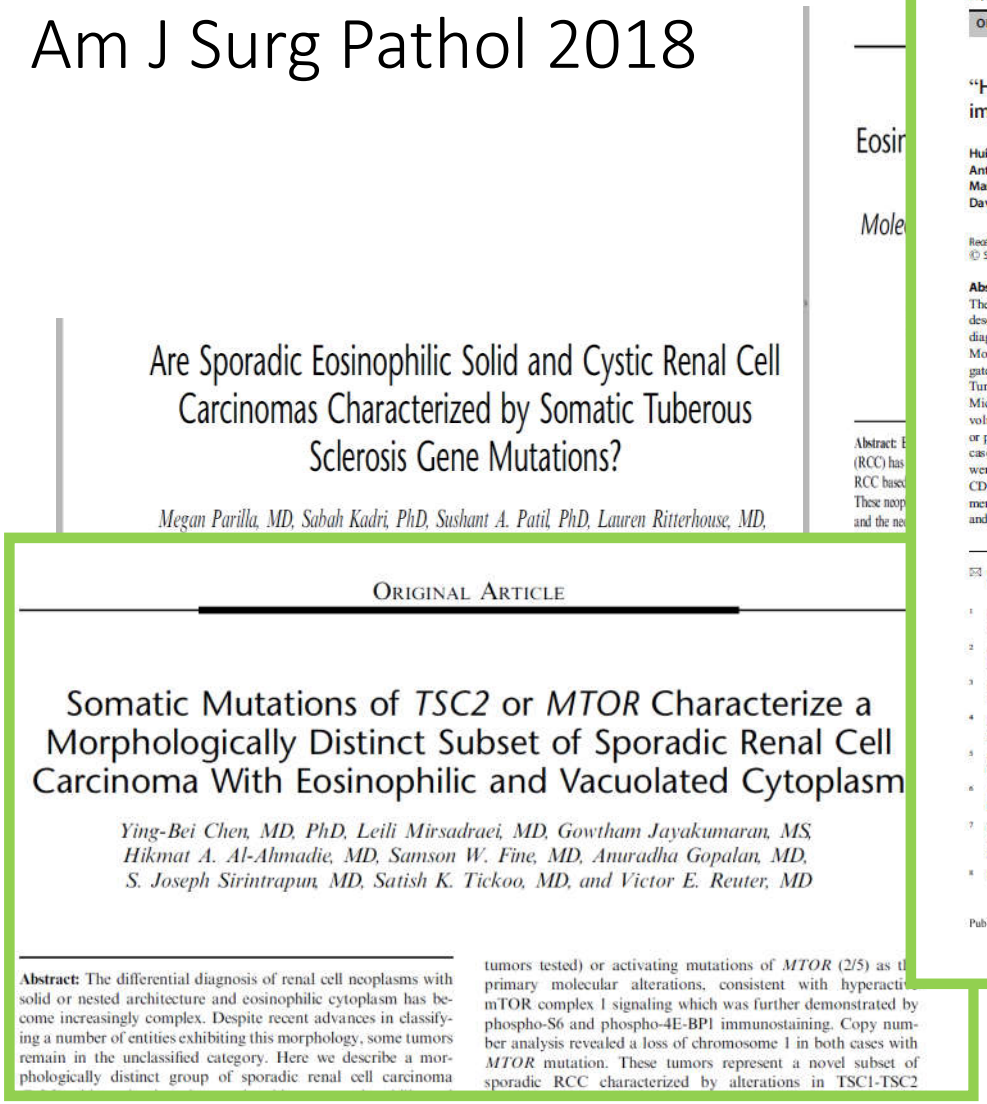
Eosinophilic Solid and Cystic (ESC) Renal Cell Carcinomas Harbor *TSC* Mutations

Molecular Analysis Supports an Expanding Clinicopathologic Spectrum

Doreen N. Palsgrove, MD, Yunjie Li, MD,* Christine A. Pratilas, MD,* Ming-Tseh Lin, MD, PhD,* Aparna Pallavajjalla, MS,* Christopher Gocke, MD,* Angelo M. De Marzo, MD, PhD,* Andres Matoso, MD,* George J. Netto, MD,*† Jonathan I. Epstein, MD,* and Pedram Argani, MD**

Abstract: Eosinophilic solid and cystic (ESC) renal cell carcinoma (RCC) has recently been described as a potentially new subtype of RCC based upon morphologic and immunohistochemical features. These neoplasms typically demonstrate solid and cystic architecture, and the neoplastic cells contain voluminous eosinophilic cytoplasm with granular cytoplasmic stippling. There is frequently focal immunoreactivity for cytokeratin 20. Although the initial cases all occurred in adult females and had benign outcome, we recently expanded the proposed spectrum of this neoplasm to include pediatric cases, multifocal neoplasms, and a case with hematogenous metastasis after neuroblastoma" with identical morphology and immunoprofile, providing a molecular link between the latter and ESC RCC. In summary, ESC RCC consistently harbors actionable *TSC1* or *TSC2* mutations, which are infrequently seen in established subtypes of RCC. These findings support *TSC1/2* mutation as a molecular marker of ESC RCC, and suggest expansion of the clinicopathologic spectrum to include neoplasms with papillary architecture, occasional cases lacking well-developed granular cytoplasmic stippling, and a subset of RCC with oncocytic features in patients who have survived neuroblastoma.

Am J Surg Pathol 2018



Are Sporadic Eosinophilic Solid and Cystic Renal Cell Carcinomas Characterized by Somatic Tuberous Sclerosis Gene Mutations?

Megan Parilla, MD, Sabah Kadri, PhD, Sushant A. Patil, PhD, Lauren Ritterhouse, MD,

ORIGINAL ARTICLE

Somatic Mutations of *TSC2* or *MTOR* Characterize a Morphologically Distinct Subset of Sporadic Renal Cell Carcinoma With Eosinophilic and Vacuolated Cytoplasm

Ying-Bei Chen, MD, PhD, Leili Mirsadraei, MD, Gowtham Jayakumaran, MS, Hikmat A. Al-Ahmadie, MD, Samson W. Fine, MD, Anuradha Gopalan, MD, S. Joseph Sirintrapun, MD, Satish K. Tickoo, MD, and Victor E. Reuter, MD

Abstract: The differential diagnosis of renal cell neoplasms with solid or nested architecture and eosinophilic cytoplasm has become increasingly complex. Despite recent advances in classifying a number of entities exhibiting this morphology, some tumors remain in the unclassified category. Here we describe a morphologically distinct group of sporadic renal cell carcinoma

tumors tested) or activating mutations of *MTOR* (2/5) as t primary molecular alterations, consistent with hyperacti mTOR complex 1 signaling which was further demonstrated by phospho-S6 and phospho-4E-BP1 immunostaining. Copy number analysis revealed a loss of chromosome 1 in both cases with *MTOR* mutation. These tumors represent a novel subset of sporadic RCC characterized by alterations in TSC1-TSC2

Virchows Archiv
https://doi.org/10.1007/s00428-018-2456-4

ORIGINAL ARTICLE

"High-grade oncocytic renal tumor": morphologic, immunohistochemical, and molecular genetic study of 14 cases

Huiying He[1] · Kiril Trpkov[2] · Petr Martinek[3] · Ozlem Tanas Isikci[4] · Cristina Maggi-Galuzzi[5] · Reza Alaghehbandan[6] · Anthony J Gill[7,8,9] · Maria Tretiakova[10] · Jose Ignacio Lopez[11] · Sean R. Williamson[12] · Delia Perez Montiel[13] · Maris Sperga[14] · Eva Comperat[15] · Fadi Brimo[16] · Ali Yilmaz[2] · Kristyna Pivovarcikova[3] · Kveta Michalova[3] · David Slouka[17] · Kristyna Prochazkova[18] · Milan Hora[18] · Michael Bonert[19] · Michal Michal[3] · Ondrej Hes[3]

Received: 11 May 2018 / Revised: 29 August 2018 / Accepted: 10 September 2018

Abstract
The spectrum of the renal oncocytic tumors has been expanded in recent years to include several novel and emerging entities. We describe a cohort of novel, hitherto unrecognized and morphologically distinct high-grade oncocytic tumors (HOT), currently diagnosed as "unclassified" in the WHO classification. We identified 14 HOT by searching multiple institutional archives. Morphologic, immunohistochemical (IHC), molecular genetic, and molecular karyotyping studies were performed to investigate these tumors. The patients included 3 men and 11 women, with age range from 25 to 73 years (median 50, mean 49 years). Tumor size ranged from 1.5 to 7.0 cm in the greatest dimension (median 3, mean 3.4 cm). The tumors were all pT1 stage. Microscopically, they showed nested to solid growth, and focal tubulocystic architecture. The neoplastic cells were uniform with voluminous oncocytic cytoplasm. Prominent intracytoplasmic vacuoles were frequently seen, but no irregular (raisinoid) nuclei or perinuclear halos were present. All tumors demonstrated prominent nucleoli (WHO/ISUP grade 3 equivalent). Nine of 14 cases were positive for CD117 and cytokeratin (CK) 7 was either negative or only focally positive in of 6/14 cases. All tumors were positive for AE1-AE3, CK18, PAX 8, antimitochondrial antigen, and SDHB. Cathepsin K was positive in 13/14 cases and CD10 was positive in 12/13 cases. All cases were negative for TFE3, HMB45, Melan-A. No *TFEB* and *TFE3* genes rearrangement was found in analyzable cases. By array CGH, complete chromosomal losses or gains were not found in any of the cases, and 3/9 cases showed absence of any abnormalities. Chromosomal losses were detected on chromosome 19 (4/9), 3 with losses of

✉ Ondrej Hes
hes@medima.cz

[1] Department of Pathology, Health Science Center, Peking University, Beijing, China
[2] Department of Pathology and Laboratory Medicine, Calgary Laboratory Services and University of Calgary, Calgary, AB, Canada
[3] Department of Pathology, Medical Faculty and Charles University Hospital Plzen, Alej Svobody 80, 304 60 Plzen, Czech Republic
[4] Department of Pathology, Ankara Education and Research Hospital, Ankara, Turkey
[5] Robert J. Tomsich Pathology and Laboratory Medicine Institute, Cleveland Clinic, Cleveland, OH, USA
[6] Department of Pathology, Faculty of Medicine, University of British Columbia, Royal Columbian Hospital, Vancouver, BC, Canada
[7] Cancer Diagnosis and Pathology Group, Kolling Institute of Medical Research, Royal North Shore Hospital, St Leonards, NSW 2065, Australia
[8] University of Sydney, Sydney, NSW 2006, Australia
[9] NSW Health Pathology Department of Anatomical Pathology, Royal North Shore Hospital, St Leonards, NSW 2065, Australia
[10] Department of Anatomic Pathology, Harborview Medical Center, Seattle, WA, USA
[11] BioCruces Institute, Cruces University Hospital, University of the Basque Country (UPV/EHU), Barakaldo, Bizkaia, Spain
[12] Department of Pathology, Henry Ford Hospital, Detroit, MI, USA
[13] Department of Pathology, Instituto Nacional de Cancerologia, Mexico City, Mexico
[14] Department of Pathology, Riga Stradin's University, Riga, Latvia
[15] Sorbonne Université Service d'Anatomie et Cytologie Pathologiques Hôpital Tenon, HUEP, Paris, France
[16] Department of Pathology, McGill University, Montreal, QC, Canada
[17] Biomedicine Center, Charles University, Medical Faculty and Charles University Hospital Plzen, Prague, Czech Republic
[18] Department of Urology, Charles University, Medical Faculty and Charles University Hospital Plzen, Prague, Czech Republic
[19] Department of Pathology and Molecular Medicine, Faculty of Health Sciences, McMaster University, Hamilton, ON, Canada

Published online: 19 September 2018

Springer

Am J Surg Pathol 2018

Skupina nádorů s mutacemi v TSC genech? Spíše ne, jen koincidence

Virchows Archiv
https://doi.org/10.1007/s00428-018-2456-4

ORIGINAL ARTICLE

"High-grade oncocytic renal tumor": morphologic, immunohistochemical, and molecular genetic study of 14 cases

Anthony J Gill[7,8,9] · Maria Tretiakova[10] · Jose Ignacio Lopez[11] · Sean R. Williamson[12] · Delia Perez Montiel[13] · Maris Sperga[14] · Eva Comperat[15] · Fadi Brimo[16] · Ali Yilmaz[2] · Kristyna Pivovarcikova[3] · Kveta Michalova[3] · Ondrej Hes[3]

Received: 11 May 2018 / Revised: 9 August 2018 / Accepted: 10 September 2018

Abstract

The spectrum of the renal oncocytic tumors has been expanded in recent years to include several novel and emerging entities. We describe a cohort of novel, hitherto unrecognized and morphologically distinct high-grade oncocytic tumors (HOT), currently diagnosed as "unclassified" in the WHO classification. We identified 14 HOT by searching multiple institutional archives. Morphologic, immunohistochemical (IHC), molecular genetic, and molecular karyotyping studies were performed to investigate these tumors. The patients included 3 men and 11 women, with age range from 25 to 73 years (median 50, mean 49 years). Tumor size ranged from 1.5 to 7.0 cm in the greatest dimension (median 3, mean 3.4 cm). The tumors were all pT1 stage. Microscopically, they showed nested to solid growth, and focal tubulocystic architecture. The neoplastic cells were uniform with voluminous oncocytic cytoplasm. Prominent intracytoplasmic vacuoles were frequently seen, but no irregular (raisinoid) nuclei or perinuclear halos were present. All tumors demonstrated prominent nucleoli (WHO/ISUP grade 3 equivalent). Nine of 14 cases were positive for CD117 and cytokeratin (CK) 7 was either negative or only focally positive in of 6/14 cases. All tumors were positive for AE1-AE3, CK18, PAX 8, antimitochondrial antigen, and SDHB. Cathepsin K was positive in 13/14 cases and CD10 was positive in 12/13 cases. All cases were negative for TFE3, HMB45, Melan-A. No *TFEB* and *TFE3* genes rearrangement was found in analyzable cases. By array CGH, complete chromosomal losses or gains were not found in any of the cases, and 3/9 cases showed absence of any abnormalities. Chromosomal losses were detected on chromosome 19 (4/9), 3 with losses of

✉ Ondrej Hes
hes@medima.cz

1 Department of Pathology, Health Science Center, Peking University, Beijing, China
2 Department of Pathology and Laboratory Medicine, Calgary Laboratory Services and University of Calgary, Calgary, AB, Canada
3 Department of Pathology, Medical Faculty and Charles University Hospital Plzen, Alej Svobody 80, 304 60 Pilsen, Czech Republic
4 Department of Pathology, Ankara Education and Research Hospital, Ankara, Turkey
5 Robert J. Tomsich Pathology and Laboratory Medicine Institute, Cleveland Clinic, Cleveland, OH, USA
6 Department of Pathology, Faculty of Medicine, University of British Columbia, Royal Columbian Hospital, Vancouver, BC, Canada
7 Cancer Diagnosis and Pathology Group, Kolling Institute of Medical Research, Royal North Shore Hospital, St Leonards, NSW 2065, Australia
8 University of Sydney, Sydney, NSW 2006, Australia
9 NSW Health Pathology Department of Anatomical Pathology, Royal North Shore Hospital, St Leonards, NSW 2065, Australia
10 Department of Anatomic Pathology, Harborview Medical Center, Seattle, WA, USA
11 BioCruces Institute, Cruces University Hospital, University of the Basque Country (UPV/EHU), Barakaldo, Bizkaia, Spain
12 Department of Pathology, Henry Ford Hospital, Detroit, MI, USA
13 Department of Pathology, Instituto Nacional de Cancerologia, Mexico City, Mexico
14 Department of Pathology, Riga Stradin's University, Riga, Latvia
15 Sorbonne Université Service d'Anatomie et Cytologie Pathologiques Hôpital Tenon, HUEP, Paris, France
16 Department of Pathology, McGill University, Montreal, QC, Canada
17 Biomedicine Center, Charles University, Medical Faculty and Charles University Hospital Plzen, Prague, Czech Republic
18 Department of Urology, Charles University, Medical Faculty and Charles University Hospital Plzen, Prague, Czech Republic
19 Department of Pathology and Molecular Medicine, Faculty of Health Sciences, McMaster University, Hamilton, ON, Canada

Published online: 19 September 2018

Springer

Are Sporadic Eosinophilic Solid and Cystic Renal Cell Carcinomas Characterized by Somatic Tuberous Sclerosis Gene Mutations?

Megan Parilla, MD, Sabah Kadri, PhD, Sushant A. Patil, PhD, Lauren Ritterhouse, MD,

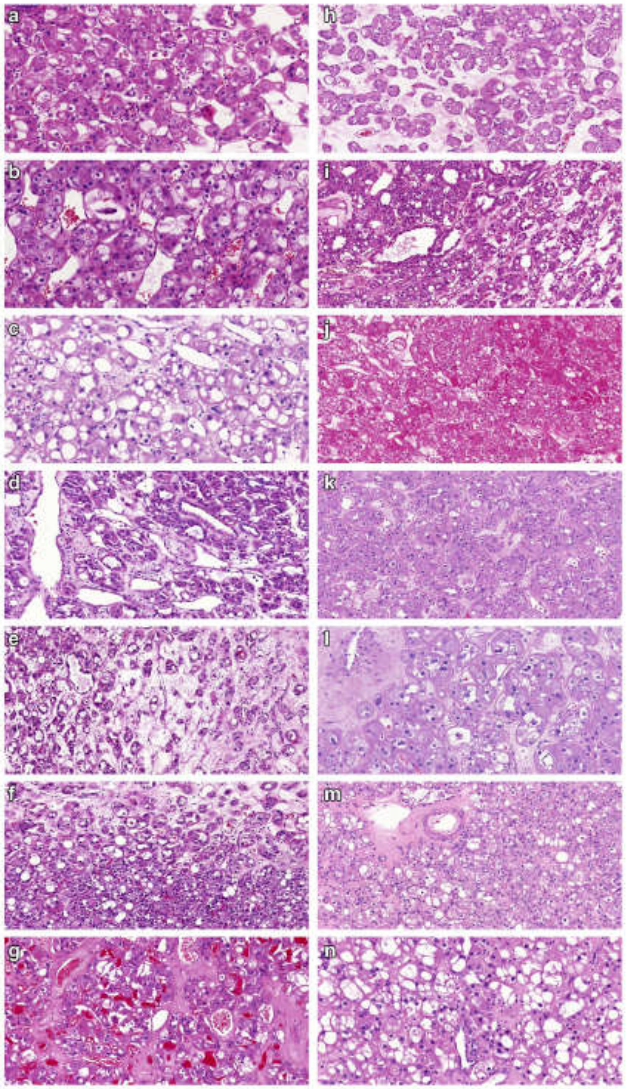
ORIGINAL ARTICLE

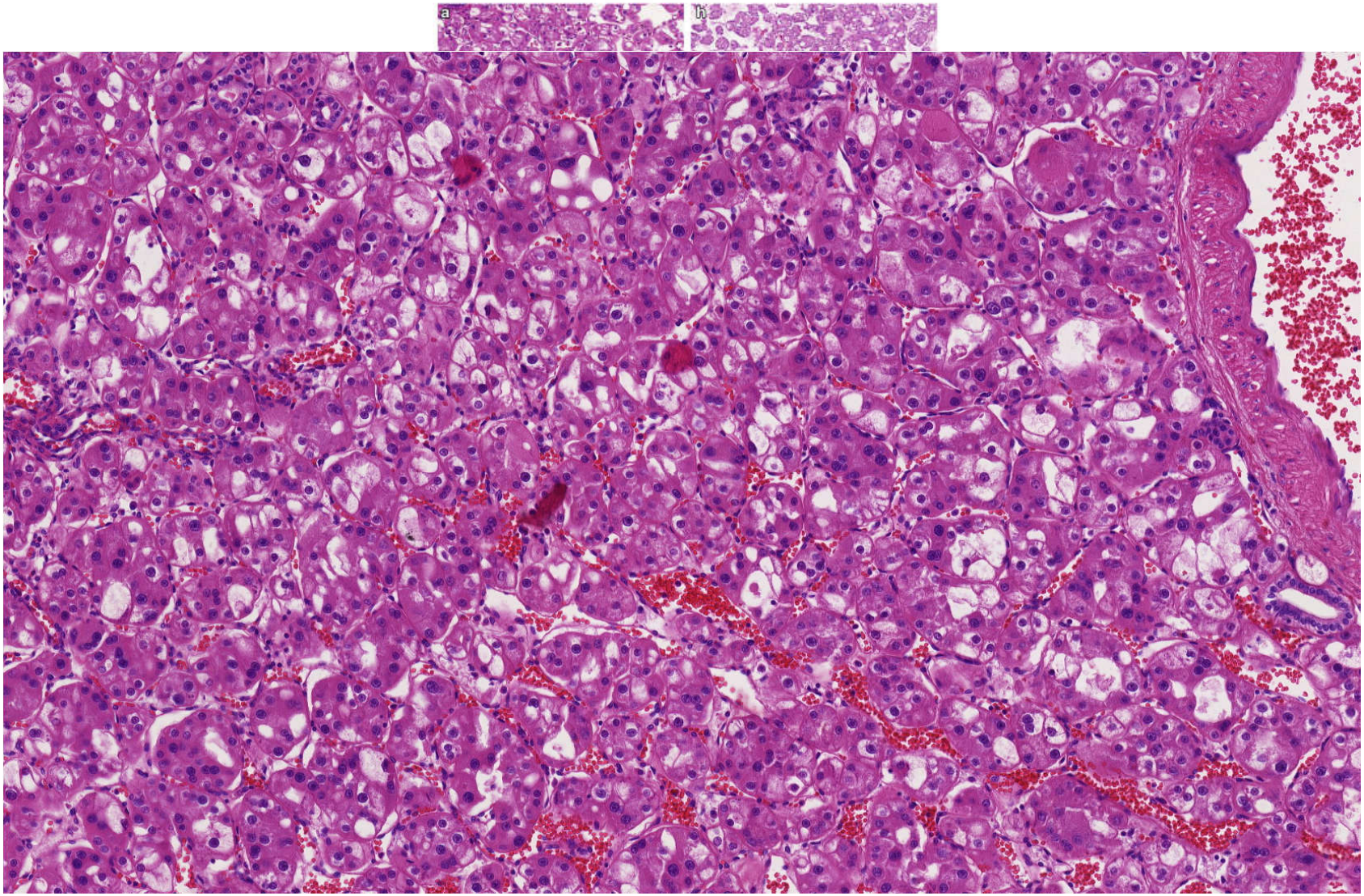
Somatic Mutations of *TSC2* or *MTOR* Characterize a Morphologically Distinct Subset of Sporadic Renal Cell Carcinoma With Eosinophilic and Vacuolated Cytoplasm

Ying-Bei Chen, MD, PhD, Leili Mirsadraei, MD, Gowtham Jayakumaran, MS, Hikmat A. Al-Ahmadie, MD, Samson W. Fine, MD, Anuradha Gopalan, MD, S. Joseph Sirintrapun, MD, Satish K. Tickoo, MD, and Victor E. Reuter, MD

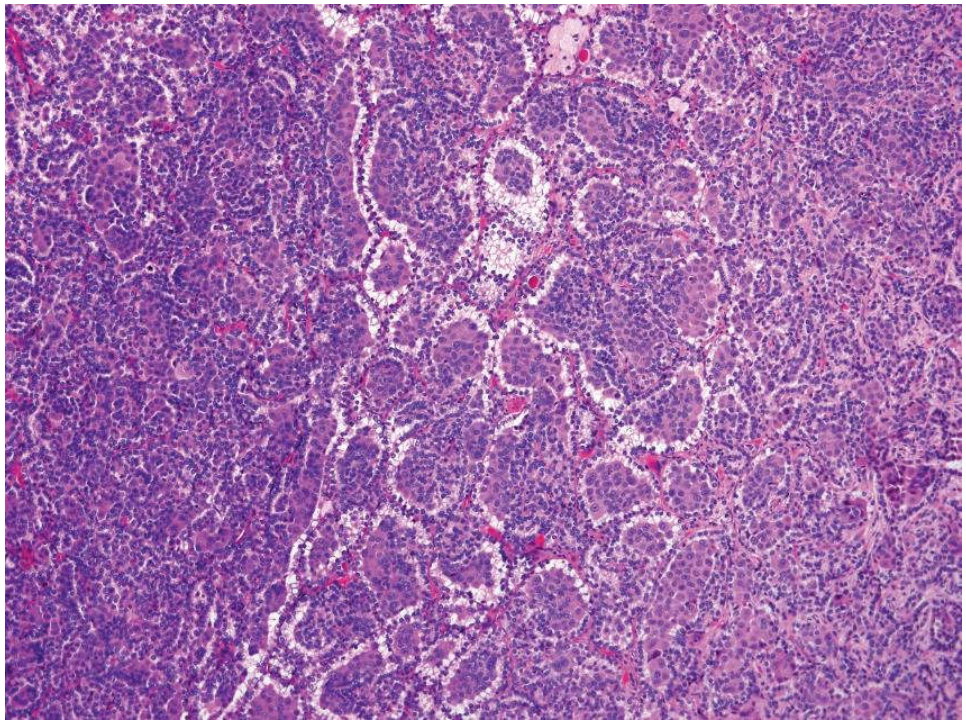
Abstract: The differential diagnosis of renal cell neoplasms with solid or nested architecture and eosinophilic cytoplasm has become increasingly complex. Despite recent advances in classifying a number of entities exhibiting this morphology, some tumors remain in the unclassified category. Here we describe a morphologically distinct group of sporadic renal cell carcinoma

tumors tested) or activating mutations of *MTOR* (2/5) as the primary molecular alterations, consistent with hyperactive mTOR complex 1 signaling which was further demonstrated by phospho-S6 and phospho-4E-BP1 immunostaining. Copy number analysis revealed a loss of chromosome 1 in both cases with *MTOR* mutation. These tumors represent a novel subset of sporadic RCC characterized by alterations in TSC1-TSC2


a
b
c
d
e
f
g
h
i
j
k
l
m
n


a
b

Squamoid Papillary RCC



Am J Surg Pathol 2016

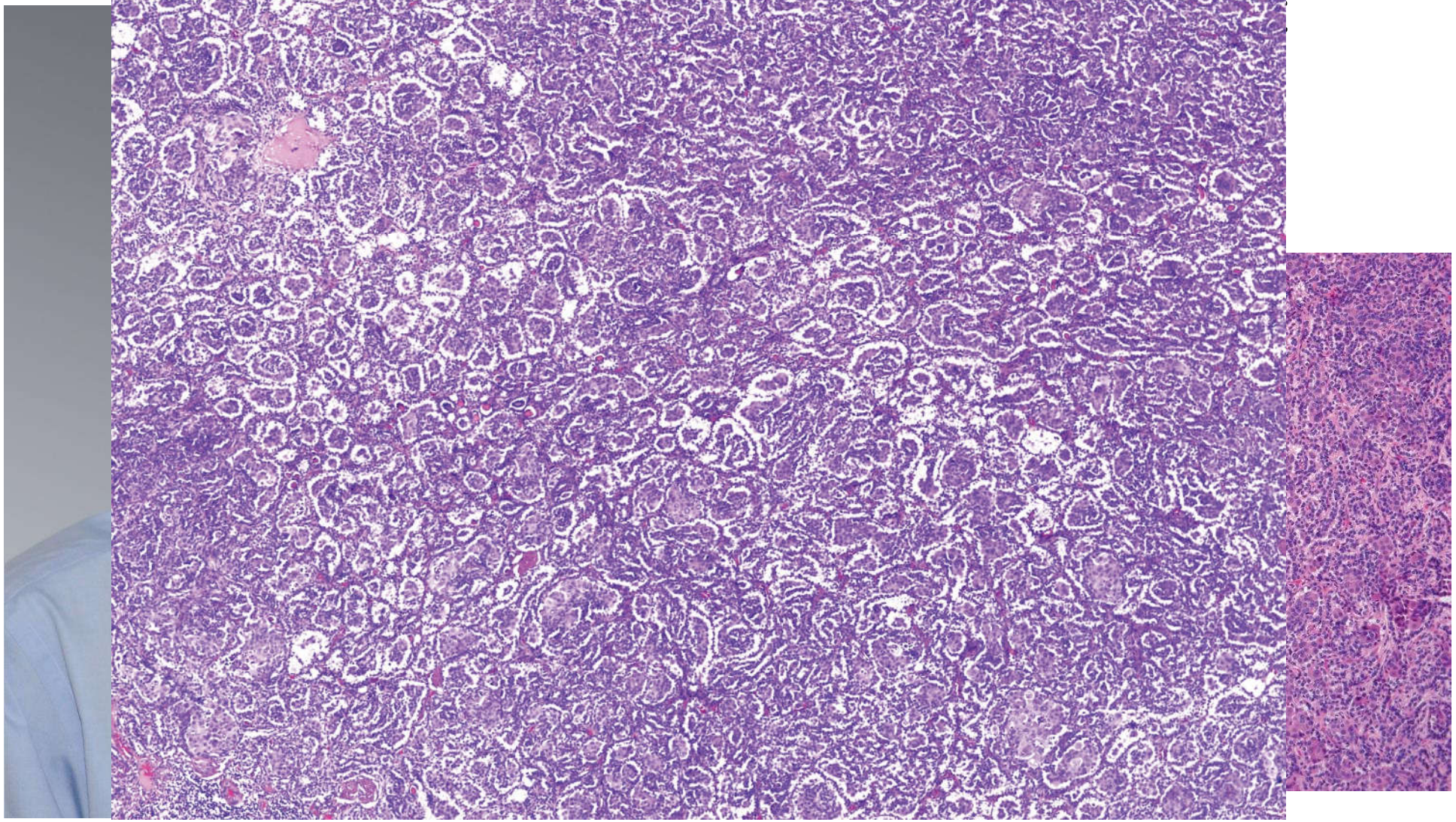
Biphasic Squamoid Alveolar Renal Cell Carcinoma

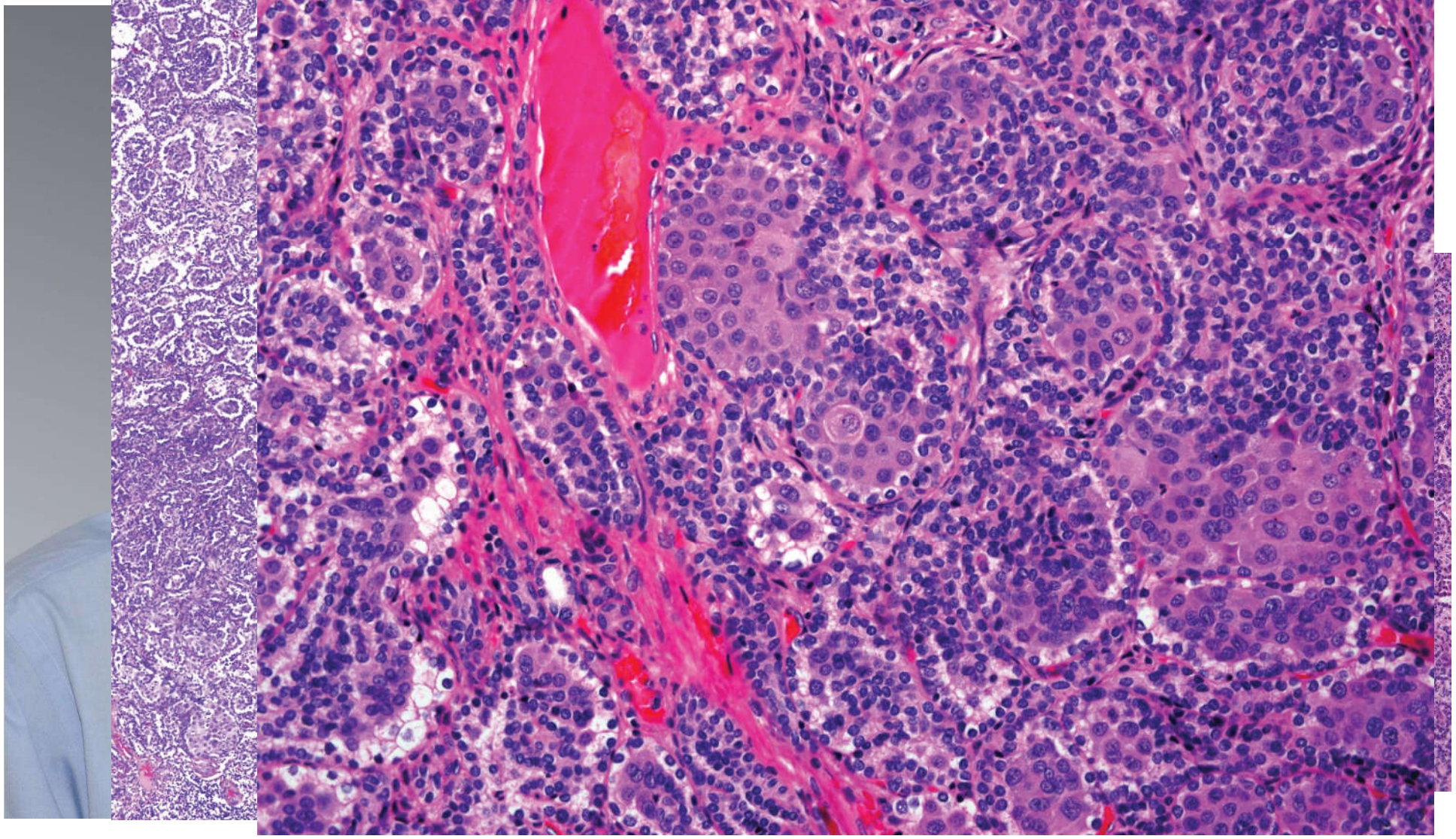
A Distinctive Subtype of Papillary Renal Cell Carcinoma?

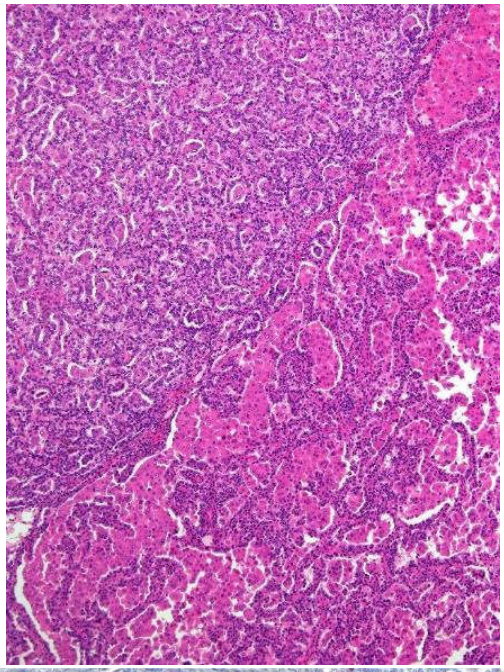
Ondrej Hes, MD, PhD, Enric Condom Mundo, MD, PhD,†‡ Kvetoslava Peckova, MD,* Jose I. Lopez, MD,§ Petr Martinek, PhD,* Tomas Vanecek, PhD,* Giovanni Falconieri, MD,‖ Abbas Agaimy, MD,¶ Whitney Davidson, MD,# Fredrik Petersson, MD, PhD,** Stela Bulimbasic, MD, PhD,†† Ivan Damjanov, MD, PhD,# Mireya Jimeno, MD,‡‡ Monika Ulamec, MD, PhD,§§ Miroslav Podhola, MD, PhD,‖‖ Maris Sperga, MD,¶¶ Maria Pane Foix, MD,†‡ Ksenya Shelekhova, MD, PhD,## Kristyna Kalusova, MD,*** Milan Hora, MD, PhD,*** Pavla Rotterova, MD, PhD,* Ondrej Daum, MD, PhD,* Kristyna Pivovarcikova, MD,* and Michal Michal, MD**

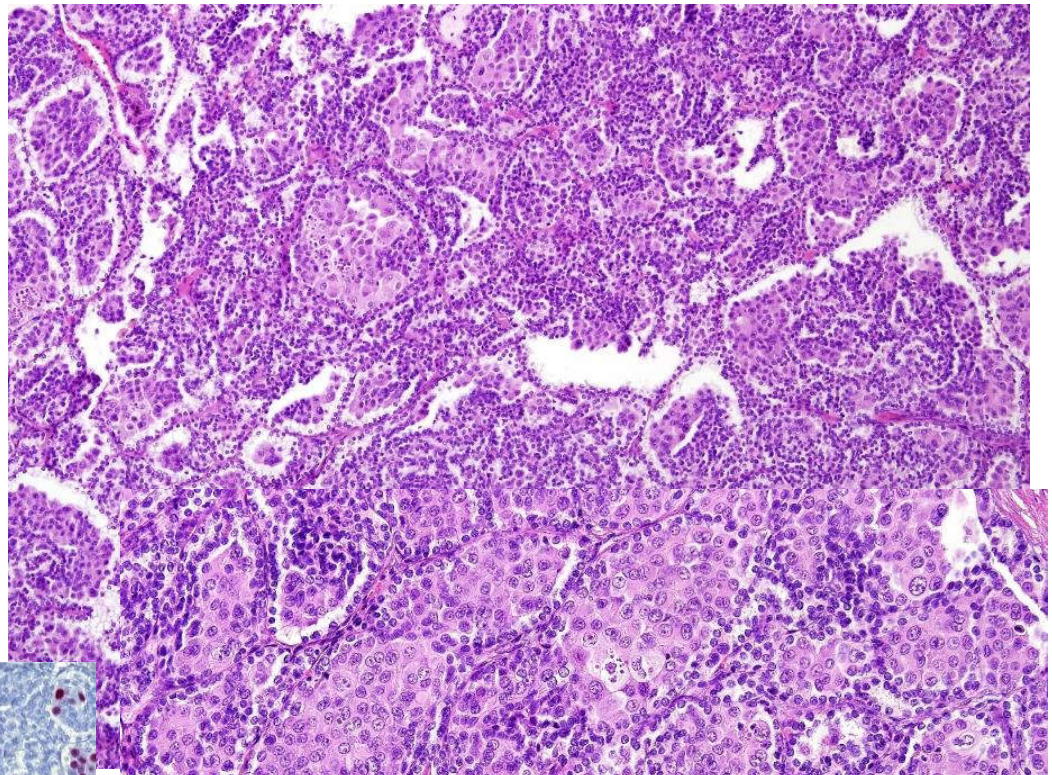
Abstract: Biphasic squamoid alveolar renal cell carcinoma (BSARCC) has been recently described as a distinct neoplasm. Twenty-one cases from 12 institutions were analyzed using routine histology, immunohistochemistry, array comparative genomic hybridization (aCGH) and fluorescence in situ hybridization. Tumors were removed from 11 male and 10 female patients, whose age ranged from 53 to 79 years. The size of tumors ranged from 1.5 to 16 cm. Follow-up information was

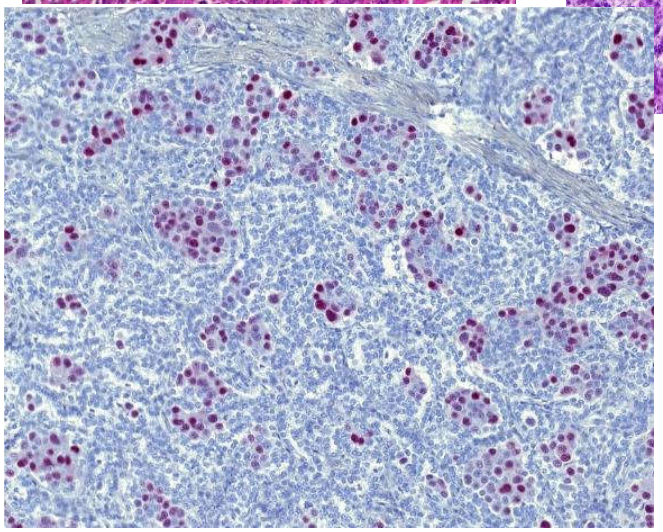
neoplastic cells with scant cytoplasm usually lining the inside of alveolar structures, and larger squamoid cells with more prominent cytoplasm and larger vesicular nuclei arranged in compact nests. In 9/21 tumors there was a visible transition from such solid and alveolar areas into papillary components. Areas composed of large squamoid cells comprised 10% to 80% of total tumor volume. Emperipolesis was present in all (21/21) tumors. Immunohistochemically, all cases were positive for cytokeratin 7, EMA, vimentin, and cyclin D1. aCGH (confirmed

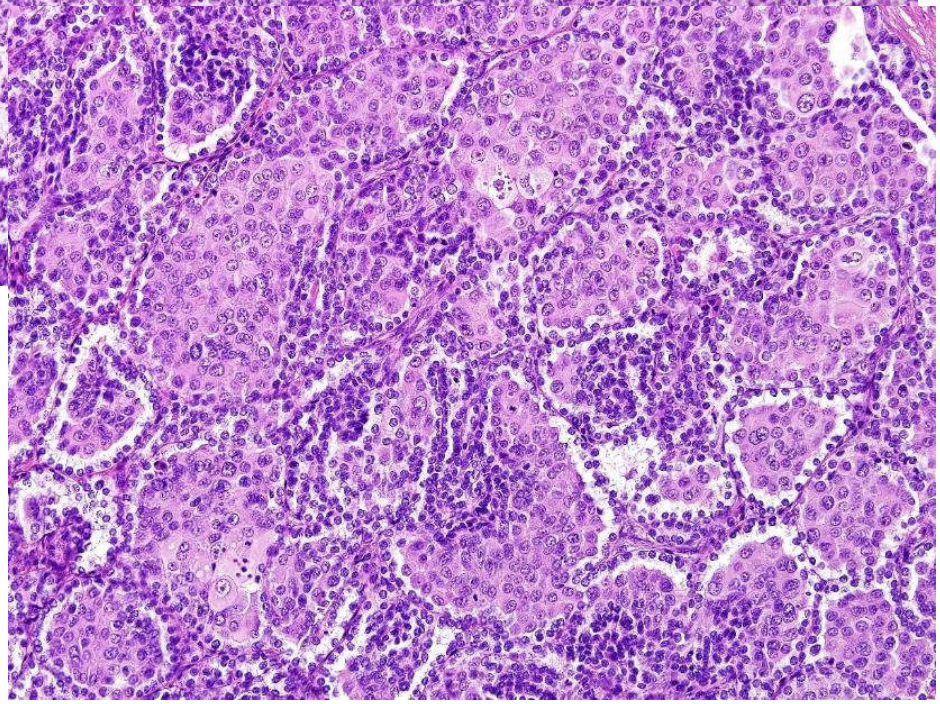


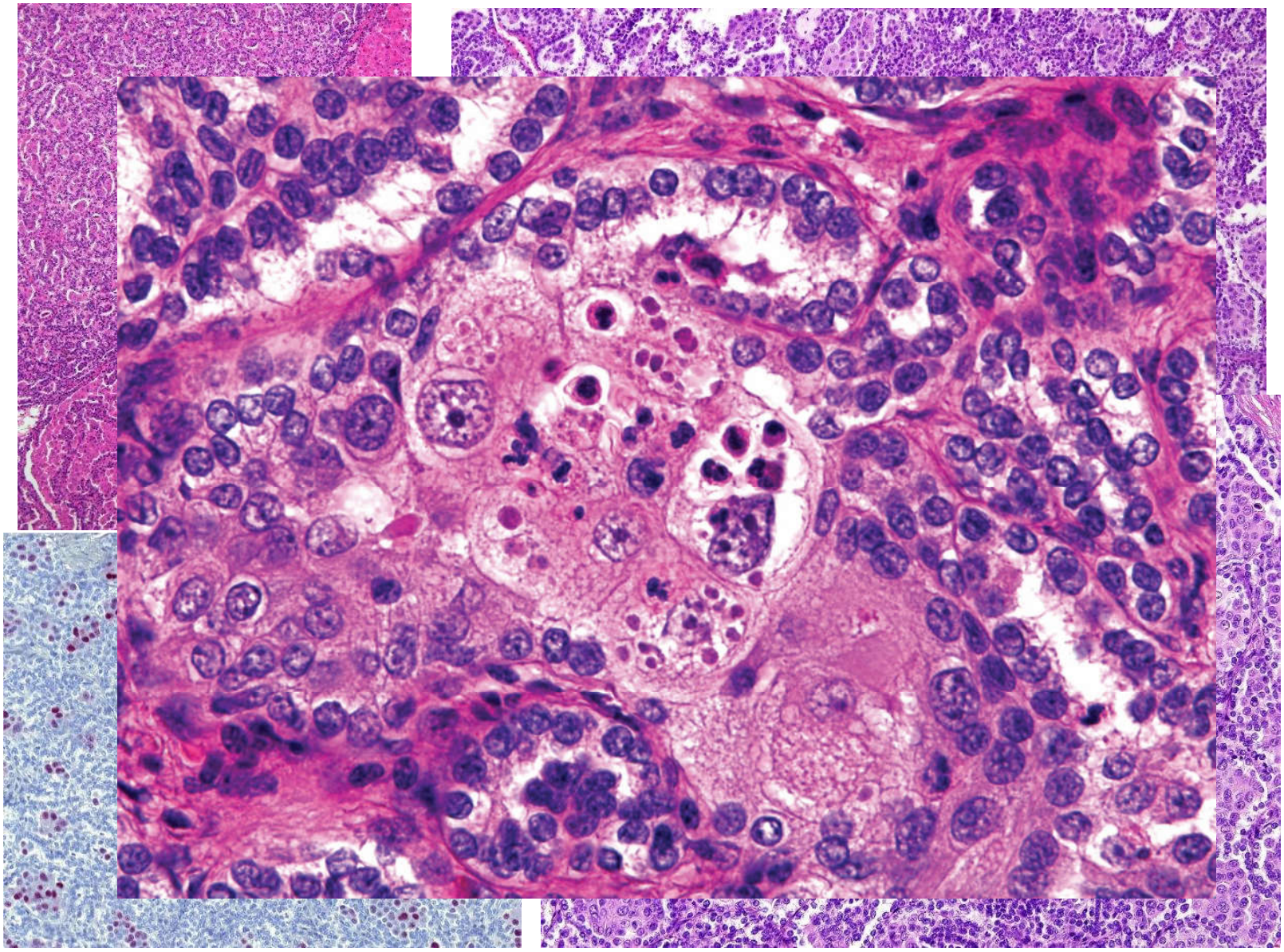












Biologické vlastnosti

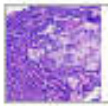
- Solitární nebo bilaterální/multifokální
- Popsány Tx pacienti
- Věk 39-79
- Až 15% agresivní chování!!!

- Podtyp PRCC blízký tzv PRCC typ 1
- IHC: CK7, AMACR, vimentin, PAX8
- Molekulární genetika: polysomie 7/17

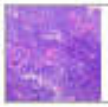
RE: Salute from Seattle

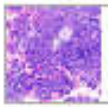
Komu Hes Ondřej

Odpověděli jste na tuto zprávu dne 14.10.2018 11:09.


Early-BSARCC-SH18-7107-20x1.jpg
639 KB


Early-BSARCC-SH18-7107-40x.jpg
509 KB


Early-BSARCC-SH18-7107-10x.jpg
788 KB

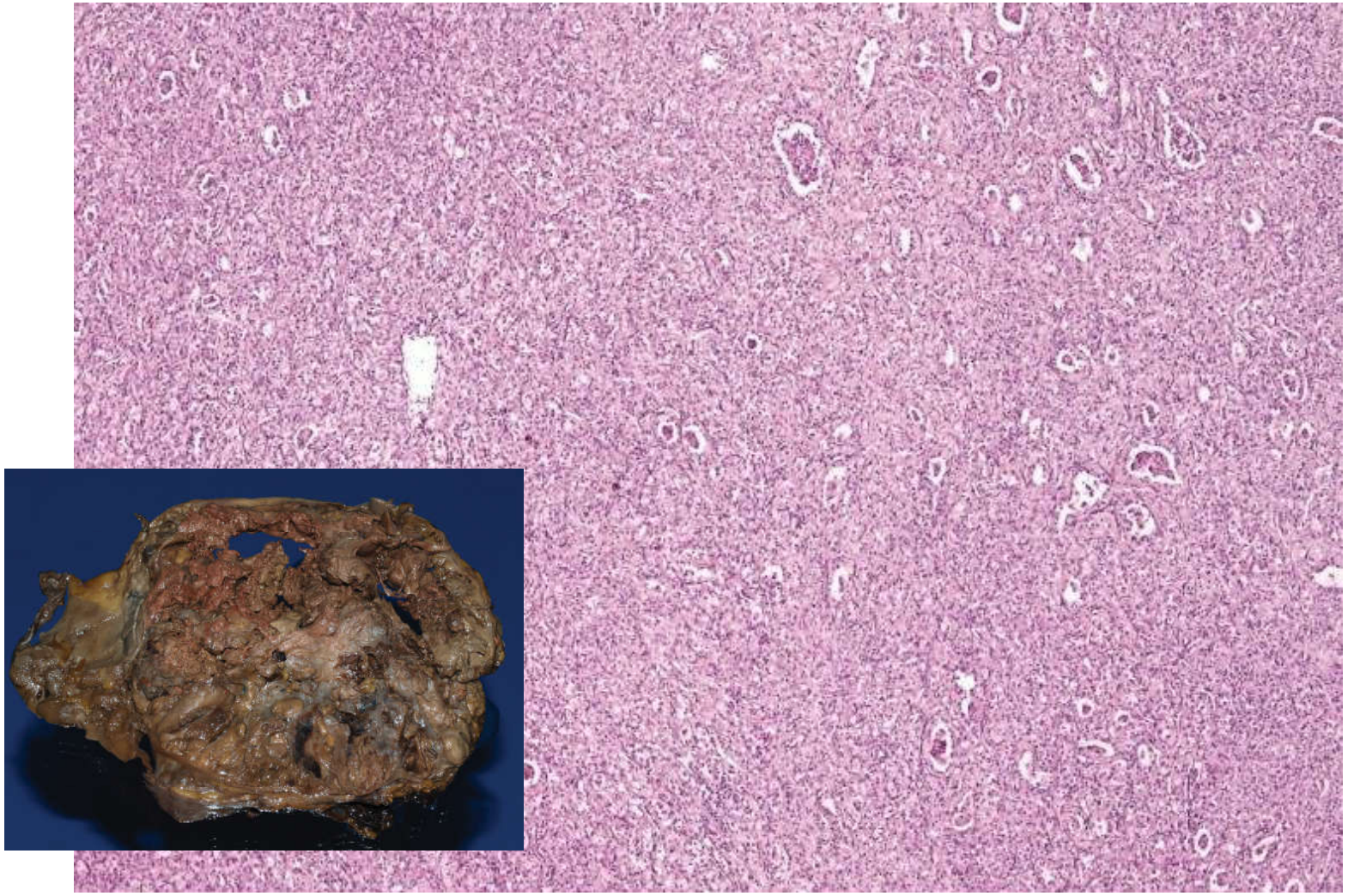

Early-BSARCC-SH18-7107-20x3.jpg
751 KB

Dear Ondra,

During sign out I had a vulgar case of papillary RCC, type1. Nothing special, except on high power I found a tiny focus of biphasic squamoid morphology with emperipolesis (<0.1% of tumor volume). It's an amazing example of early BSARCC morphology. Thought I would share. Perhaps it's more common than we think...

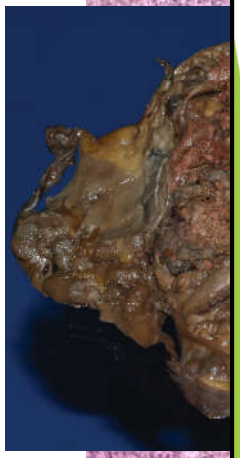
Maria

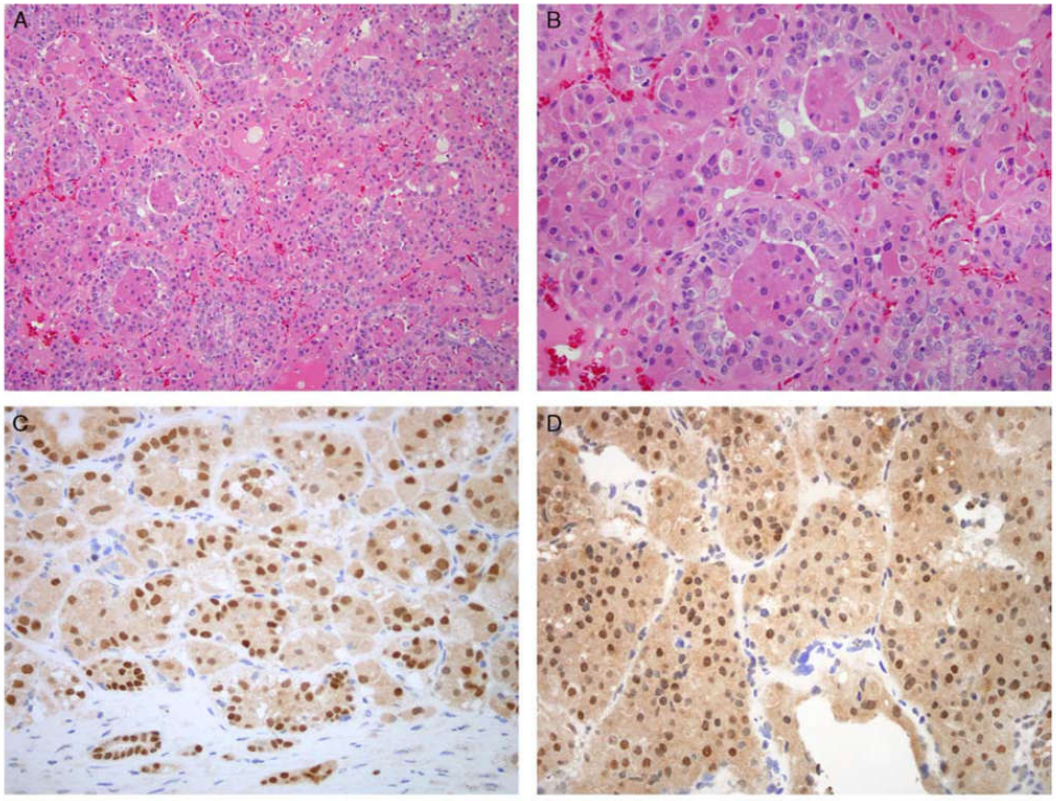
Peckova et al: Ann Diagn Pathol 2014 *TFEB* break AND amplification



Peckova et al: Ann Diagn Pathol 2014 *TFEB* break

RCC with *TFEB* amplification- Argani et al: AJSP 2016

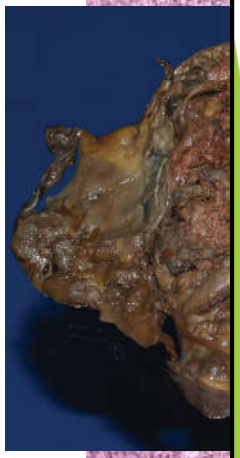


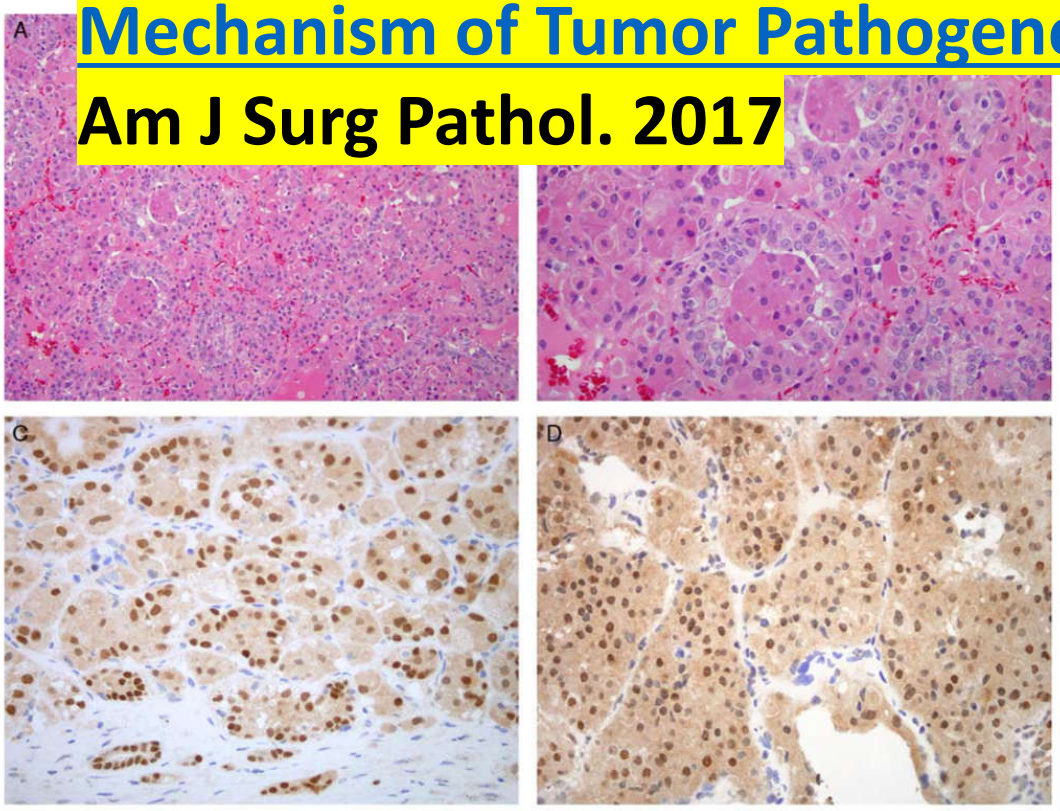


Peckova et al: Ann Diagn Pathol 2014 *TFEB*
break

RC
Ar

Williamson SR: Renal Cell Carcinoma With Chromosome 6p Amplification Including the TFEB Gene: A Novel Mechanism of Tumor Pathogenesis? Am J Surg Pathol. 2017

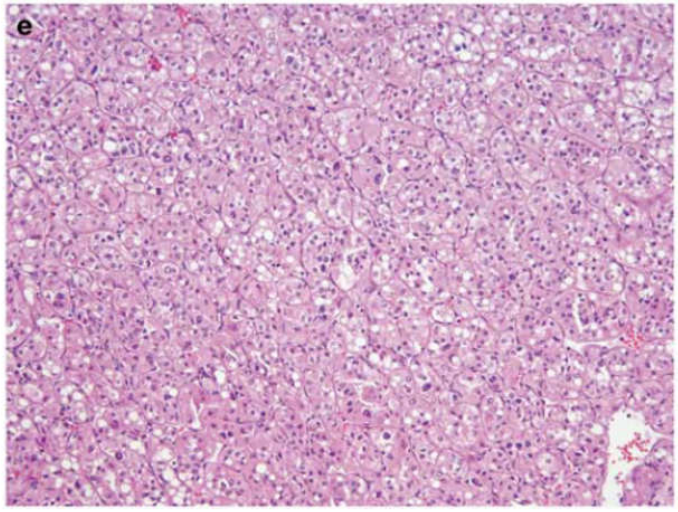


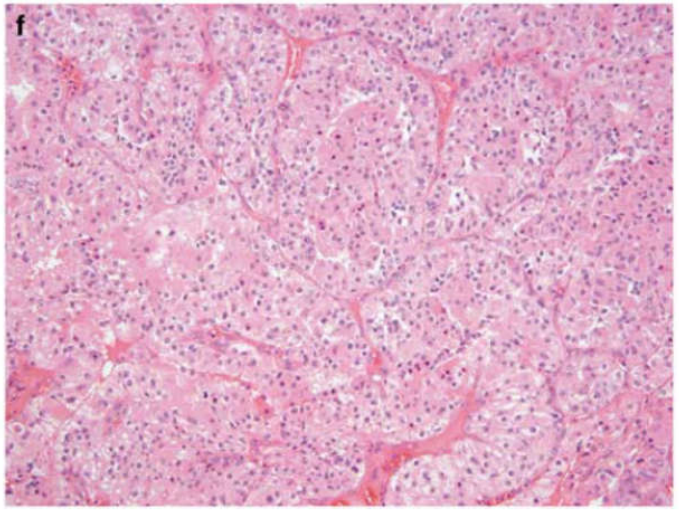


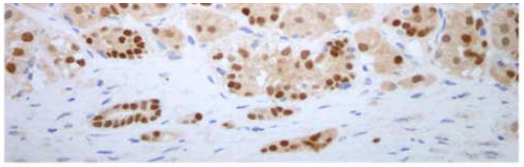
Peckova et al: Ann Diagn Pathol 2014 *TFEB* break

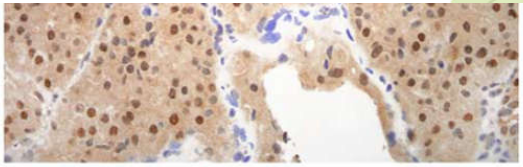
Williamson SR: Renal Cell Carcinoma

Amplification of *TFEB* gene in RCC (Skala et al: Mod Pathol 2018)









TFEB amplifikované RCC

- Zvláštní molekulárně genetické nádory
- High grade RCC
- Agresivní chování
- Variabilní morfologie
- Aberrantní exprese melanocytárních markerů

Histopathology

Histopathology 2019, **74**, 31–59. DOI: 10.1111/his.13727

REVIEW

New and emerging renal entities: a perspective post-WHO 2016 classification

Kiril Trpkov[1] & Ondřej Hes[2]

[1]*University of Calgary and Calgary Laboratory Services, Calgary, Alberta, Canada, and* [2]*Charles University and University Hospital Pilsen, Pilsen, Czech Republic*

Trpkov K & Hes O

(2019) *Histopathology* **74**, 31–59. https://doi.org/10.1111/his.13727

New and emerging renal entities: a perspective post-WHO 2016 classification

Renal tumours include a heterogeneous and diverse spectrum of neoplasms. Recent advances in this field have significantly improved our understanding of the morphological, immunohistochemical, molecular, epidemiological and clinical characteristics of renal tumours, which led to the new Vancouver classification of renal neoplasia and the new World Health Organization (WHO) classification of renal cell tumours. This review aims to summarise the new information and evidence on several new and emerging/provisional renal entities, which were mostly generated after the recent classification of renal neoplasia. stroma, fumarate hydratase-deficient renal cell carcinoma, biphasic squamoid papillary renal cell carcinoma, eosinophilic solid and cystic renal cell carcinoma, atrophic kidney-like renal cell carcinoma, clear cell renal cell carcinoma with giant cells and emperipolesis, Warthin-like papillary renal cell carcinoma, and low-grade oncocytic renal tumour (CD117-negative; cytokeratin 7-positive). Some of these entities, such as succinate dehydrogenase-deficient renal cell carcinoma, have already been recognised as new entities in the WHO classification, and some have been recognised as provisional/emerging entities. However,

Optimistický vzkaz na závěr?

Děkuji za pozornost a přeji hezké léto u vody

Shitlhave, Kruger, JAR
Listopad 2018