Fumarate hydratase deficient renal cell carcinoma and fumarate hydratase deficient-like renal cell carcinoma: Morphologic comparative study of 23 genetically tested cases

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SUMMARY

Hereditary leiomyomatosis and renal cell carcinoma-associated renal cell carcinoma (HLRCC)/ fumarate hydratase deficient renal cell carcinoma (FHRCC) is an aggressive tumor defined by molecular genetic changes - alteration in fumarate hydratase (*FH*) gene. The morphologic spectrum of HLRCC/FHDRCC is remarkably variable. The presence of large nuclei and prominent dark red inclusion-like nucleoli and perinucleolar clearing are considered as helpful morphologic clue. We selected 23 renal neoplasms primarily based on their morphologic features suspicious for HLRCC/FHDRCC. Morphological, basic immunohistochemical, and genetic analysis was performed. The tumors were divided in two groups according to the molecular genetic findings. The first group included 13 tumors with detected *FH* mutation/LOH (compatible with diagnosis FHRCC), and the second group included 10 tumors without *FH* mutation/LOH (FH-like RCCs). In the FHRCC group, the vast majority of cases (9/13) had mixed morphology with different architectural growth patterns. All cases showed prominent macronucleoli, and perinucleolar clearing was found in 10/13 cases. Immunohistochemically, 6/7 FHRCC cases were negative for FH antibody, while one case showed strong diffuse FH reactivity. The FH-like RCC group showed more uniform architectural growth pattern. All 10 tumors had prominent macronucleoli, and perinucleolar clearing was present in 8/10 cases. Eight FH-like RCC cases showed diffuse strong positivity for FH, although 2 cases were completely negative for FH. It is evident that neither morphologic feature nor immunohistochemical analysis can be reliably used in routine practice for the diagnosis of HLRCC/FHRCC. In suspected cases, the diagnosis of HLRCC/FHRCC can be confirmed by molecular-genetic testing for *FH* mutation. It should be noted that the traditionally described morphologic features of HLRCC/FHRCC (prominent eosinophilic macronuclei with perinucleolar halos) can frequently be seen in other renal neoplasms.

Keywords: fumarate hydratase – HLRCC – renal cell carcinoma

Fumarát hydratáza deficientní karcinom z renálních buněk a jemu podobný karcinom z renálních buněk: Komparativní studie 23 geneticky testovaných případů

SOUHRN

S hereditární leiomyomatózou a renálním karcinomem asociovaný renální karcinom (HLRCC)/ fumarát hydratáza deficientní renální karcinom (FHRCC) je agresivní tumor definovaný na základě přítomnosti molekulárně genetické změny – alterace genu pro fumarát hydratázu (FH). Morfologické spektrum těchto neoplázií je široké, avšak přítomnost objemných jader s prominentními tmavě červenými „inklusními" jadérky a s perinukleolárním projasněním byla dlouho považována za důležitý morfologický diagnostický znak. Z Plzeňského registru nádorů bylo vyhledáno a opětovně hodnoceno 23 renálních neoplázií suspektní z FHRCC, primárně na podkladě morfologie. U všech případů byla provedena molekulárně genetická analýza (průkaz mutace/LOH genu pro fumarát hydratázu), detailní morfologické hodnocení (architektonika, cytologické znaky) a základní imunohistochemické barvení (FH). Genetické vyšetření prokázalo alteraci v FH genu u 13 případů (FHRCC), u 10 případů nebyla detekována žádná alterace *FH* genu (FH-like RCC). Tumory s geneticky potvrzenou diagnózou FHRCC měly heterogenní architektoniku kombinující různé růstové vzorce ve většině případů (9/13). Ve všech případech FHRCC byly zastiženy prominentní jadérka, u 10 případů i perinukleolární projasnění. Imunohistochemický průkaz protilátkou FH byl proveden u 7 FHRCC, u 6/7 případů bylo barvení negativní, avšak 1/7 FHRCC vykazoval silnou difúzní reaktivitu. Skupina FH-like RCC byla více uniformní v architektonice, pouze jeden případ kombinoval různé růstové varianty. Všechny případy FH-like RCC měly prominentní jadérka a perinukleolární projasnění bylo zastiženo v 8/10 případů. Osm FH-like RCCs bylo pozitivní v imunohistochemickém průkazu FH, dva případy však vykazovali kompletní negativitu. Z výsledků je patrné, že čistě na podkladě morfologie či imunohistochemického vyšetření je zcela nemožné odlišit FHRCC od nádorů, které FHRCC jen napodobují (FH-like RCC). Diagnostika těchto lézí se tak zcela opírá o molekulárně genetické vyšetření FH genu. Typicky u FHRCC popisované morfologické znaky (prominentní eosinofilní jadérka s perinukleolárním projasněním) jsou často nacházeny i u jiných renálních neoplázií.

Klíčová slova: fumarát hydratáza – HLRCC – renální karcinom

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Hereditary leiomyomatosis and renal cell carcinoma-associated renal cell carcinoma (HLRCC) is an aggressive tumor defined by molecular genetic changes, namely mutation in fumarate hydratase (*FH*) gene. It has been recently proposed that renal tumors associated with impaired *FH* gene to be named fumarate hydratase deficient renal cell carcinoma (FHRCC). The term HLRCC is used for patients with germline mutation of *FH* gene, autosomal dominant heredity and syndromic presentation with

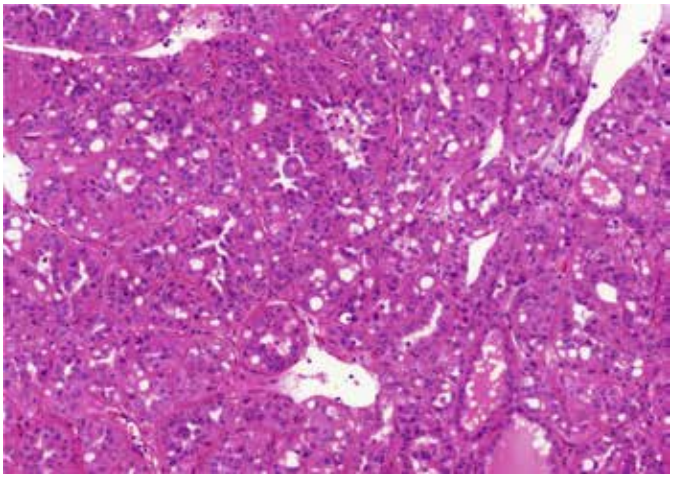

Fig. 1. Cribriform pattern in case of renal cell carcinoma mimicking FHRCC (FH-like RCC). HE 100x

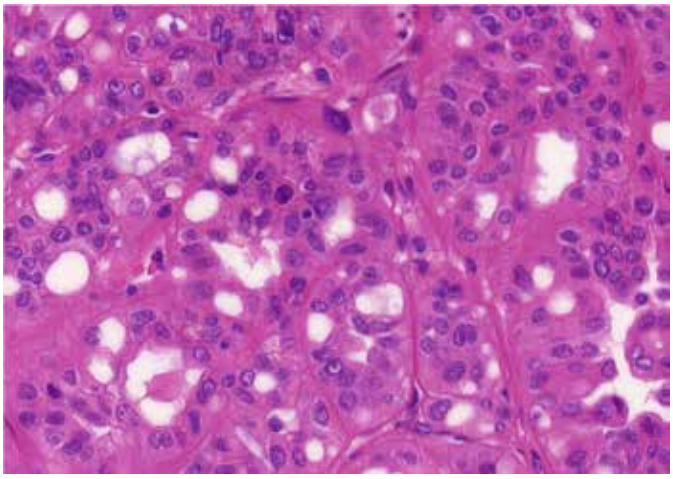

Fig. 2. Deep red macronucleoli and perinucleolar clearing in same case, showed in Figure 1. HE 400x

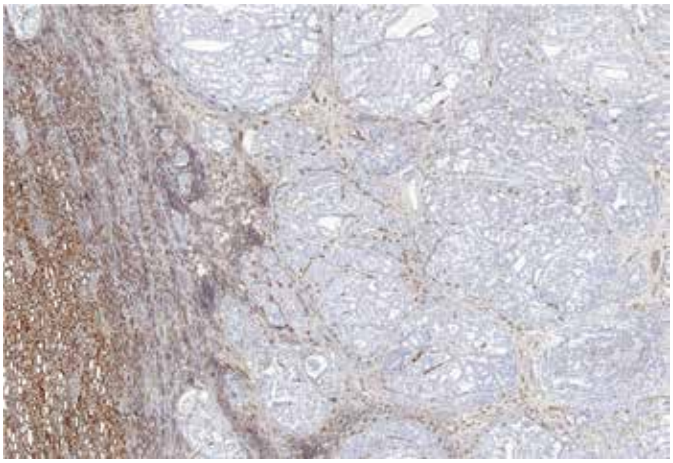

Fig. 3. Renal cell carcinoma mimicking FHRCC (no mutation/LOH of *FH gene* detected) with negative immunohistochemical staining for FH. 40x

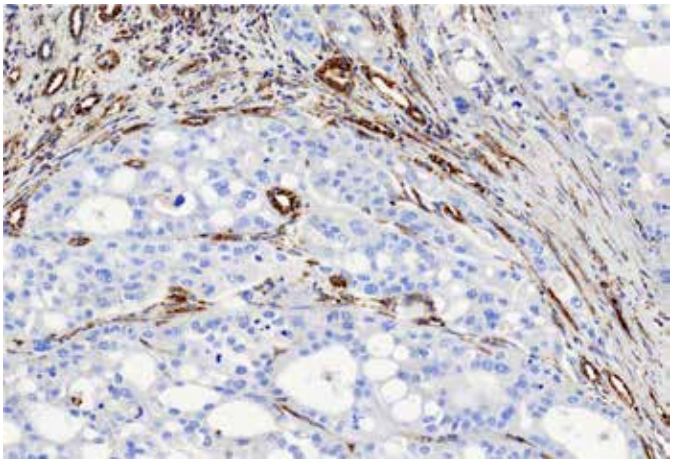

Fig. 4. Immunohistochemical staining for FH – detail. 200x

concurrent presence of cutaneous and/or uterine leiomyomas (1, 2). On the other hand, the term FHRCC is recommended for tumors with suggestive morphology and typical immunophenotype in the setting of uncertain clinical and family history and unknown genetic status. FHRCC also allows designation of cases that might represent apparently sporadic forms, harboring somatic (not germline) alterations in the *FH* gene (3-5). Overall, HLRCC/FHRCC is a distinct histomolecular entity.

The morphologic spectrum of HLRCC/FHRCC is remarkably variable, with various architectural and histologic features being reported in the literature (4-19). Immunohistochemical examination can be helpful in the diagnosis of these tumors with combined negative staining for fumarate hydratase (FH) and strong positive staining for 2-succinocysteine (2SC), demonstrating good sensitivity and excellent specificity (4, 20). Nonetheless, molecular genetic testing for *FH* mutation/LOH still remains the gold standard for the diagnosis of HLRCC/FHRCC.

While HLRCC/FHRCC is one of the most challenging renal tumors in routine practice, its detection can have a significant impact on family members and potentially the patient. Thus, pathologists should be aware of this entity, given its highly variable morphology and difficult immunohistochemical evaluation, to be able to identify suspect cases to be genetically tested.

In this study, we compared morphologic, immunohistochemical and molecular-genetic features between FHRCC (confirmed cases) and FH-like RCC tumors (suspicious cases).

MATERIAL AND METHODS

Case identification

Twenty three tumors suspect for FHRCC primarily based on morphology were identified in the Plzen Tumor Registry out of 26,000 renal neoplasms. Nine cases in this study were previously published (4), and 13 cases were included which were previously published by our group (21). All cases were reviewed by two Urologic Pathologists (KP and OH). Tissues for light microscopy were fixed in 4% formaldehyde and embedded in paraffin using routine procedure. Sections 4 μm thick were cut from tissue blocks and stained with hematoxylin and eosin (H&E). There were 1 to 48 tissue blocks (median 1) for each case. However all original HE slides were reviewed and evaluated. One representative block was selected for immunohistochemical and molecular–genetic studies (usually block with internal positive control of non-neoplastic renal parenchyma).

Tumors were divided in two groups after molecular genetic analysis. The first group included 13 tumors with detected *FH* mutation/LOH (compatible with diagnosis FHRCC), and the second group included 10 tumors without *FH* mutation/LOH (these cases are hereafter referred as FH-like RCC).

Architectural patterns, and morphologic features including the presence of prominent macronucleoli and perinucleolar clearing were analyzed in all 23 tumors. Macronucleoli were described as a prominent dark red inclusion-like nucleoli, and

a perinucleolar clearing was defined as an clear area between the nucleus and the cytoplasm (as seen by light microscopy at high magnification). Different growing patterns were detected in the tumors (papillary, tubulary, solid, cribriform, sarcomatoid, multicystic), every architectural pattern representing more than 5% of the whole tumor mass were count into definitive architectural results.

Immunohistochemistry

The immunohistochemical analysis was performed using a VentanaBenchMark ULTRA (Ventana Medical System, Inc., Tucson, Arizona), FH antibody (J-13, Santa Cruz Biotechnology, dilution 1:3000) was used. Appropriate positive controls were included.

Molecular genetic testing

All cases demonstrating suspicious morphology for FHRCC underwent molecular evaluation for *FH* gene mutation status by Sanger sequencing and loss of heterozygosity studies on DNA extracted from macrodissected FFPE tissue. We also evaluated 10 cases with retained *FH* expression for *FH* mutation, as a negative control group. Previously described custom primer sets were used for Sanger sequencing, and the whole coding sequence including exon-intron junctions was sequenced using primers designed to produce short amplicons suitable for degraded formalin fixed DNA(22). Loss of heterozygosity studies were performed using a previously described set of 6 polymorphic short tandem repeat markers (D1S517, D1S2785, D1S180, AFM214xe11, D1S547, and D1S2842), surrounding the *FH* gene (22).

RESULTS

Fumarate hydratase renal cell carcinoma group (FH RCC group)

FHRCC cohort included 13 tumors from 12 patients. Patients were 8 males and 4 females, with age range of 24-65 years (mean 50.8 years). Tumor size ranged from 0.9-18 cm (mean 9.6 cm).

Molecular genetic analysis confirmed the presence of *FH* mutation/LOH in all 13 cases (Table 1).

Histologic assessment showed mixed patterns in majority of cases (9/13 cases). Pure papillary architecture was detected only in 3/13 cases. Sarcomatoid differentiation was identified in 2/13 tumors. Cytoplasm of the neoplastic cells were bright eosinophilic in 9/13 cases, and weak to scant eosinophilic in four cases. All 13 tumors had prominent macronucleoli (focally in 4 tumors). Perinucleolar clearing was found in 10/13 (focally in 7 tumors).

Material for seven tumors was available for immunohistochemical examination with FH antibody (7/13). Negative staining for FH was found in six cases (with presence of an appropriate positive internal control in adjacent non-neoplastic renal parenchyma), while one case showed strong diffuse FH reactivity (this case demonstrated genetically *FH* mutation c.1118A>G p.Asn373Ser).

Fumarate hydratase-like renal cell carcinoma group (FH-like RCC group)

Five males and five females with age range of 21-82 years (mean 62.4 years) were included in this group. Tumor size ranged from 2.6-11 cm (mean 7.5 cm).

No mutations/LOH of *FH* gene was identified in these 10 cases.

All 10 cases were considered suspicious for FHRCC based on morphology. These tumors were purely papillary in 4 cases, tubulopapillary in 4 cases, tubular in one case, and combined tubulo-cystic and cribriform in one case. Cytoplasm of the neoplastic cells was bright eosinophilic in 8/10 cases, while only focally in two cases. All 10 tumors had prominent macronucleoli (in one case only focally), and perinucleolar clearing was present in 8/10 cases (in 2 cases focally).

Immunohistochemistry showed diffuse strong positivity for FH in 8 cases, which was confirmed by the absence of *FH* mutations. Although 2 cases were completely negative for FH by immunohistochemistry (with an appropriate positive internal control), we were unable to demonstrate *FH* mutations in these cases.

Finally, all these 10 cases were classified as papillary renal cell carcinoma (PRCC), according to the current WHO classification (2). Two cases fulfilled the criteria for diagnosis PRCC type 1, and 8 tumors were classified as PRCC not otherwise specified (NOS).

DISCUSSION

In early publications, even in WHO 2004, the HLRCC/FHRCC was described as displaying typically PRCC type 2 histology (6,9). In recent years, the morphologic spectrum of HLRCC/FHRCC has expanded. It is now evident that the histologic appearance of this tumor is nearly unpredictable. HLRCC/FHRCC includes tumors with predominantly papillary or tubulocystic architecture, usually mixed with other growing patterns (cystic, tubulary, tubulopapillary, tubulocystic, solid). Sometimes, these tumors can closely mimic other renal neoplastic entities – e.g. collecting duct carcinoma, clear cell RCC, tubulocystic RCC, unclassified oncocytic tumor, or even oncocytic type of RCC resembling SDH-deficient RCC (4,5,7,8,10-13,15-19).

Historically, the presence of large nuclei, prominent dark red inclusion-like nucleoli and perinucleolar clearing were considered as helpful morphologic clue (11). However, it is now recognized that even these morphologic features are not consistently present. Recent study by Muller´s group clearly showed that these histologic features are not distinctive for HLRCC/FHRCC. They compared pathological features and imunohistochemical profile (FH/2SC immunohistochemistry) of 24 renal cell carcinomas from proven *FH* mutations carriers and 12 PRCC type 2 from patients without *FH* mutations. In this study, they reported the presence of prominent eosinophilic macronuclei with perinucleolar clearing in 58% PRCC type 2 from patients with no *FH* germline mutation. Further, they concluded that multiplicity of architectural patterns, rhabdoid/sarcomatoid components and combined FH/2SC staining can differentiate HLRCC from type 2 PRCC with efficient *FH* gene (20).

We investigated 23 renal tumors with suspicious histology for HLRCC/FHRCC. The vast majority of these cases were send to us by experienced uropathologists, either for a second opinion or for a molecular-genetic study. The histology was indeed suggestive of FHRCC in all cases, with predominantly papillary growth, often mixed with other patterns, prominent macronuclei (23/23), and perinucleolar clearing (18/23). The *FH* mutation/LOH was confirmed genetically in 13 cases. Four of the 13 genetically proven FHRCC in our cohort showed uniform architecture (3 with papillary and one with tubulocystic pattern), while 9 FHRCCs demonstrated mixed architectural patterns. On the other hand, the tumors that resembled FHRCC (FH-like RCC) were more architecturally uniform. Only one FH-like RCC had mixed growth pattern. Our study along with Muller's study clearly showed that the multiplicity of architectural patterns in conjunction with pertinent immunohistochemical profile may help differentiate HLRCC/FHRCC from PRCC. It should be noted

Table 1. FH deficient RCC and FH deficient-like RCC - Basic clinical data and results of morphologic, immunohistochemical a molecular-genetic study.

Case	Age (years)	Sex	Size (cm)	*FH* mutation	Pattern	Cytoplasm	Macronucleoli	Perinucleolar clearing	FH - IHC	Final diagnosis
Case 1	51	F	Multiple 1.4, 1.0, 1.6, 0.6	c.698G>A p.(Arg233His)	Papillary, tubulocystic, cribriform	eosin	+	+	NP	FHRCC
Case 2**	52	F	Multiple 0.9, 0.6, 0.3, 0.9, 0.2, 0.4	c.698G>A p.(Arg233His)	Papillary	eosin	+ (foc.)	+ (foc.)	NP	FHRCC
Case 3	44	M	7	c.911_917delCTTTTGT p.(Phe305Leufs*22)	Tubulocystic	Scant, Weak eosin	+	+ (foc.)	-	FHRCC
Case 4	45	F	7	c.805delA p.(Ile269fs*15)	Papillary, tubulary	eosin	+ (foc.)	+ (foc.)	NP	FHRCC
Case 5	42	M	10	c.395_398delTAAAT p.(Leu132*)	Papillary, tubulary, cystic	eosin	+	+ (foc.)	NP	FHRCC
Case 6	65	M	18	c.1189G>A p.(Gly397Arg) + LOH	Sarcomatoid, tubulocystic	Scant, eosin	+	-	-	FHRCC
Case 7	60	M	8	c.174_177dupTGAAA p.(Leu60*)	Papillary, cystic, tubulopapillary	eosin	+	-	-	FHRCC
Case 8	50	F	10.9	c.139C>T p.(Gln47Ter) + LOH	Papillary	eosin	+ (foc.)	+ (foc.)	NP	FHRCC
Case 9	60	M	8	c.496G>T p.(Gly166*)	Papillary, tubulocystic, cystic	Weak, eosin	+	+	-	FHRCC
Case 10	52	M	14	c.1385_1390+6del	Solid, sarcomatoid	eosin	+	-	NP	FHRCC
Case 11	54	M	14	c.239dupA p.(Ile81Aspfs*14)	Papillary	eosin	+	+ (foc.)	-	FHRCC
Case 12	61	M	12.5	c.589A>T p.(Ile197Phe) + LOH	Solid-papillary, tubulocystic	eosin	+	+	-	FHRCC
Case 13	24	F	Multiple 2.3 and 13	c.1118A>G p.Asn373Ser	Tubulary, multicystic	Scant, eosin	+ (foc.)	+ (foc.)	+++	FHRCC
Case 14	35	M	11	Neg.	Tubulopapillary	eosin	+	-	+++	PRCC NOS (oncocytic)
Case 15	81	F	4.2	Neg.	Papillary compressed	Weak eosin	+	+	++	PRCC NOS
Case 16	72	F	2.6	Neg.	Tubulocystic, cribriform	eosin	+	+ (foc.)	-	PRCC NOS
Case 17	21	F	5.5	Neg.	papillary	eosin	+	+	-	PRCC NOS (with mucin-like)
Case 18	50	M	10.1	Neg.	papillary	Weak eosin	+	+	+++	PRCC NOS (with clear cell changes)
Case 19	80	M	11	Neg.	tubulopapillary	Weak eosin	+	+	+++	PRCC NOS (solid)
Case 20	62	M	6.4	Neg.	tubulary	eosin	+	+	+++	PRCC NOS
Case 21	67	F	8.5	Neg.	papillary	eosin*	+ (foc.)	-	+++	PRCC type 1
Case 22	74	F	4.2	Neg.	tubulopapillary	eosin	+	+ (foc.)	+++	PRCC type 1
Case 23	82	M	11	Neg.	tubulopapillary	eosin	+	+	+++	PRCC NOS

Yellow block FHdeficient RCC, *green block* FHdeficient-like RCC, *M* male, *F* female, *Neg.* negative, *eosin*eosinophilic, *largedepositsofhemosiderin, *foc.*focally, +present, - absent, *NP* not performed, ** recurrence of case 1, *FH-IHC* immunohistochemical examination with FH antibody

that prominent macronucleoli and perinucleolar clearing are not very specific for this type of neoplasia, and as such it should not be used as a determining criteria for the diagnosis of HLRCC/FHRCC.

Immunohistochemistry can be a useful diagnostic tool in these tumors. Concurrent negative staining for FH and positive staining for 2SC should demonstrate a very good sensitivity and specificity for detecting HLRCC/FHRCC (4). Unfortunately, 2SC immunohistochemistry is still not commercially available. In this study, we found that separate immunohistochemistry for FH, although useful as a screening test, is not 100% sensitive and specific. We identified 2 cases which showed negative FH reactivity by immunohistochemistry, in which we could not confirm a mutation/LOH of the *FH* gene by molecular-genetic tests (FH-like RCCs). Concurrently, immunohistochemical staining with FH antibody reached the sensitivity of 86% in our FHRCC/HLRCC cases. Other recently published study determined that single use of FH antibody shows specificity of 100% but sensitivity of 87.5% (20). This illustrates the limitations of the immunohistochemistry screening for FH in suspicious cases with overlapping histomorphologic patterns. In our view, all morphologically suspicious cases should be evaluated for *FH* gene mutations to separate the true HLRCC/FHRCC from their mimickers, regardless of the FH immunohistochemistry findings.

It is evident that neither morphologic feature nor immunohistochemical analysis can solely be used in routine practice for the diagnosis of HLRCC/FHRCC. Yet morphology and immunohistochemistry could aid and be used as a further screening tool in detecting suspicious cases for genetic testing.

CONCLUSIONS

Our findings showed that it was virtually impossible to separate genuine HLRCC/FHRCC from cases that demonstrate morphologic similarities (FH-like RCC) solely based on morphologic features. Considering the limitations of immunohistochemistry, analysis of *FH* gene is currently the only reliable method for distinguishing HLRCC/FHRCC from their mimickers. Traditionally described histologic features of HLRCC/FHRCC (prominent eosinophilic macronuclei with perinucleolar halos) are frequently found in other renal neoplasms.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this paper.

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Spomienka na emeritného primára MUDr. Petra Kosseya, CSc.

V júli 2019 si slovenská obec patológov a spolupracujúcich klinikov, najmä onkológov pripomenula nedožité 100. výročie narodenia prim. MUDr. Petra Kosseya, CSc., zakladateľa slovenskej onko-patológie.

Peter Kossey sa narodil 14. júla 1919 v Kopašneve, okr. Chust (Podkarpatská Rus) na území vtedajšieho Československa (tč. Zakarpatská oblasť Ukrajiny) v rodine grécko-katolíckeho farára a učiteľky. Detstvo prežil v Strážskom v okrese Michalovce. Stredoškolské štúdium absolvoval na reálnom gymnáziu v Užhorode, kde roku 1938 maturoval. Štúdium medicíny začal na Karlovej univerzite v Prahe, avšak po vyhlásení Protektorátu Čiech a Moravy v r. 1939 pokračoval vo svojich štúdiách na Lekárskej fakulte Semmelweisovej univerzity v Budapešti, kde v septembri 1944 promoval. Po promócii narukoval do maďarskej armády, spočiatku slúžil vo vojenskej nemocnici v Budapešti, ale napokon bol odvelený do vojenského tábora v Nemecku, kde sa v apríli 1945 dostal do amerického zajatia, odkiaľ sa vrátil domov v novembri 1945. V decembri 1945 nastúpil ako sekundárny lekár štátnej nemocnice v Lučenci, kde pôsobil dva roky. Medzitým v apríli 1947 nostrifikoval svoj lekársky diplom na Univerzite Komenského v Bratislave. V rokoch 1947-1953 bol asistentom na Patologicko-anatomickom ústave LFUK v Bratislave, kde sa venoval aj pedagogickej činnosti - viedol praktické cvičenia, prednášal a skúšal medikov. Bol spoluautorom učebných textov i vysokoškolskej učebnice patológie (Základy všeobecnej patologickej anatómie). V rokoch 1953-1974 vykonával funkciu histopatológa na Výskumnom onkologickom ústave, kde sa venoval patológii experimentálnych zvierat a hlbšie patológii ľudských nádorov. V roku 1968 obhájil kandidátsku dizertačnú prácu „Patomorfológia a diferenciálna diagnostika fibrocystických onemocnení kostí", v roku 1970 získal špecializáciu II. stupňa z patologickej anatómie. Založil oddelenie onko-patológie, prvé oddelenie klinickej patológie na Slovensku. V rokoch 1974-1989 vykonával funkciu prednostu Oddelenia klinickej patológie a cytológie Ústavu klinickej onkológie (ÚKO) v Bratislave. Absolvoval niekoľko študijných pobytov doma i v zahraničí, aktívne sa zúčastnil viacerých vedeckých konferencií a kongresov doma i v zahraničí, ako aj pracovných zasadaní WHO v Ženeve ako člen expertnej skupiny pre testikulárne nádory. V rokoch 1978-1981 pôsobil na expertíze v Kuwaite. Ako samostatne pracujúci lekár pracoval na plný úväzok do veku 75 rokov (1994) a do 80 rokov (do 1999) ešte na polovičný úväzok.

Bohatá bola jeho spolupráca s akademikom Viliamom Thurzom, prvým riaditeľom Ústavu experimentálnej onkológie SAV, spolupráca na výskumných úlohách s viacerými klinickými pracoviskami vtedajšieho ÚKO. Dlhoročná bola aj spolupráca s akademikom Jánom Červeňanským, prednostom vtedajšej Ortopedickej kliniky v Bratislave a akademikom Vladimírom Zvarom, prednostom vtedajšej Urologickej kliniky v Bratislave.

Venoval sa diagnostike celého spektra nádorových ochorení, pôsobil ako onko-patológ, konzultant prakticky pre celé Slovensko. Stal sa priekopníkom histopatologickej diagnostiky najmä kostných nádorov, lymfómov, nádorov prsníka a testikulárnych nádorov na Slovensku.

S manželkou Vierou, ktorá pôsobila ako u pacientov veľmi obľúbená praktická lekárka, vychovali 7 detí, z ktorých najstaršie dve dcéry pokračovali v „šľapajách" rodičov ako lekárky.

K jeho záľubám patrila predovšetkým vážna hudba, pravidelne navštevoval abonentné koncerty Slovenskej filharmónie a kupoval gramofónové platne s vážnou hudbou. Rád sa učil cudzie jazyky, hovoril dobre po anglicky, nemecky, rusky, ukrajinsky, poľsky i maďarsky a čiastočne aj po francúzsky a arabsky.

Dr. Peter Kossey, CSc. zomrel 19. septembra 2002 v Bratislave.

Vážený pán primár, chcem sa Vám v mene Vašich bývalých spolupracovníkov, kolegov, i rodinných priateľov, ktorým ste odovzdávali kus seba, poďakovať a vysloviť presvedčenie, že ostávate natrvalo v našich spomienkach a srdciach.

Prof. MUDr. Dalibor Ondruš, DrSc.