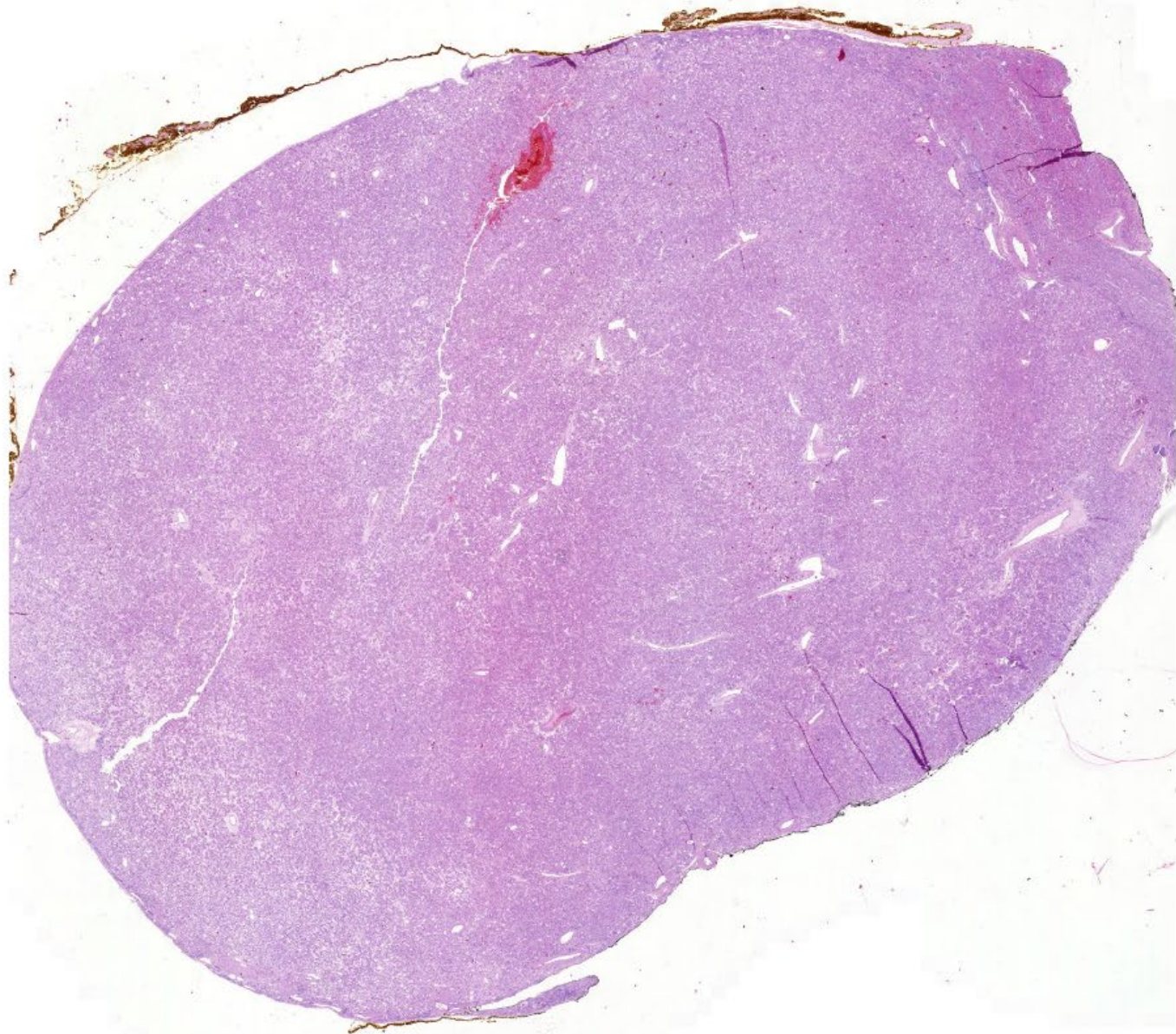
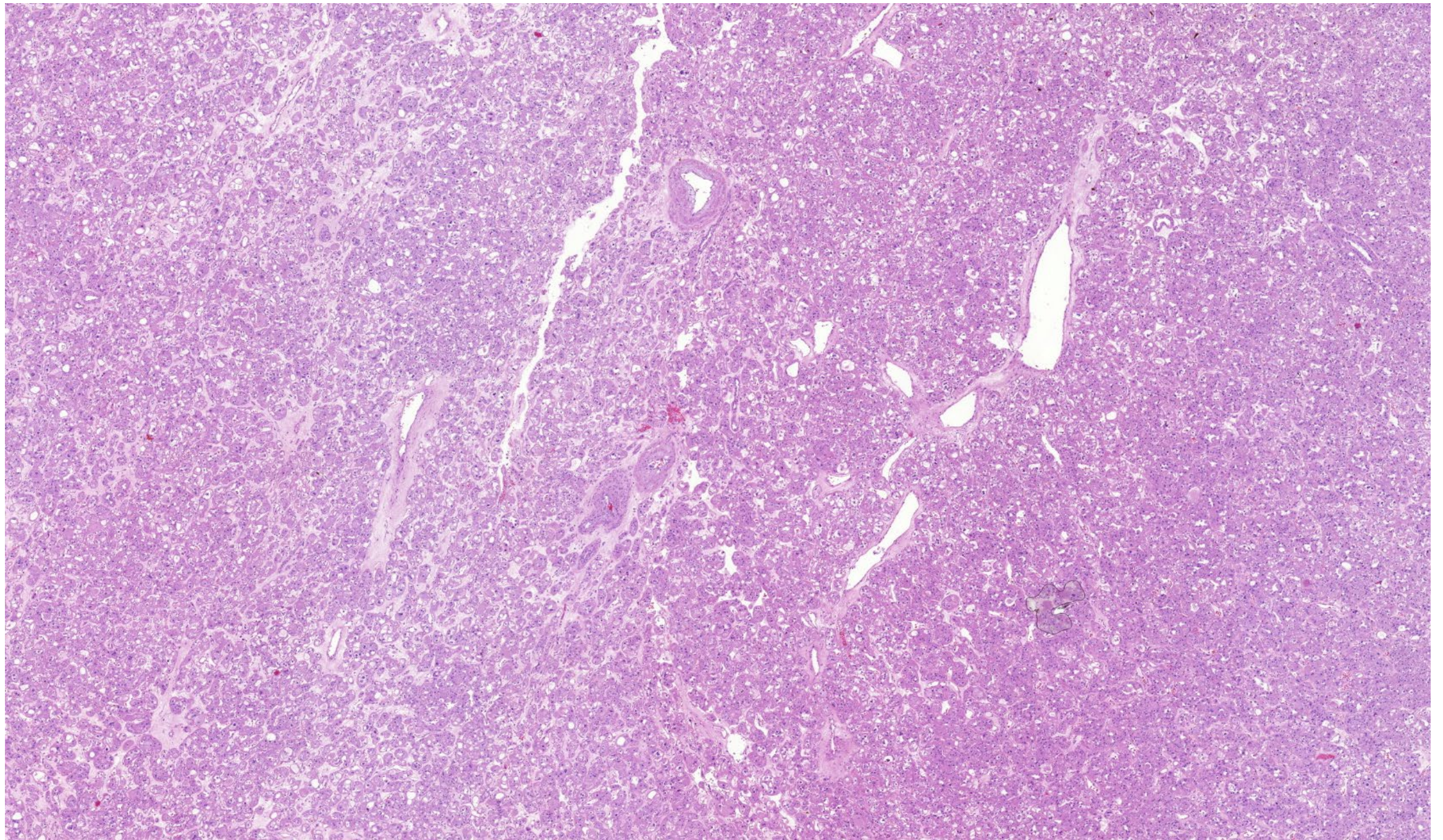
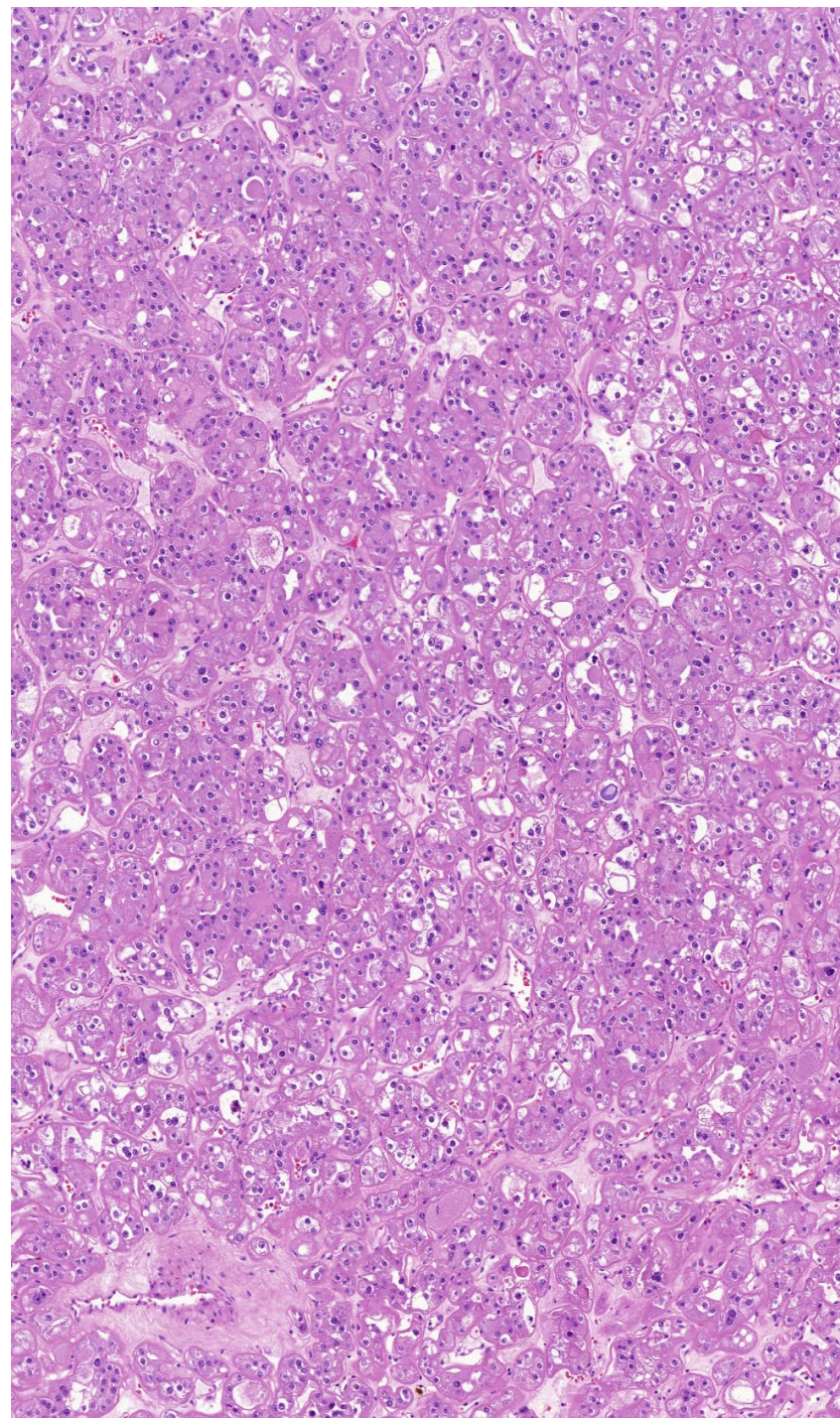
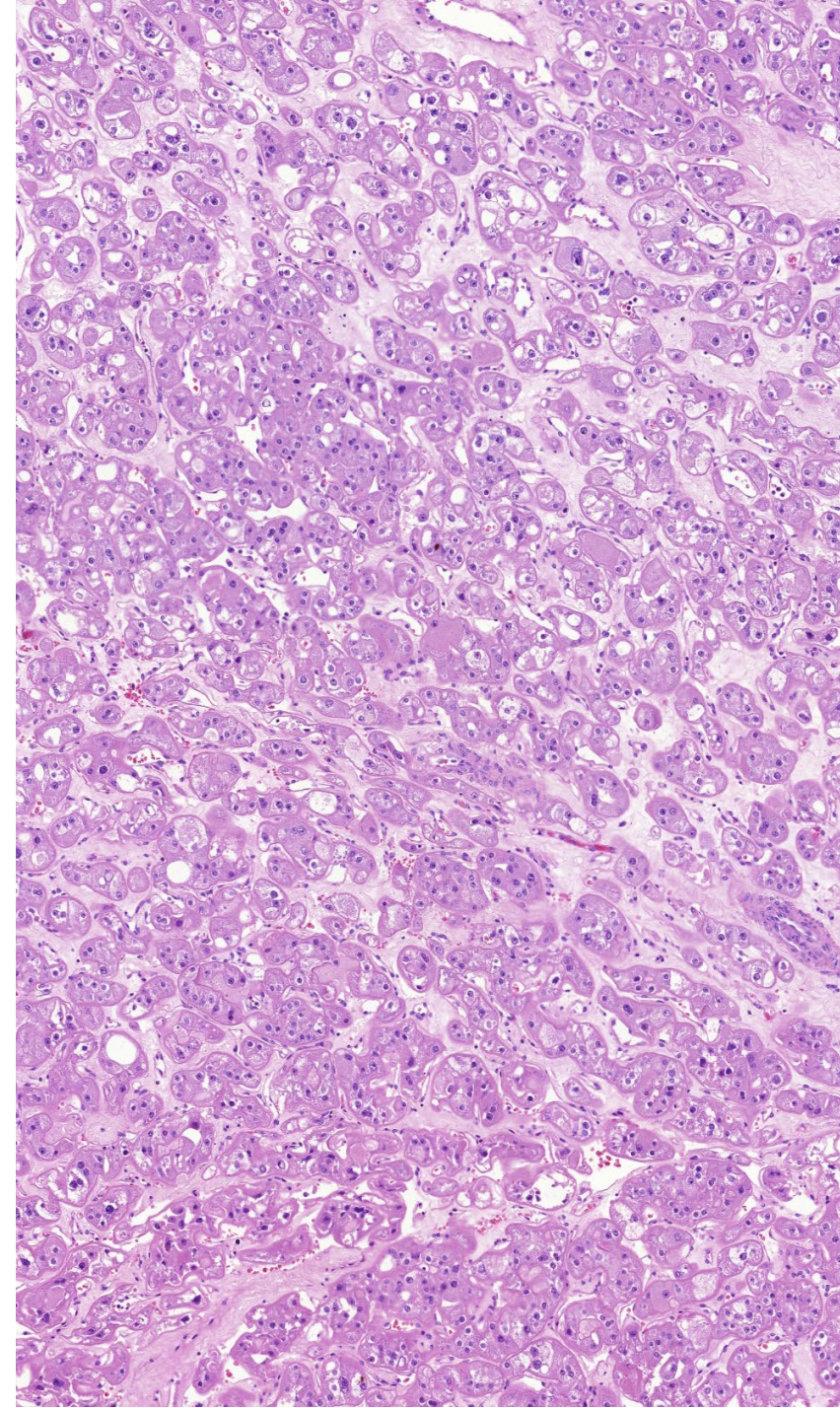


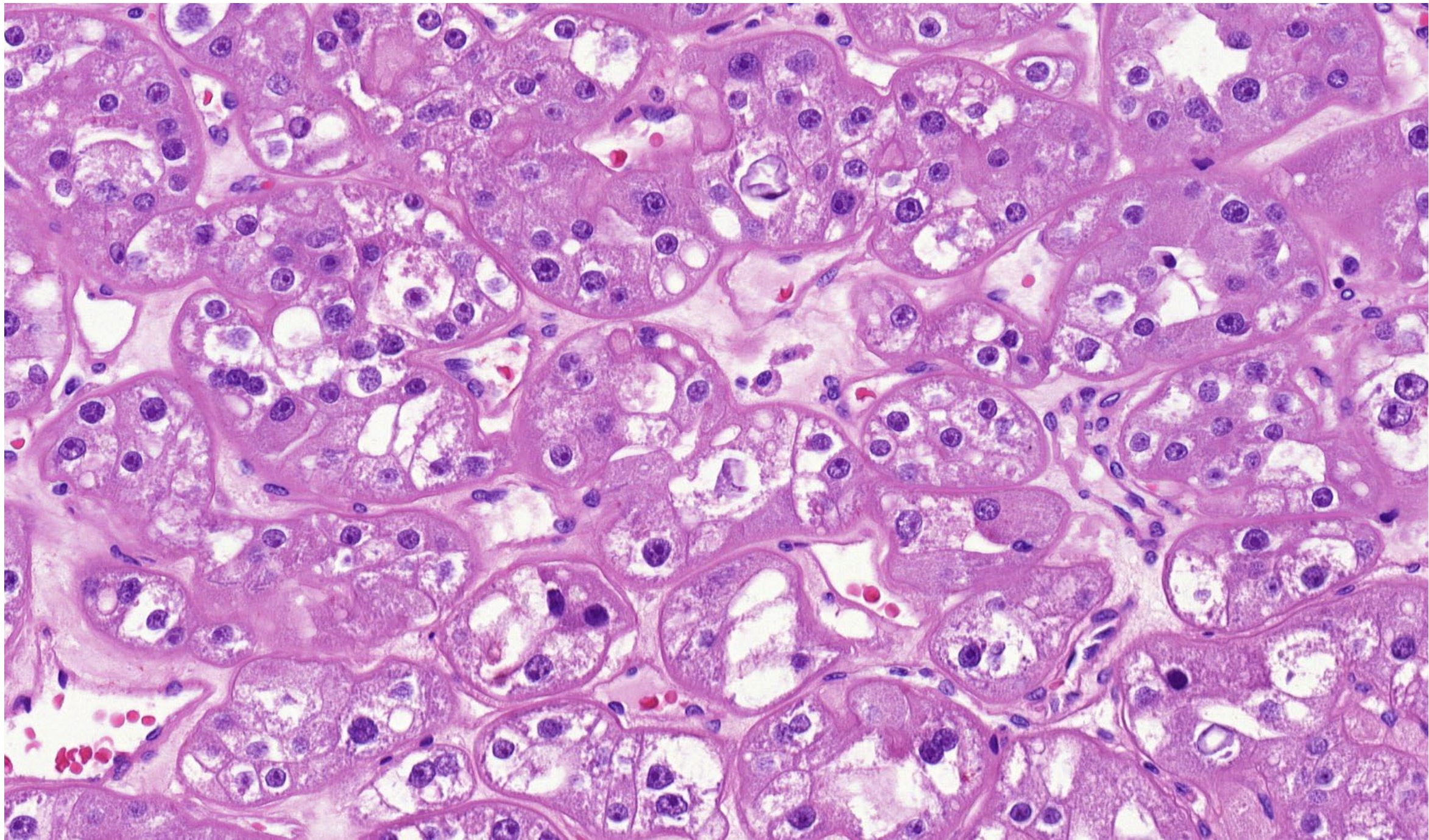
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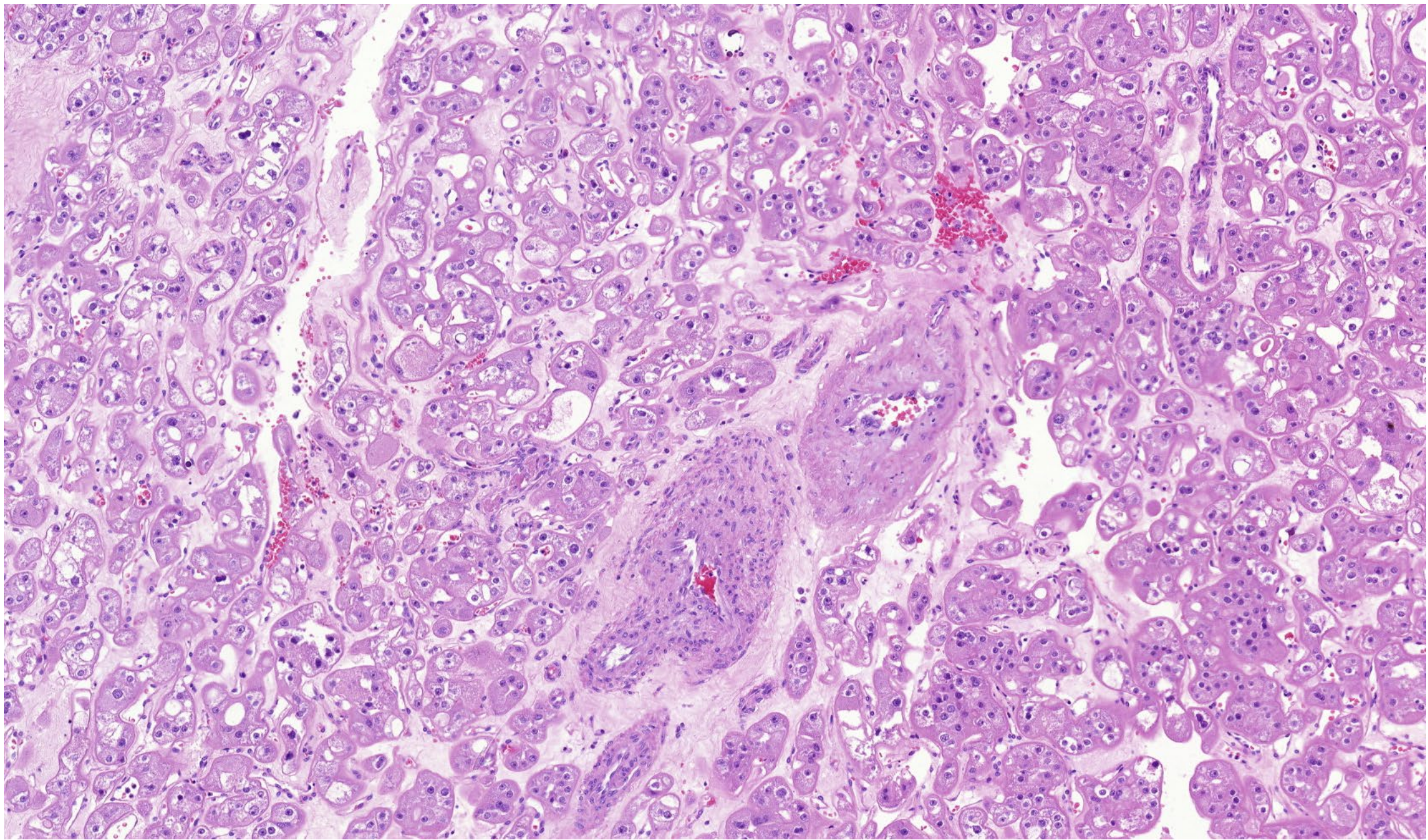
Ondřej Hes

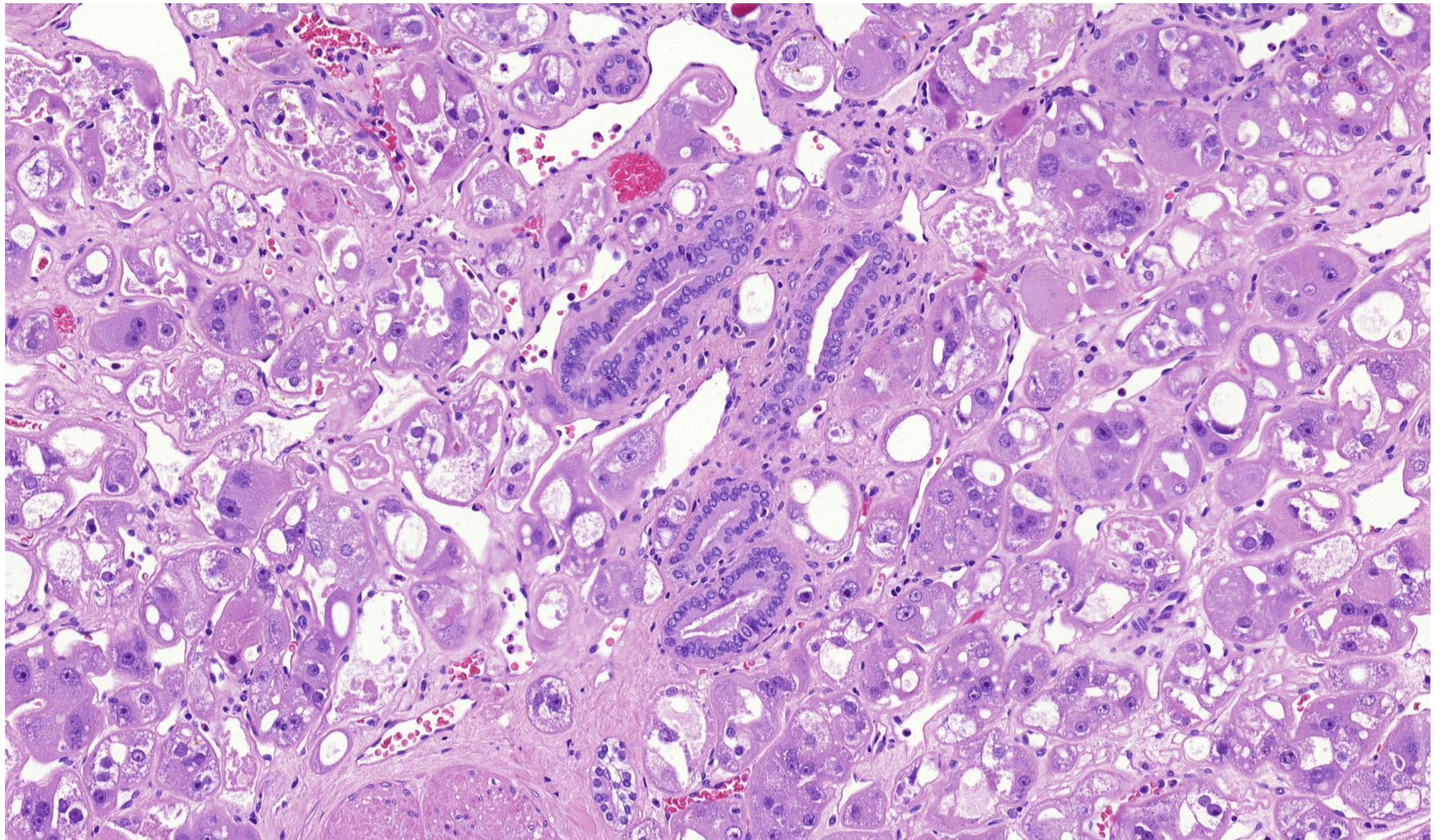




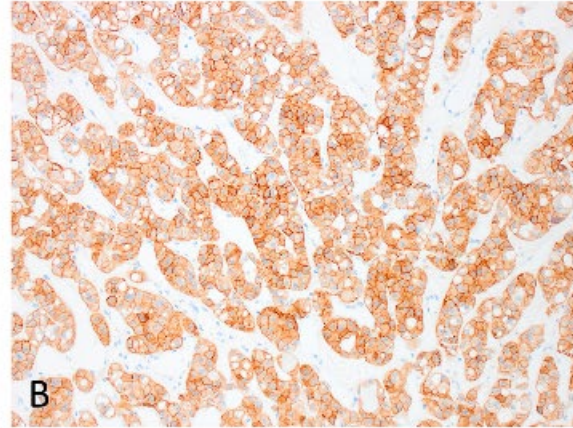
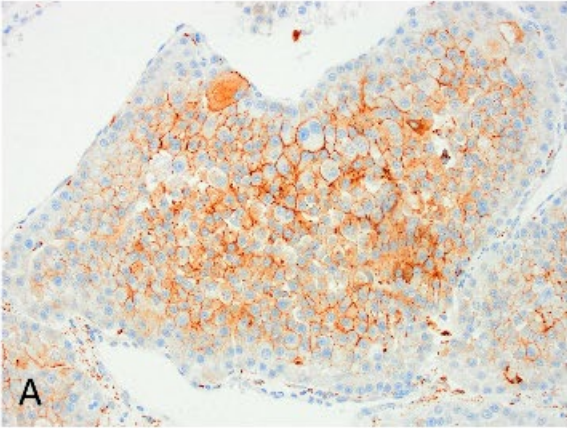




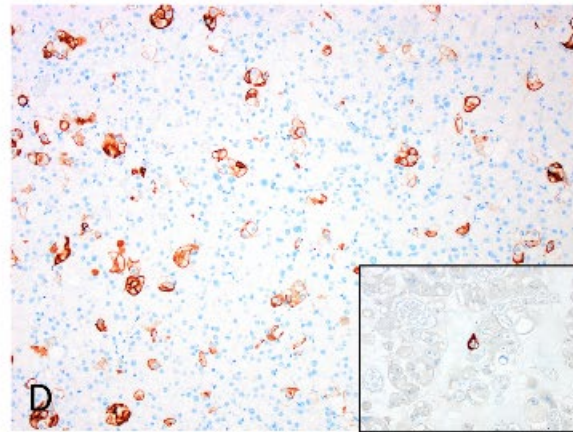
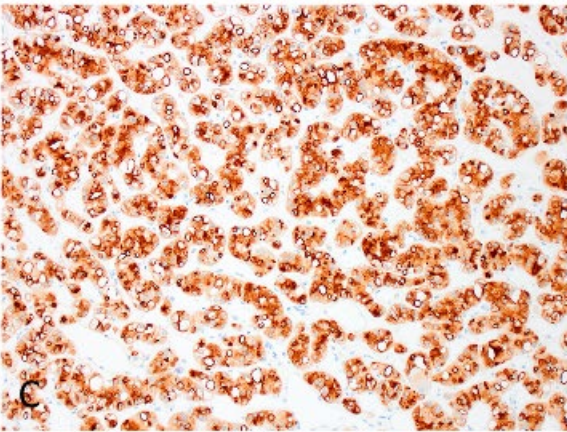




Immunohistochemický profil



- A: Cathepsin K
- B: CD117
- C: CD10
- D: CK 7





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

Huiying He¹ · Kiril Trpkov² · Petr Martinek³ · Ozlem Tanas Isikd⁴ · Cristina Maggi-Galuzzi⁵ · Reza Alaghebandan⁶ · Anthony J Gill^{7,8,9} · Maria Tretiakova¹⁰ · Jose Ignacio Lopez¹¹ · Sean R. Williamson¹² · Delia Perez Montiel¹³ · Maris Sperga¹⁴ · Eva Comperat¹⁵ · Fadi Brimo¹⁶ · Ali Yilmaz² · Kristyna Pivovarcikova³ · Kveta Michalova³ · David Slouka¹⁷ · Kristyna Prochazkova¹⁸ · Milan Hora¹⁸ · Michael Bonert¹⁹ · Michal Michal³ · Ondrej Hes³

Received: 11 May 2018 / Revised: 29 August 2018 / Accepted: 10 September 2018
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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 6/14 cases. All tumors were positive for AE1-AE3, CK18, PAX8, 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

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

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

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*



Novel, emerging and provisional renal entities: The Genitourinary Pathology Society (GUPS) update on renal neoplasia

Kiril Trpkov¹ · Sean R. Williamson² · Anthony J. Gill³ · Adebawale J. Adeniran⁴ · Abbas Agaimy⁵ · Reza Alaghebandan⁶ · Mahul B. Amin⁷ · Pedram Argani⁸ · Ying-Bei Chen⁹ · Liang Cheng¹⁰ · Jonathan I. Epstein¹¹ · John C. Cheville¹² · Eva Comperat¹³ · Isabela Wemeck da Cunha¹⁴ · Jennifer B. Gordetsky¹⁵ · Sounak Gupta¹² · Huiying He¹⁶ · Michelle S. Hirsch¹⁷ · Peter A. Humphrey⁴ · Payal Kapur¹⁸ · Fumiyoshi Kojima¹⁹ · Jose I. Lopez²⁰ · Fiona Maclean^{21,22} · Cristina Magi-Galluzzi²³ · Jesse K. McKenney² · Rohit Mehra²⁴ · Santosh Menon²⁵ · George J. Netto²³ · Christopher G. Przybycin² · Priya Rao²⁶ · Qiu Rao²⁷ · Victor E. Reuter⁹ · Rola M. Saleeb²⁸ · Rajal B. Shah²⁹ · Steven C. Smith³⁰ · Satish Tickoo⁹ · Maria S. Tretiakova³¹ · Lawrence True³¹ · Virginie Verkarre³² · Sara E. Wobker³³ · Ming Zhou³⁴ · Ondrej Hes³⁵

Received: 19 October 2020 / Revised: 15 December 2020 / Accepted: 15 December 2020
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Abstract

The Genitourinary Pathology Society (GUPS) undertook a critical review of the recent advances in renal neoplasia, particularly focusing on the newly accumulated evidence post-2016 World Health Organization (WHO) classification. In the era of evolving histo-molecular classification of renal neoplasia, morphology is still key. However, entities (or groups of entities) are increasingly characterized by specific molecular features, often associated either with recognizable, specific morphologies or constellations of morphologies and corresponding immunohistochemical profiles. The correct diagnosis has clinical implications leading to better prognosis, potential clinical management with targeted therapies, may identify hereditary or syndromic associations, which may necessitate appropriate genetic testing. We hope that this undertaking will further facilitate the identification of these entities in practice. We also hope that this update will bring more clarity regarding the evolving classification of renal neoplasia and will further reduce the category of “unclassifiable renal carcinomas/tumors”. We propose three categories of novel entities: (1) “Novel entity”, validated by multiple independent studies; (2) “Emerging entity”, good compelling data available from at least two or more independent studies, but additional validation is needed; and (3) “Provisional entity”, limited data available from one or two studies, with more work required to validate them. For some entities initially described using different names, we propose new terminologies, to facilitate their recognition and to avoid further diagnostic dilemmas. Following these criteria, we propose as novel entities: eosinophilic solid and cystic renal cell carcinoma (ESC RCC), renal cell carcinoma with fibromyxomatous stroma (RCC FMS) (formerly RCC with leiomyomatous or smooth muscle stroma), and anaplastic lymphoma kinase rearrangement-associated renal cell carcinoma (ALK-RCC). Emerging entities include: eosinophilic vacuolated tumor (EVT) and thyroid-like follicular renal cell carcinoma (TLFRCC). Finally, as provisional entities, we propose low-grade oncocytic tumor (LOT), atrophic kidney-like lesion (AKLL), and biphasic hyalinizing psammomatous renal cell carcinoma (BHP RCC).

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Novel, emerging and provisional renal entities: The Genitourinary Pathology Society (GUPS) update on renal neoplasia

Kiril Trpkov¹ · Sean R. Williamson² · Anthony J. Gill³ · Adebowale J. Adeniran⁴ · Abbas Agaimy⁵ ·
Rebecca J. Jones⁶ · John S. Bellizzi⁷ · G. Przybycin² · Satish Tickoo⁹ · Ondrej Hes³⁵

Rebecca J. Jones⁶ · John S. Bellizzi⁷ · G. Przybycin² · Satish Tickoo⁹ · Ondrej Hes³⁵

Abstract Renal neoplasia is a complex entity, particularly focusing on the newly accumulated evidence post-2016 World Health Organization (WHO) classification. In the era of evolving histo-molecular classification of renal neoplasia, morphology is still key. However, entities (or groups of entities) are increasingly characterized by specific molecular features, often associated either with recognizable, specific morphologies or constellations of morphologies and corresponding immunohistochemical profiles. The correct diagnosis has clinical implications leading to better prognosis, potential clinical management with targeted therapies, may identify hereditary or syndromic associations, which may necessitate appropriate genetic testing. We hope that this undertaking will further facilitate the identification of these entities in practice. We also hope that this update will bring more clarity regarding the evolving classification of renal neoplasia and will further reduce the category of “unclassifiable renal carcinomas/tumors”. We propose three categories of novel entities: (1) “Novel entity”, validated by multiple independent studies; (2) “Emerging entity”, good compelling data available from at least two or more independent studies, but additional validation is needed; and (3) “Provisional entity”, limited data available from one or two studies, with more work required to validate them. For some entities initially described using different names, we propose new terminologies, to facilitate their recognition and to avoid further diagnostic dilemmas. Following these criteria, we propose as novel entities: eosinophilic solid and cystic renal cell carcinoma (ESC RCC), renal cell carcinoma with fibromyomatous stroma (RCC FMS) (formerly RCC with leiomyomatous or smooth muscle stroma), and anaplastic lymphoma kinase rearrangement-associated renal cell carcinoma (ALK-RCC). Emerging entities include: eosinophilic vacuolated tumor (EVT) and thyroid-like follicular renal cell carcinoma (TLFRCC). Finally, as provisional entities, we propose low-grade oncocytic tumor (LOT), atrophic kidney-like lesion (AKLL), and biphasic hyalinizing psammomatous renal cell carcinoma (BHP RCC).

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TSC1-TSC2

Eosinophilic Vacuolated Tumor (EVT) of Kidney Demonstrates Sporadic *TSC/MTOR*

Mutations:

Next Generation Sequencing Multi-institutional Study of 19 Cases

Farcaș Mihaela^{1,2}, Gatalica Zoran³, Trpkov Kiril⁴, Swensen Jeffrey⁵, Zhou Ming⁶,
Alaghebandan Reza⁷, Williamson Sean R⁸, Magi-Galluzzi Cristina⁹, Gill Anthony J^{10,11},
Tretiakova Maria¹², Lopez Jose I¹³, Perez Montiel Delia¹⁴, Sperga Maris¹⁵, Comperat Eva¹⁶,
¹⁷, Brimo Fadi¹⁸, Yilmaz Asli⁴, Siadat Farshid⁴, Sangoi Ankur¹⁹, Gao Yuan²⁰, Ptáková
Nikola²¹, Kuthi Levente²², Pivovarcikova Kristyna²³, Rogala Joanna²³, Agaimy Abbas²⁴,
Hartmann Arndt²⁴, Fraune Cristoph²⁵, Rychly Boris²⁶, Hurnik Pavel²⁷, Durcansky Dušan²⁸,
Bonnert Michael²⁹, Gakis Georgios³⁰, Michal Michal²³, Hora Milan³¹, and Hes Ondrej²³

¹Department of Pathology, Colentina Clinical Hospital, Bucharest, Romania

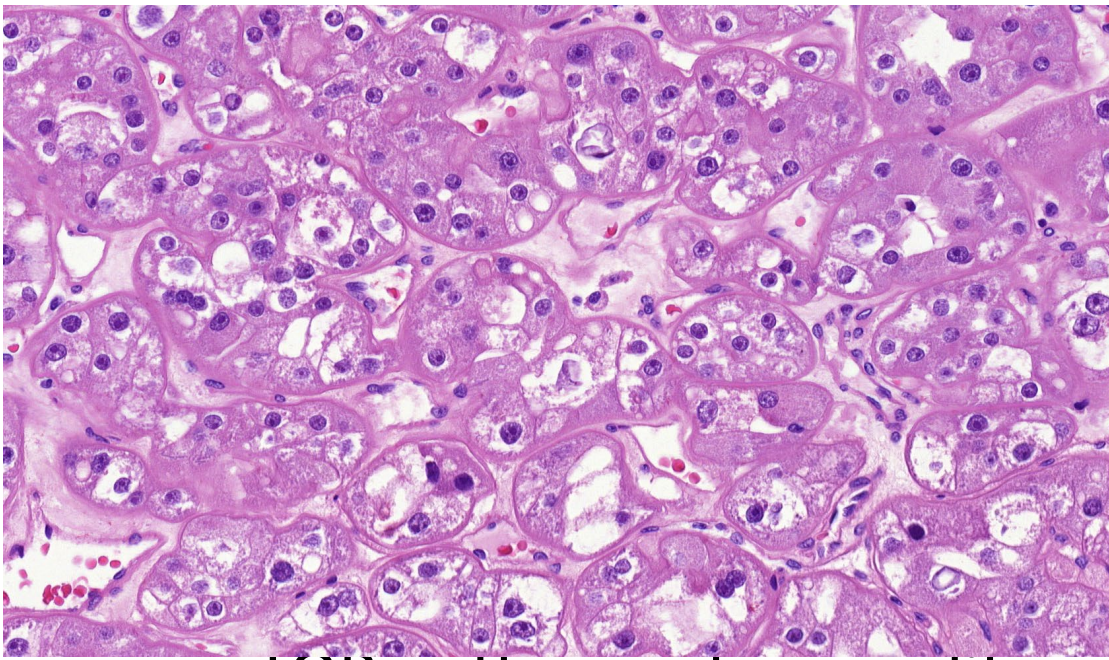
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cell carcinoma (TLFRCC). Finally, as provisional entities, we propose low-grade oncocytic tumor (LOT), atrophic kidney-like lesion (AKLL), and biphasic hyalinizing psammomatous renal cell carcinoma (BHP RCC).

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both cases with
vel subset of
TSC1-TSC2

Diferenciální diagnóza

- **RO**- postrádá vakuoly, jiný IHC profil, postrádá mTOR pathway abnormality
- CH RCC- jiná architektura a cytologie, CK7 je obvykle +++, postrádá mTOR pathway abnormality
- ESC- jiná architektura, nemá vakuoly, častá CK20 pozitivita, genetika je podobná
- BHD syndrom tumory- takřka identické, včetně IHC profilu- nutno vyloučit geneticky



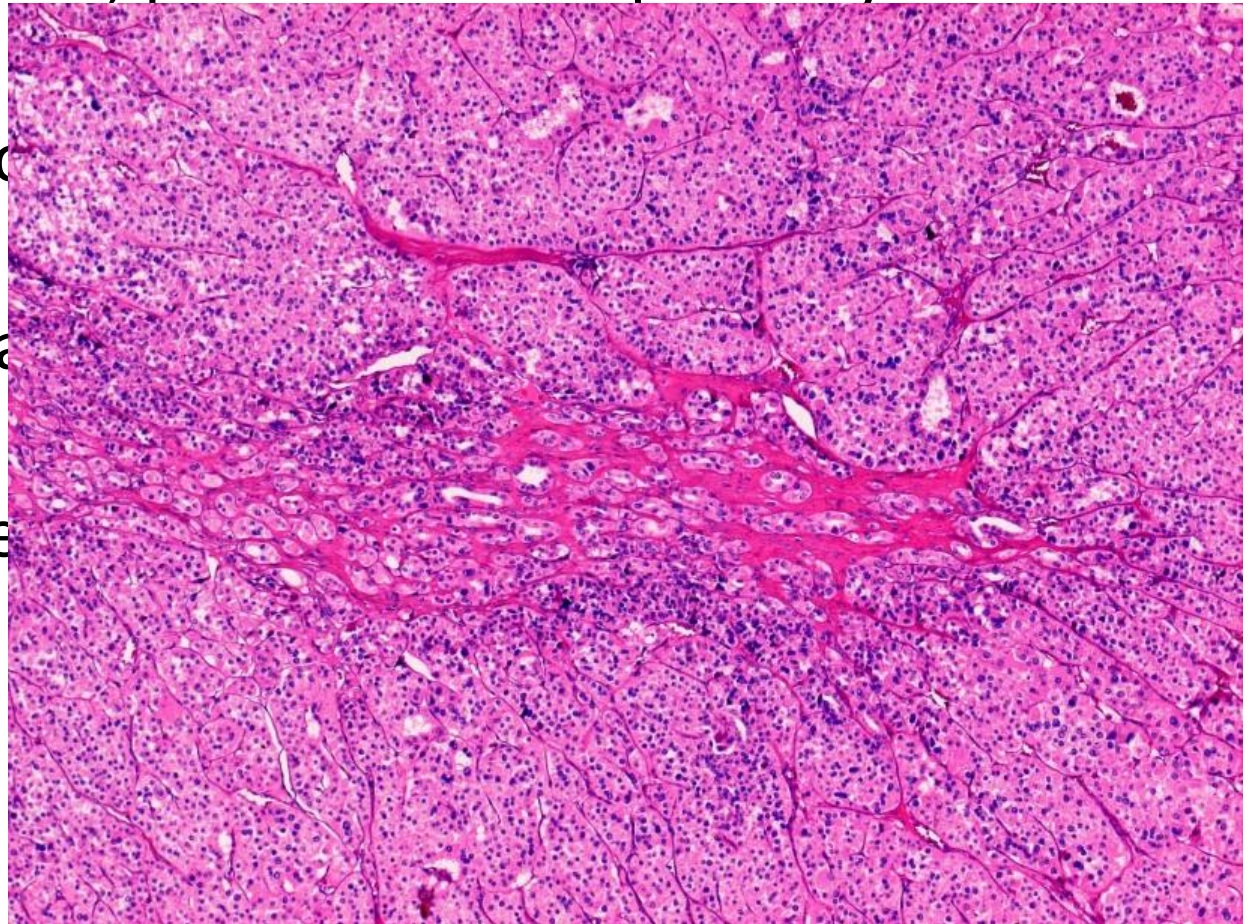
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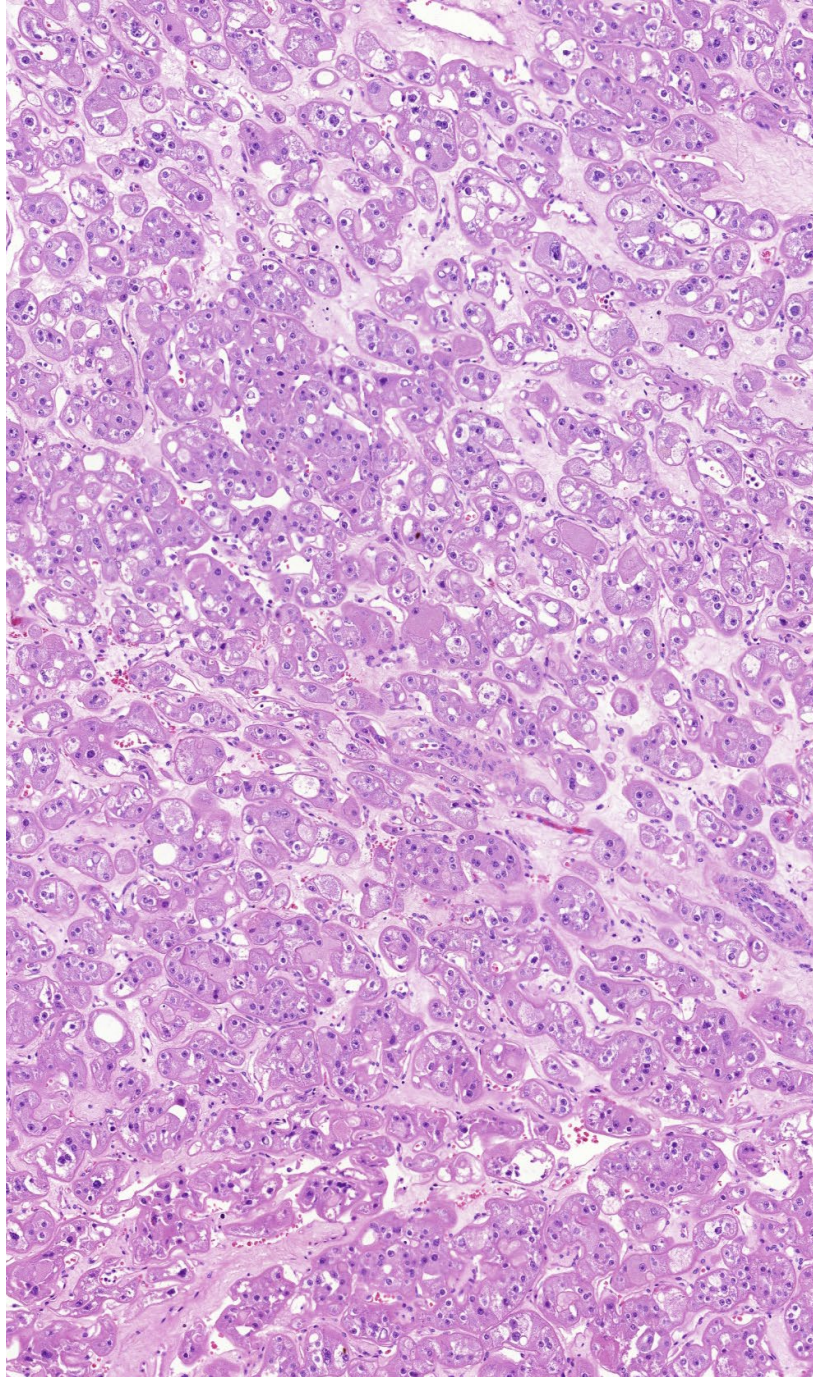
mTOR pathway abnormality

- ESC- jiná architektura, nemá vacuoly, je podobná
- BHD syndrom tumory- takřka ideálně vyloučit geneticky

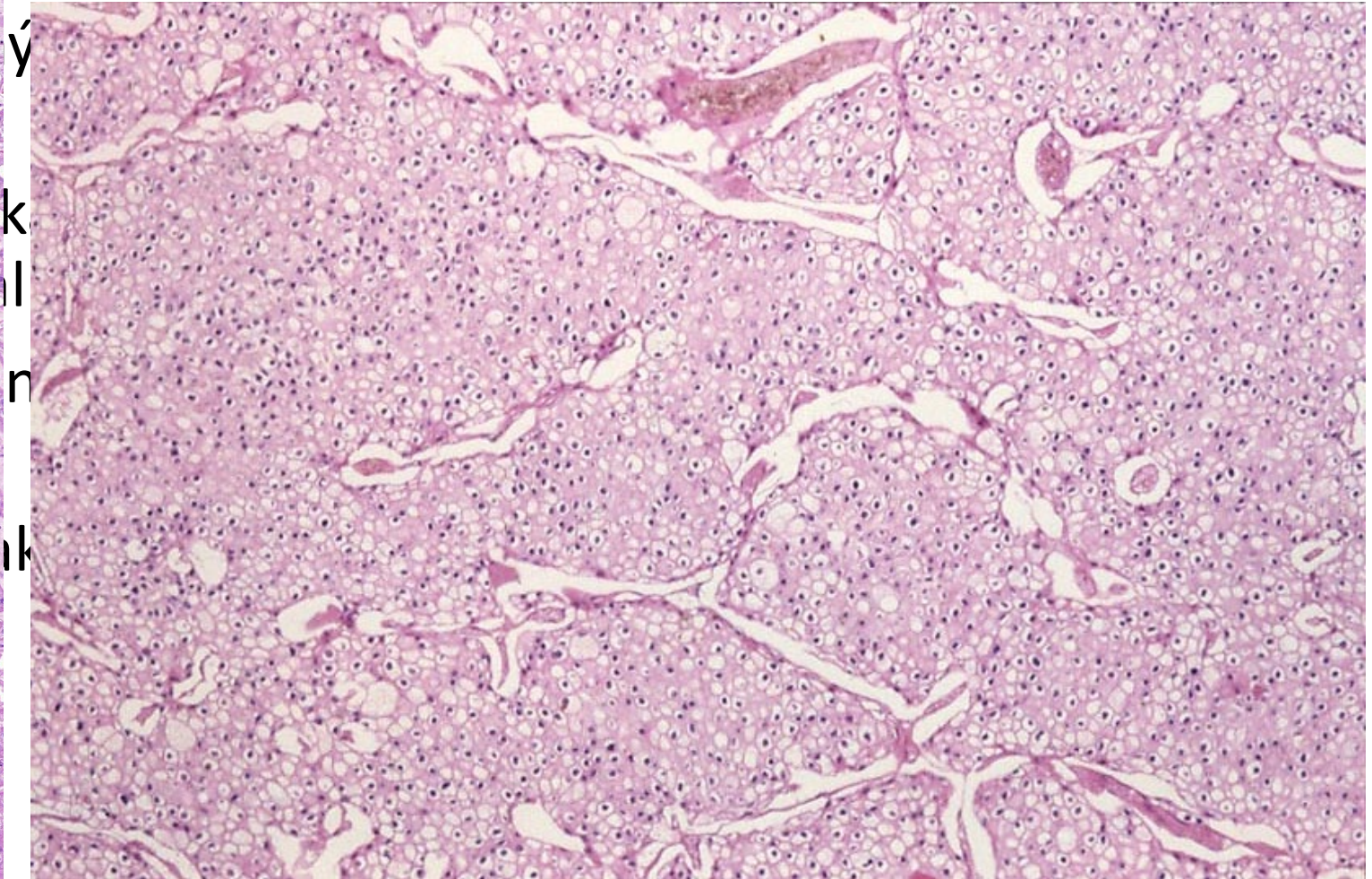


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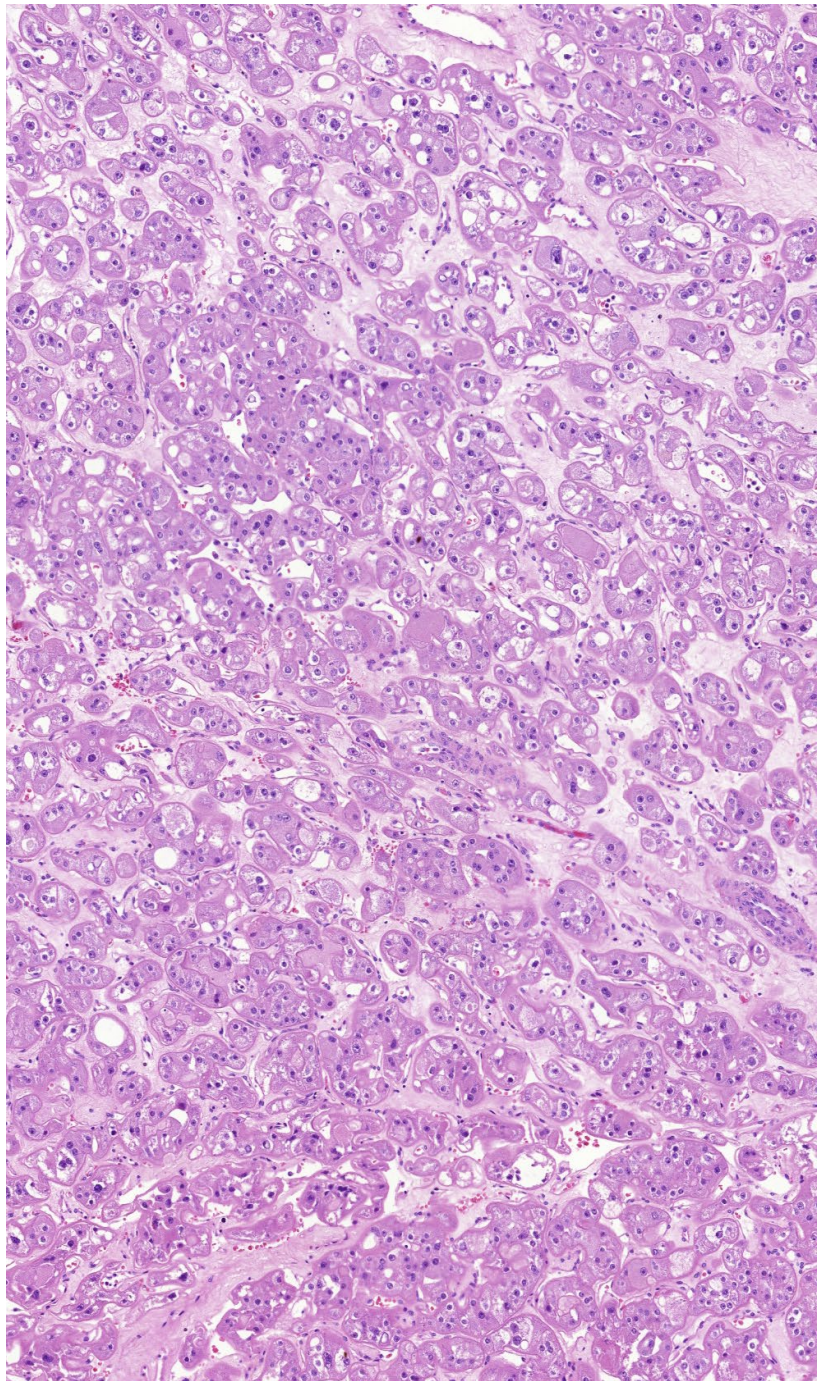


gnóza



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- BHD syndrom tumory- takřka identické, včetně IHC profilu- nutno vyloučit geneticky

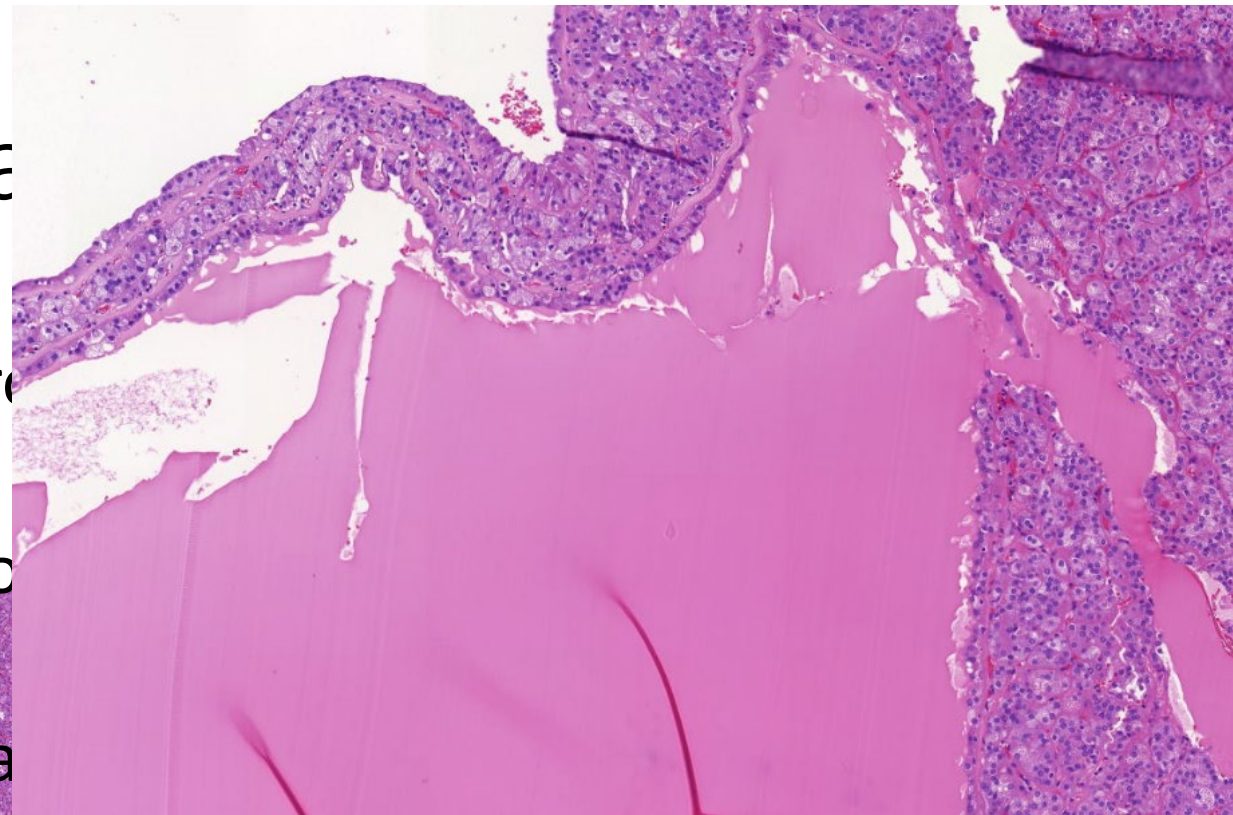


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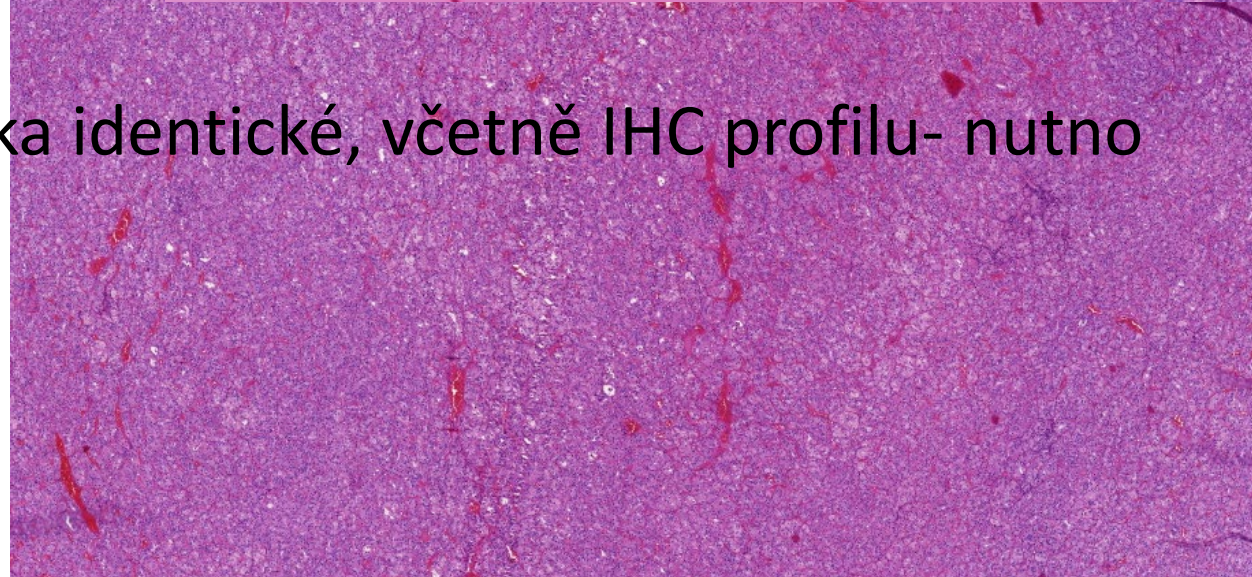
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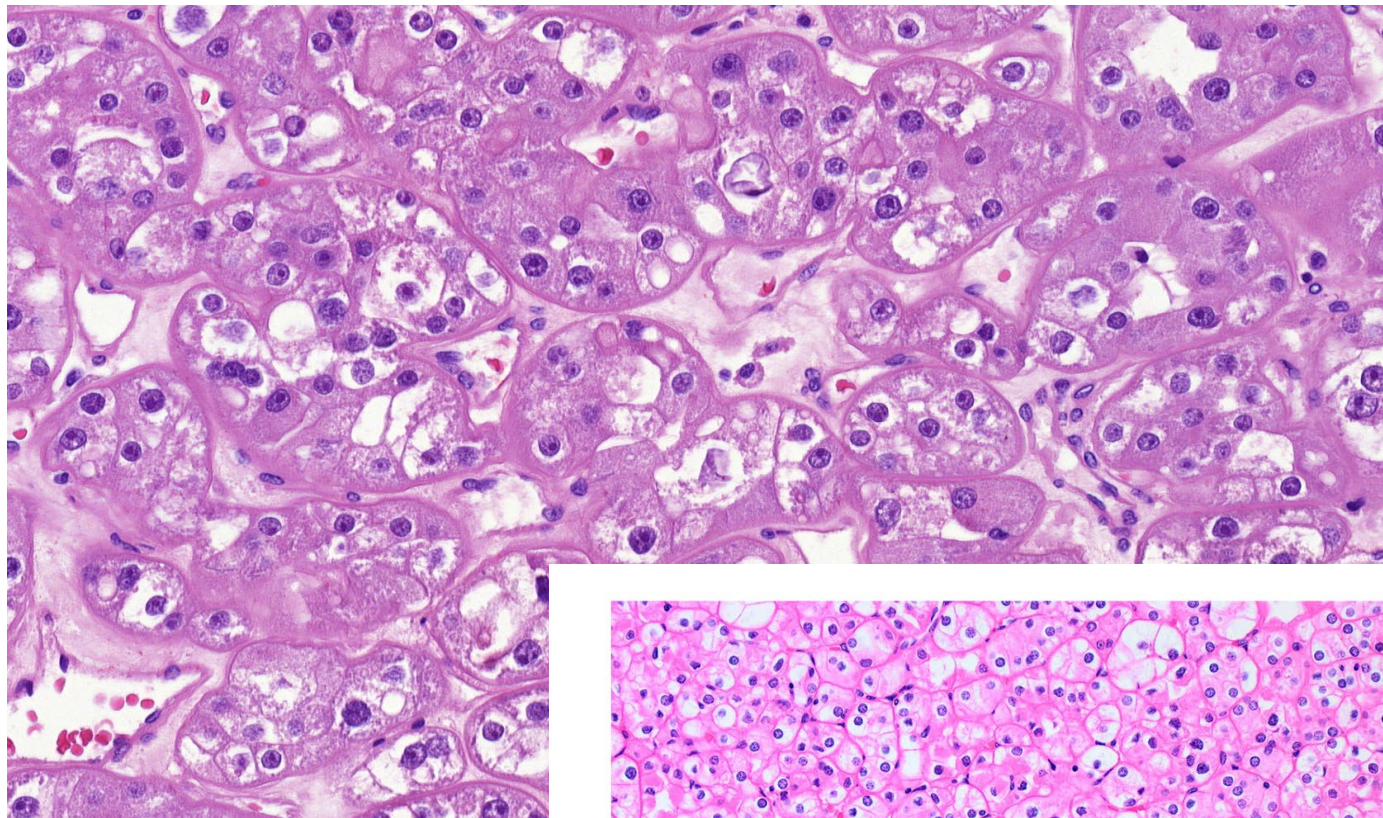


křka identické, včetně IHC profilu- nutno



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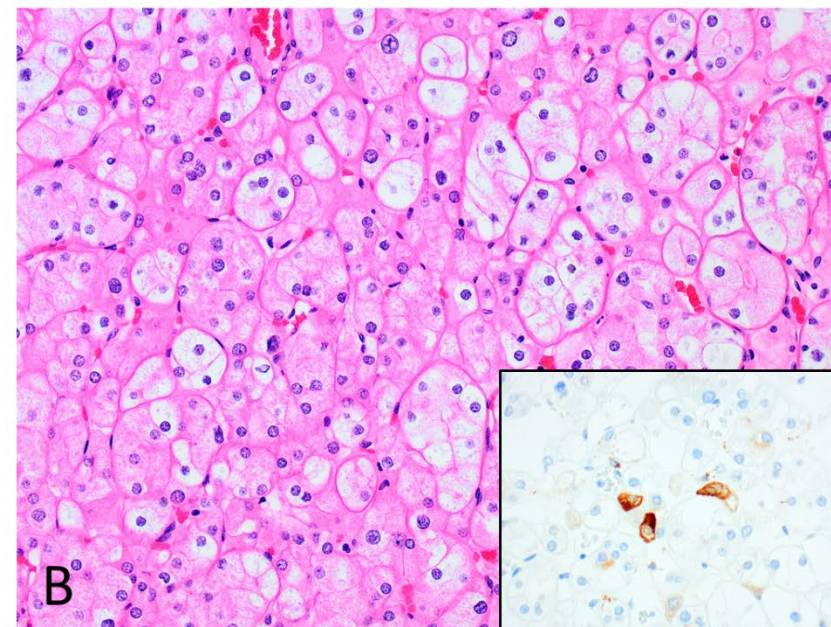
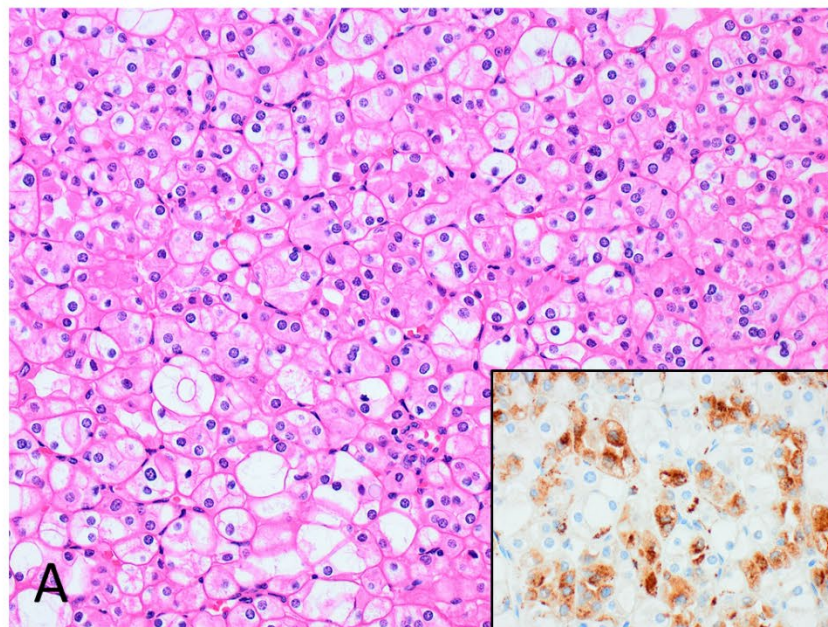


nostrádá mTOR pathway

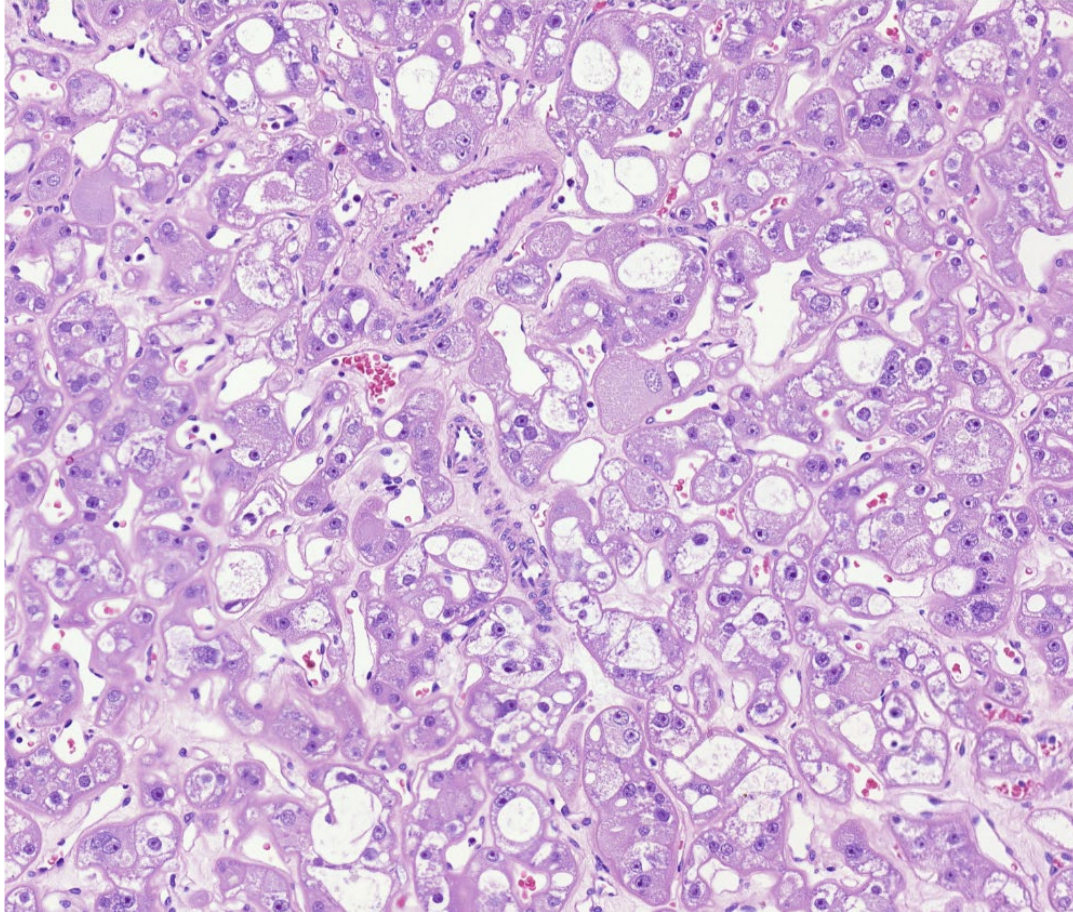
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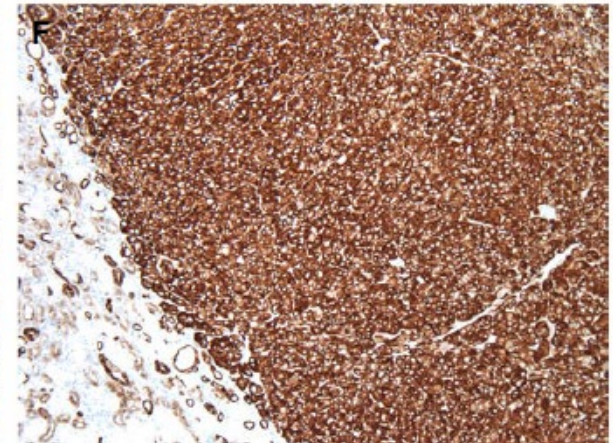
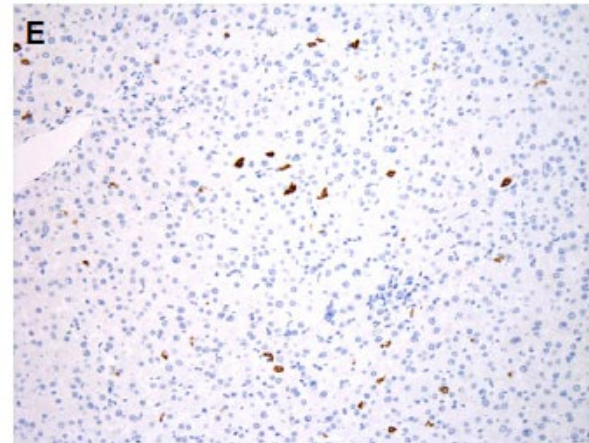
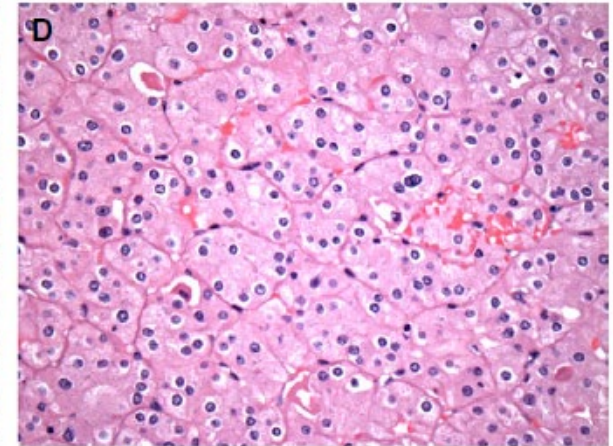
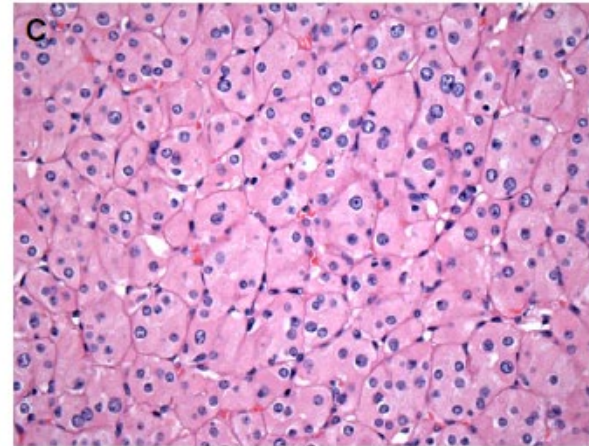
- BHD syndrom
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EVT



LOT



Eosinophilic Vacuolated Tumor

- Low-stage tumors
- Zatím bez agresivního případu, přestože vypadají divoce
- Kompaktní růst
- Eosinofilní buňky s výraznými vakuolami a nepravidelnými jádry
- Pozitivní s cathepsinem K, CD117, CD10, CK 7- onkocytický typ reakce
- Abnormality v *TSC1*, *TSC2*, *mTOR*

Kidney Tumor Friends ~~2020~~ 2021, 5. ročník

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+420 737 220 447

Bioptical laboratory
Mikulasske sq 4, Pilsen, Czech Republic

SPEAKERS

Amin Mahul (*Memphis*)
Comperat Eva (*Vienna/Paris*)
Tretiakova Maria (*Seattle*)
Vujanic Gordan (*Dauha*)
Zhou Ming (*Boston*)
Jose Lopez (*Bilbao*)
Nesi Gabriella (*Florence*)
Agaimy Abbas (*Erlangen*)
Hardtmann Arndt (*Erlangen*)
Osunkoya Boye (*Atlanta*)
Gatalica Zoran (*Oklahoma*)
Yang Ximing (*Chicago*)

Reza Alaghebandan (*Vancouver*)
Siadat Farshid (*Calgary*)
Calio Anna (*Verona*)
Martignoni Guido (*Verona*)
Kristyna Pivovarcikova (*Plzen*)
Kiril Trpkov (*Calgary*)
Joanna Rogala (*Wroclaw*)
Kvetoslava Michalova (*Plzen*)
Rajal Shah (*Dallas*)
Monika Ulamec (*Zagreb*)
Michal Michal (*Plzen*)
Ondřej Hes (*Plzen*)

COURSE STRUCTURE

The meeting will take place in the
Biopticka laborator s.r.o.

The format of the meeting will be a combination of a **slide seminar** (multihead microscope, Thursday, OCT 14) **and lectures** (Friday-Saturday, OCT 15-16th).

The meeting will focus mainly on diagnostics problems in general GU pathology, rare and new kidney, testicular tumors and prostatic lesions. WHO 2021 and GUPS updates were/will be published in 2021. Vast majority of the speakers were authors of both classifications, therefore it is possible to expect brand new reviews of GU problematic. Due to the limited

Kidney

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www.patologie.cz

14.-16.10.2021 Plzeň

Děkuji za pozornost



Žinkovy, Czech Republic,
2/2021