CHARLES UNIVERSITY IN PRAGUE
FACULTY OF MEDICINE IN PILSEN
SIKLS' DEPARTMENT OF PATHOLOGY

SELF-REPORT TO THE DISSERATION

CORRELATION OF IMMUNOHISTOCHEMISTRY AND MOLECULAR BIOLOGIC METHODS IN THE DIAGNOSIS OF TUMORS
KORELACE IMUMOHISTOCHEMIE A MOLEKULÁRNĚ BIOLOGICKÝCH METOD V DIAGNOSTICE NÁDORŮ

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Self-report was sent:_____

Defense of the dissertation in front of the commission for the defense of the dissertation of the study program D4PA5145 PATOLOGIE is taking place on 11th of June, 2018 at 1 p.m. in the auditorium of Bioptical Laboratory Ltd., Rejskova 10, Pilsen

The dissertation is available at the dean's office of the Faculty of Medicine in Pilsen, Charles University in Prague, Husova 3, 30100 Pilsen, Czech Republic.

CONTENT

FOREWORD

While morphology is, and for many decades to come will remain the mainstay of the histopathological diagnosis, an accurate classification of neoplastic disorders is today in many cases impossible without the adjuvant methods of immunohistochemistry (IHC) and molecular genetics. Although there is a continuing effort to discover new sensitive and specific IHC antibodies that would be useful in laboratory practice, an even more intense effort is being exerted to widen our understanding of the molecular underpinnings of neoplastic diseases, particularly since the advent of next-generation sequencing (NGS) in the recent years. Such understanding can be later utilized in many ways. For instance, the knowledge of a rearrangement of a given tumor can later lead to the development of the very specific and sensitive antibody. Secondly, it can become itself diagnostically useful and be easily detected by some relatively cheap molecular genetic method such as fluorescence in situ hybridization (FISH), or by other methods that are becoming more widely available and affordable, including NGS itself. Thus, in both cases, it facilitates rendering of an accurate diagnosis. Thirdly, such rearrangement can lead to the development of novel, highly specific drugs which may target these rearrangements and improve patient's survival. Lastly, the knowledge of the molecular background of tumors allows for the refinement of the tumor classification which in turn leads to the availability of a better risk stratification groups for malignant tumors but also to an increase of pure academic knowledge. At first sight, for examples, when one type of a benign tumor is separated from a heterogeneous group of others, completely innocuous tumors, it may appear that mere academic progress has been achieved. However, such progress usually concomitantly leads to an increase of a deeper understanding of tumorigenesis whose impact and significance are impossible to predict.

Apart from hematopathology and perhaps neuropathology, there are very few areas of surgical pathology where IHC and molecular genetics play such a critical role as in the diagnosis of soft tissue tumors. In fact, it is our experience that today a diagnosis of any soft tissue tumor is rarely made without the use of a least a few IHC markers, and when rendering the diagnosis of sarcoma, IHC and increasingly, molecular genetics, is used almost invariably.

Since soft tissue tumors represent a highly complex group of usually very rare neoplasms whose diagnosis often necessitates advanced laboratory equipment, much of these lesions are usually concentrated in only a few large pathology centers. The author of this thesis is fortunate enough to work at an institution which receives arguably one the highest amount of both routine and consultation soft tissue tumor cases in the whole Central European region. In the last quarter of a century, this institution has also been very effective in the creation and administration of its tumor registry. In this archive of rare tumors, of which the soft tissue tumors represent a very significant part, all cases are precisely assorted using specific keywords. When necessary, any given case can be searched and obtained for review within few hours. For those interested, these circumstances along with the presence of several acknowledged soft tissue experts at the department, provide a unique environment to learn and study soft tissue tumors, as well as many other neoplasms. Therefore, the author of this thesis focused his research mostly (but not exclusively) on mesenchymal neoplasms. The intent of his publications was to study and find novel ways and clues which could help others to arrive at the correct diagnosis as well as to propose novel approaches and categories for classification of certain tumors. To

achieve this goal, he and his colleagues approached every topic the same way a pathologist works in practice. With a novel hypothesis in mind, we first strived for a precise morphological assessment of the material, followed by the IHC analysis. In cases where it was desirable and necessary, molecular genetic analysis followed.

Using this approach, the author of this thesis produced altogether 13 manuscripts as the main researcher, 11 of which focused on mesenchymal lesions. The remaining two studies reported one peculiar penile tumor and one head and neck neoplasm which, along with most of the 20 publications he co-authored, are dealing with the other areas of surgical pathology largely researched at his institution – head and neck pathology and the pathology of testicular and penile tumors. Apart from two contributions deliberately sent to non-impacted journals, all other studies were published in international journals with an impact factor, in many cases representing some of the best journals in this field of medicine.

The thesis is conceived as a collection of commentaries on each manuscript followed by a copy of every publication. It is divided into two main parts. In the initial one, the first authored manuscripts are discussed, the second summarizes the co-authored publications. Each of the two parts is then divided based on the body system it concerns.

SUMMARY

This thesis is a collection of commentaries on altogether 13 first-authored and 20 co-authored publications where morphology, immunohistochemistry (IHC) and molecular genetic methods were used to provide novel clues for arriving at an accurate diagnosis of tumors, as well as to propose novel approaches and refinement of classification of certain tumors. The presented manuscripts are the result of the postgraduate studies of MUDr. Michael Michal at the Charles University in Prague, Faculty of Medicine in Pilsen in the period between 2015-2018. The author focused the main part of his research, particularly his first-authored manuscripts, on soft tissue tumors but also largely participated in research activities focusing on other body systems. Over the course of his studies, four main areas of interests within the topic of soft tissue pathology emerged.

The first is oriented on soft tissue tumors of presumed (but unconfirmed) fibroblastic lineage. First two publications regard two related low-grade sarcomas called Myxoinflammatory fibroblastic sarcoma (MIFS) and Pleomorphic hyalinizing angiectatic tumor (PHAT). In the first manuscript, a high-grade variant of the former is described. The latter publication is focused on the morphological and IHC similarities between both MIFS and PHAT. The third and very recent publication describes 4 novel cases of an emerging entity provisionally called acral fibroblastic spindle cell neoplasm with EWSR1-SMAD3 fusion. Only one previous report of this tumor has been published, and our contribution thus helps to further characterize this apparently very rare tumor.

The second group of publications concerns tumors of the peripheral nerve sheath origin. Overall three papers from this area are presented. One reports on a novel, so far undescribed morphological feature of a plexiform neurofibroma. Other presents a special, highly cellular variant of perineurioma which may be easily mistaken for monophasic fibrous synovial sarcoma. The last manuscript is a review of hybrid peripheral nerve sheath tumor pathology.

The third part concerns peculiar histiocytic proliferations. Although most of them do not primarily affect soft tissue structures, since they may be easily mistaken for a carcinoma and occur over a wide anatomic range, they are often signed out by the soft tissue pathologists. As mentioned, they occur in many different organs and tissues and in most of them they bear a different name. We proposed a unifying concept and a common name for all these lesions and also studied their expression of various IHC markers.

The fourth area of interest are tumors of adipose tissue which became the center of the author's research in one larger paper and two letters to the editor. First paper scrutinized the relatively common lipomatous tumor called spindle cell/pleomorphic lipoma for the presence of lipoblasts. Since general pathologists often consider the presence of lipoblasts as an important feature for rendering the diagnosis of liposarcoma, their presence in spindle cell/pleomorphic lipoma, a benign mimic of liposarcoma, may lead to overdiagnosis. The first letter to the editor reports another worrisome and commonly present feature of spindle cell/pleomorphic lipoma – the occurrence of atypical mitosis. The latter letter to the editor is a reply to a comment made by another group of investigators in a reaction to our studies of spindle cell/pleomorphic lipoma.

Due to a large number of co-authored manuscripts, their summary was omitted, and they will be introduced only at the particular section of the thesis.

ABSTRAKT

Předkládaná dizertační práce je kolekcí komentářů k celkem 13 prvoautorským a 20 spoluautorským pracím, ve kterých bylo použito metod histomorfologického hodnocení, imunohistochemie (IHC) a molekulární genetiky. Tyto metody byly použity za účelem nalezení nových znaků, které by umožnily zpřesnění diagnostiky a také zdokonalily současnou klasifikaci nádorů. Prezentovaná práce je výsledkem postgraduálního studia MUDr. Michaela Michala, které proběhlo na Karlově Univerzitě, konkrétně pak na Lékařské fakultě v Plzni v období mezi roky 2015-2018. Autor se během svého výzkumu, zvláště pak ve svých prvoautorských pracích, zaměřil především na problematiku nádorů měkkých tkání, rovněž se však podílel na výzkumných činnostech zaměřujících se na jiné orgánové systémy. V průběhu studia pak v rámci široké kapitoly nádorů měkkých tkání vykrystalizovala čtyři hlavní témata zájmu.

První téma je tvořeno měkkotkáňovými nádory s (předpokládanou) fibroblastickou diferenciací. Úvodní 2 publikace se týkaly 2 vzájemně příbuzných low-grade sarkomů nazývaných Myxoinflammatorní fibroblastikcý sarkom (MIFS) a Pleomorfní hyalinizující angiektatický tumor (PHAT). V první práci byla poprvé publikována high-grade varianta MIFS. Druhá práce se zaměřovala na morfologické a IHC porovnání obou nádorů. Nedávno vypracovaná třetí práce popisuje 4 nové případy vycházející jednotky s prozatímním názvem Akrální fibroblastická vřetenobuněčná neoplazie s EWSR1-SMAD3 fúzí. Tento tumor byl zatím popsán pouze v jediné předchozí publikaci a naše studie tak výrazně přispívá k přesnější charakterizaci této jednotky.

Druhá skupina publikací se zabývala tumory vznikajícími z pochev periferních nervů. Celkem byly sepsány 3 publikace. Jedna se zabývala novým, dosud nepopsaným morfologickým znakem plexiformních neurofibromů. Další prezentovala speciální, vysoce celulární variantu perineuriomu, která může být snadno zaměněna za monofazický synoviální sarkom. Poslední prací byl přehledový článek o patologii hybridních neurogenních tumorů.

Třetím tématem byly zvláštní histiocytické léze, které sice většinou nepostihují primárně měkké tkáně, ale protože mohou být snadno zaměněny za metastatický karcinom a postihují mnoho různých anatomických struktur, jsou často odečítány „měkkotkáňovými“ patology. Jak již bylo zmíněno, tyto léze se vyskytují v mnoha orgánech a téměř v každém se nazývají jinak. My jsme různými způsoby, včetně IHC, prokázali, že se jedná o identické léze a navrhli koncept, který všechny tyto jinak identické léze sdružuje pod jeden souhrnný název.

Poslední oblastí byly nádory tukové tkáně, které se staly předmětem autorova výzkumu v jedné rozsáhlejší práci a dále ve dvou dopisech editorovi. První původní práce se zabývala relativně častým lipomatózním tumorem nazývaným vřetenobuněčný/pleomorfní lipom. Konkrétně zkoumala frekvenci výskytu lipoblastů, které všeobecní patologové často považují za důležitý diagnostický znak pro stanovení diagnózy liposarkomu. Jejich přítomnost ve vřetenobuněčném/pleomorfním lipomu - benigním tumoru, který často napodobuje liposarkom - může vézt k nesprávné diagnóze malignity. První ze dvou dopisů vydavateli reportoval další matoucí a relativně častý znak pleomorfním lipomů – přítomnost atypických mitóz. Druhý dopis vydavateli byl odpovědí na předchozí korespondenci od jiné skupiny autorů, kteří reagovali na oba přechozí články týkající se vřetenobuněčného/pleomorfního lipomu.

Vzhledem k vysokému počtu spoluautorských prací bude jejich souhrnný popis vynechán a budou představeny vždy v komentáři na příslušném místě této práce.

OBJECTIVES AND AIMS

The intent of the presented research was to study and find novel ways and clues which could help other surgical pathologists to arrive at the correct diagnosis as well as to propose novel approaches and categories for classification of certain tumors.

MATERIALS AND METHODS

To achieve this goal, we first retrieved the desired tumors from the Pilsner Tumor Registry using pertinent keywords. The obtained hematoxylin and eosin slides were morphologically reviewed to confirm to oftentimes several decades old diagnosis. After such refining, the entire cohort underwent a precise morphological assessment for given features, followed by the IHC analysis. For the IHC analysis, more than 700 primary antibodies were available at both the Bioptical Laboratory Ltd. and Sikl's Department of Pathology in Pilsen. In cases where it was desirable and necessary, molecular genetic analysis followed as well. Most common molecular genetic methods used were fluorescence in situ hybridization, reverse transcription polymerase chain reactive, Sanger sequencing, HUMARA assay and in the recent years also next-generation Sequencing, all available at the Bioptical Laboratory Ltd. In Pilsen.

Invaluable part of most of the publications were also detailed clinic-pathological information and follow-up.

RESULTS

Using this approach, the author of this thesis produced altogether 13 manuscripts as the main researcher, 11 of which focused on mesenchymal lesions. The remaining two studies reported one peculiar penile tumor and one head and neck neoplasm which, along with most of the 20 publications he co-authored, are dealing with the other areas of surgical pathology largely researched at his institution – head and neck pathology and the pathology of testicular and penile tumors. Apart from two contributions deliberately sent to non-impacted journals, all other studies were published in international journals with an impact factor, in many cases representing some of the best journals in this field of medicine.

CONCLUSION

This dissertation finalizes the postgraduate study of MUDr. Michael Michal. All the objectives were fulfilled over the course of the study. With the help of the colleagues, the student presented altogether 13 research papers as the first author and participated as a co-author on another 20 studies, all aimed at the use and correlation of IHC and molecular genetic methods in the diagnosis of tumors.

OVERVIEW OF THE PUBLICATIONS

Over the course of the doctoral study program, altogether 33 research papers were finalized. I wrote 13 of them as the first author and participated as a co-author on another 20 studies.

1. Michael Michal, Ryan S. Berry, Brian P. Rubin, Scott E. Kilpatrick, Abbas Agaimy, Dmitry V. Kazakov, Petr Steiner, Nikola Ptakova, Petr Martinek, Ladislav Hadravsky, Kvetoslava Michalova, Zoltan Szep, Michal Michal: *EWSR1-SMAD3-rearranged Fibroblastic Tumor: An Emerging Entity in an Increasingly More Complex Group of Fibroblastic/Myofibroblastic Neoplasms. American Journal of Surgical Pathology, Accepted for publication*
2. Kvetoslava Michalova, Michael Michal, Monika Sedivcova, Dmitry V. Kazakov, Carlos Bacchi, Tatjana Antic, Marketa Miesbauerova, Ondrej Hes, Michal Michal: *Solid pseudopapillary neoplasm (SPN) of the testis: Comprehensive mutational analysis of 6 testicular and 8 pancreatic SPNs*. Annals of Diagnostic Pathology 04/2018; 35., DOI:10.1016/j.anndiagpath.2018.04.003
3. Martina Baneckova, Abbas Agaimy, Simon Andreasen, Tomas Vanecek, Petr Steiner, David Slouka, Tomas Svoboda, Marketa Miesbauerova, Michael Michal, Alena Skálová: *Mammary Analog Secretory Carcinoma of the Nasal Cavity: Characterization of 2 Cases and Their Distinction From Other Low-grade Sinonasal Adenocarcinomas*. American Journal of Surgical Pathology 03/2018; 42(6):1., DOI:10.1097/PAS.0000000000001048
4. Dmitry V. Kazakov, Liubov Kyrpychova, Petr Martinek, Petr Grossmann, Petr Steiner, Tomas Vanecek, Michal Pavlovsky, Vladimir Bencik, Michael Michal, Michal Michal: *ALK Gene Fusions in Epithelioid Fibrous Histiocytoma: A Study of 14 Cases, With New Histopathological Findings*. American Journal of Dermatopathology 01/2018;, DOI:10.1097/DAD.0000000000001085
5. Michael Michal, Dmitry V. Kazakov, Kvetoslava Michalova, Michal Michal: *Atypical multivacuolated lipoblasts and atypical mitoses are not compatible with the diagnosis of spindle cell/pleomorphic lipoma—reply*. Human pathology 01/2018; 74., DOI:10.1016/j.humpath.2017.11.024
6. Abbas Agaimy, Michael Michal, Ladislav Hadravsky, Michal Michal: *Dedifferentiated liposarcoma composed predominantly of rhabdoid/epithelioid cells: a frequently misdiagnosed highly aggressive variant*. Human pathology 01/2018;, DOI:10.1016/j.humpath.2017.12.025
7. Kenji Yorita, Naoto Kuroda, Takushi Naroda, Masato Tamura, Chisato Ohe, Mukul Divatia, Mahul B. Amin, Antonio L. Cubilla, Dimitry V. Kazakov, Ondrej Hes, Michael Michal, Michal Michal: *Penile warty-mucoepidermoid carcinoma with features of stratified mucin-producing intraepithelial lesion and invasive stratified mucin-producing carcinoma*. Histopathology 11/2017; 72(5)., DOI:10.1111/his.13438

8. Alena Skalova, Tomas Vanecek, Petr Martinek, Ilan Weinreb, Todd M. Stevens, Roderick H.W. Simpson, Martin Hyrcza, Niels J. Rupp, Martina Baneckova, Michael Michal, David Slouka, Tomas Svoboda, Alena Metelkova, Arghavan Etebarian, Jaroslav Pavelka, Steven J. Potts, Jason Christiansen, Petr Steiner, Michal Michal: *Molecular Profiling of Mammary Analog Secretory Carcinoma Revealed a Subset of Tumors Harboring a Novel ETV6-RET Translocation: Report of 10 Cases*. American Journal of Surgical Pathology 10/2017; 42(2):1., DOI:10.1097/PAS.0000000000000972
9. Kristyna Srbecka, Kvetoslava Michalova, Radmila Curcikova, Michael Michal, Magdalena Dubova, Marian Svajdler, Michal Michal, Ondrej Daum: *Spectrum of lesions derived from branchial arches occurring in the thyroid: from solid cell nests to tumors*. Virchows Archiv. A, Pathological anatomy and histopathology 07/2017; 471(3)., DOI:10.1007/s00428-017-2201-4
10. Kvetoslava Michalova, Michael Michal, Dmitry V Kazakov, Ondrej Hes, Ladislav Hadravsky, Abbas Agaimy, Maria Tretiakova, Carlos Bacchi, Arndt Hartmann, Stela Bulimbasic, marijana coric, Tatjana Antic, Monika Sedivcova, Michal Michal: *Primary Signet Ring Stromal Tumor of the Testis: A Study of 13 Cases Indicating Their Phenotypic and Genotypic Analogy to Pancreatic Solid Pseudopapillary Neoplasm*. Human Pathlogy 07/2017; 67., DOI:10.1016/j.humpath.2017.07.010
11. Abbas Agaimy, Michael Michal, Simion Chiosea, Fredrik Petersson, Ladislav Hadravsky, Glenn Kristiansen, Raymund E Horch, Jan Schmolders, Arndt Hartmann, Florian Haller, Michal Michal: *Phosphaturic Mesenchymal Tumors: Clinicopathologic, Immunohistochemical and Molecular Analysis of 22 Cases Expanding their Morphologic and Immunophenotypic Spectrum*. The American journal of surgical pathology 06/2017; 41(10)., DOI:10.1097/PAS.0000000000000890
12. Michael Michal, Berrin Babaoglu, Dmitry V Kazakov, Michal Michal, Kemal Kosemehmetoglu: *Atypical Mitoses in Pleomorphic Lipomas*. Human pathology 06/2017; 70., DOI:10.1016/j.humpath.2017.06.024
13. Michael Michal, Dmitry V Kazakov, Ladislav Hadravsky, Kvetoslava Michalova, Petr Grossmann, Petr Steiner, Tomas Vanecek, Valentina Renda, Saul Suster, Michal Michal: *Lipoblasts in Spindle Cell and Pleomorphic Lipomas: a Close Scrutiny*. Human pathology 05/2017; 65., DOI:10.1016/j.humpath.2017.05.006
14. Michael Michal, Dmitry V. Kazakov, Michal Michal: *Hybrid peripheral nerve sheath tumors: A review*. Ceskoslovenska patologie 05/2017; 53(2):81-88.
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16. Michael Michal, Michal Michal: *The unifying concept of histiocytosis with raisinoid nuclei: A new evidence that intravascular/intralymphatic histiocytosis*

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17. Abbas Agaimy, Michael Michal, Johannes Giedl, Ladislav Hadravsky, Michal Michal: *Superficial Acral Fibromyxoma: Clinicopathologic, Immunohistochemical and Molecular Study of 11 Cases Highlighting Frequent Rb1 Loss/Deletions*. Human pathology 11/2016; 60., DOI:10.1016/j.humpath.2016.10.016
18. Kvetoslava Michalova, Michael Michal, Dmitry V. Kazakov, Michal Michal: *Solid pseudopapillary tumor: a new tumor entity in the testis? Reply*. Human pathology 11/2016; 62., DOI:10.1016/j.humpath.2016.08.012
19. Kvetoslava Michalova, Dmitry V. Kazakov, Michael Michal, Ladislav Hadravsky, Denisa Kacerovska, Boris Rychly, Marketa Miesbauerova, Michal Michal: *Differentiated squamous intraepithelial lesion (dSIL)-like changes in the epidermis overlying anogenital melanocytic nevi: A diagnostic pitfall*. Annals of Diagnostic Pathology 11/2016; 26., DOI:10.1016/j.anndiagpath.2016.11.002
20. Michael Michal, Dmitry V Kazakov, Ladislav Hadravsky, Kvetoslava Michalova, Boris Rychly, Michal Michal: *Multivacuolated mucin-filled cells: a unique cell characteristic of plexiform neurofibroma. A report of 11 cases*. Human pathology 11/2016; 60., DOI:10.1016/j.humpath.2016.10.010
21. Marián Švajdler, Michael Michal, Pavol Dubinský, Peter Švajdler, Ondrej Ondič: *Endometrial Endometrioid Carcinoma With Large Cystic Growth Configuration and Deceptive Pattern of Invasion Associated With Abundant Nodular Fasciitis-like Stroma: A Unique Hitherto Unreported Histology in Endometrioid Carcinoma*. Advances in Anatomic Pathology 11/2016; 23(6):381-384.., DOI:10.1097/PAP.0000000000000130
22. Abbas Agaimy, Matthias Bieg, Michael Michal, Helene Geddert, Bruno Märkl, Jan Seitz, Evgeny A. Moskalev, Matthias Schlesner, Markus Metzler, Arndt Hartmann, Stefan Wiemann, Michal Michal, Thomas Mentzel, Florian Haller: *Recurrent Somatic PDGFRB Mutations in Sporadic Infantile/Solitary Adult Myofibromas But Not in Angioleiomyomas and Myopericytomas*. American Journal of Surgical Pathology 10/2016; 41(2):1., DOI:10.1097/PAS.0000000000000752
23. Michael Michal, Alena Skálová, Dmitry V. Kazakov, Květoslava Pecková, Filip Heidenreich, Petr Grossmann, Michal Michal: *Mixed Epithelial and Stromal Tumor of the Middle Ear*. Human pathology 10/2016; 61., DOI:10.1016/j.humpath.2016.09.020
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25. Kvetoslava Peckova, Ondrej Daum, Michael Michal, Radmila Curcikova, Michal Michal: *Selected Case From the Arkadi M. Rywlin International Pathology Slide Seminar: Benign Warthin Tumor of the Thyroid*. Advances in Anatomic Pathology 07/2016; 23(5):1., DOI:10.1097/PAP.0000000000000123
26. Kvetoslava Peckova, Michael Michal, Ladislav Hadravsky, Saul Suster, Ivan Damjanov, Marketa Miesbauerova, Dmitry V. Kazakov, Zdenka Vernerova, Michal Michal: *Littoral cell angioma of the spleen: a study of 25 cases with confirmation of frequent association with visceral malignancies*. Histopathology 07/2016; 69(5)., DOI:10.1111/his.13026
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28. Michal Michal, Stela Bulimbasic, Marijana Coric, Monika Sedivcova, Dmitry V. Kazakov, Michael Michal, Ondrej Hes: *Pancreatic analogue solid pseudopapillary neoplasm arising in the paratesticular location. The first case report*. Human pathology 06/2016; 56., DOI:10.1016/j.humpath.2016.06.007
29. Abbas Agaimy, Michael Michal, Ladislav Hadravsky, Michal Michal: *Follicular Dendritic Cell Sarcoma: Clinicopathological Study of 15 Cases with Emphasis on Novel Expression of MDM2, Somatostatin Receptor 2A and PD-L1*. Annals of diagnostic pathology 05/2016; 23., DOI:10.1016/j.anndiagpath.2016.05.003
30. Michael Michal, Michal Michal, Marketa Miesbauerova, Jana Hercogova, Barbora Skopalikova, Dmitry V Kazakov: *Penile Analogue of Stratified Mucin-Producing Intraepithelial Lesion of the Cervix: The First Described Case. A Diagnostic Pitfall*. The American Journal of dermatopathology 05/2016; 38(5):e64-e67., DOI:10.1097/DAD.0000000000000462
31. Michael Michal, Dmitry V. Kazakov, Ladislav Hadravský, Abbas Agaimy, Marián Švajdler, Naoto Kuroda, Michal Michal: *Pleomorphic hyalinizing angiectatic tumor revisited: all tumors manifest typical morphological features of myxoinflammatory fibroblastic sarcoma further suggesting two morphological variants of a single entity*. Annals of diagnostic pathology 10/2015; 20., DOI:10.1016/j.anndiagpath.2015.10.006
32. Abbas Agaimy, Michael Michal, Lester D R Thompson, Michal Michal: *Angioleiomyoma of the Sinonasal Tract: Analysis of 16 Cases and Review of the Literature*. Head and Neck Pathology 06/2015; 9(4)., DOI:10.1007/s12105-015-0636-y
33. Michael Michal, Dmitry V Kazakov, Ladislav Hadravský, Zdeněk Kinkor, Naoto Kuroda, Michal Michal: *High-grade myxoinflammatory fibroblastic sarcoma: a report of 23 cases*. Annals of diagnostic pathology 04/2015; 19(3)., DOI:10.1016/j.anndiagpath.2015.03.012

OVERVIEW OF THE PRESENTATIONS

1) **Novinky v patologii zažívacího systému (Hot topics in the pathology of the GI tract), 23.5. 2015 Bioptická laboratoř, Pilsen**

Presentation: Precancerous lesions and tumors of the anal mucosa and perianal area including new entities.

Presentations: Neuroendocrine tumors of the GI tract

2) **8th International Arkadi M. Rywlin Pathology Slide Seminar in Anatomic Pathology, 22. -24.6.2015, Bratislava**

Presentation: High-Grade Myxoinflammatory Fibroblastic Sarcoma

3) **Nové jednotky a diagnostická úskalí v patologii (New entities and diagnostic pitfalls in pathology), 25.-26.1. 2016, Bioptická laboratoř, Pilsen**

Presentation: Penile Analogue of Stratified Mucin-Producing Intraepithelial Lesion of the Cervix

Presentation: Myxoinflammatory fibroblastic sarcoma and related lesions

4) **Novinky v patologii zažívacího systému (Hot topics in the pathology of the GI tract), 13.2. 2016 Bioptická laboratoř, Pilsen**

Presentation: Precancerous lesions and tumors of the anal mucosa and perianal area including new entities.

Presentations: Neuroendocrine tumors of the GI tract

5) **105th Annual Meeting of the United States** & **Canadian Academy of Pathology (USCAP), 12.-18.3.2016 Washington State Convention Center, Seattle, WA, USA**

Poster: Littoral cell angioma of the spleen: a study of 25 cases with confirmation of frequent association with visceral malignancies

6) **Seminář mladých patologů a 44. Sjezd českých patologů (Seminar of young pathologists and 44th congress of Czech pathologists), 31.3-1.4 2017, Litomyšl**

Presentation: Lambls' award (2016): the best publication of the year published by a Czech pathologist under 35 years of age. Granted by the Czech society of pathologists for publications numbers 27. and 31. in the list of publications – presentation about these two publications.

7) **106th Annual Meeting of the United States & Canadian Academy of Pathology (USCAP), 4.-10.3.2017 Henry B. Gonzalez Convention Center, San Antonio, TX, USA**

Poster: Lipoblasts in Spindle Cell and Pleomorphic Lipomas: a Close Scrutiny

Poster: Whorling cellular perineurioma: A previously undescribed variant closely mimicking monophasic fibrous synovial sarcoma.

Poster: Differentiated squamous intraepithelial lesion (dSIL)-like changes in the epidermis overlying anogenital melanocytic nevi. A diagnostic pitfall

8) **9th Internationnal Arkadi M.Rywlin Pathology Slide Seminar Club Symposium in Anatomic Pathology, 26.-28.6.2017, Cracow, Poland**

Presentation: Biphenotypic sinonasal sarcoma

Presentation: Histiocytosis With Raisinoid Nuclei: A Unifying Concept for Lesions Reported Under Different Names as Nodular Mesothelial/Histiocytic Hyperplasia, Mesothelial/Monocytic Incidental Cardiac Excrescences, Intralymphatic Histiocytosis, and Others

Presentation: Whorling cellular perineurioma: A previously undescribed variant closely mimicking monophasic fibrous synovial sarcoma.

9) **107th Annual Meeting of the United States & Canadian Academy of Pathology (USCAP), 3. - 9.3.2017 Vancouver, Canada**

Poster: Subcutaneous Atypical Fatty Tumors with P53 Overexpression, RB1 Gene Abnormalities and a Lack of MDM2 Gene Amplification. Expanding the Morphologic Spectrum of "Anisometric Cell Lipoma (ACL)"

Poster: Tenosynovitis with psammomatous calcifications: A clinicopathologic study of 23 cases

10) **8. Východoslovenský bioptický seminář (Eastern Slovakian bioptic seminar), 27.-28.4. 2018, Košice.**

Presentation: Pathology of peripheral nerve sheath tumors

Presentation: Virtual slide seminar of interesting cases

11) **Sklíčkový seminář (Slide seminar) SD-IAP, 27.-28.4. 2018, Košice.**

Presentation: Anisometric/Dysplastic lipoma

12)10th Internationnal Arkadi M.Rywlin Pathology Slide Seminar Club Symposium in Anatomic Pathology, 21.-23.5.2018, Split, Croatia

Presentation: Fibrolipomatous hamartoma of the nerve

Presentation: Inflammatory leiomyosarcoma

Presentation: High-grade myxoinflammatory fibroblastic sarcoma

13) 58. Studentská vědecká konference, 30.5.2018, Šafránkův pavilon, Plzeň

Presentation: Dysplastic lipoma: a distinctive atypical lipomatous neoplasm with anisocytosis, focal nuclear atypia, p53 overexpression and a lack of MDM2 gene amplification by FISH. A report of 66 cases demonstrating occasional multifocality and a rare association with retinoblastoma.

Presentation: EWSR1-SMAD3-rearranged Fibroblastic Tumor: An Emerging Entity in an Increasingly More Complex Group of Fibroblastic/Myofibroblastic Neoplasms.