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Dissertation Opponent's Report



Author: **Joanna Rogala, MD**

Workplace: Charles University, Faculty of Medicine in Pilsen, Department of Pathology

Study program: Pathology

Title: **Clinicopathological, morphological, immunohistochemical, and molecular biological features of tumors of the genitourinary tract.**

Supervisor: prof. MUDr. Ondřej Hes, Ph.D., doc. MUDr. Kristýna Pivovarčíková, Ph.D.

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The submitted dissertation was prepared at the Šikl Institute of Pathology under the guidance of the supervisors: Prof. MUDr. Ondřej Hes, Ph.D. and Doc. MUDr. Kristýna Pivovarčíková, Ph.D. The work is content-rich and written in the form of comments on published articles in which the applicant is the first author or co-author. The topic of the work is kidney tumors. The nature of the workplace allowed to collect several rare kidney neoplasms for the work.

Choice and relevance of topic, goals

The topic of this work is kidney tumors with an emphasis on chromophobe renal cell carcinoma. The following tumors are also discussed: eosinophilic vacuolated tumor, papillary renal cell carcinoma, renal cell carcinomas with tubulopapillary architecture, and oncocytic cells. In recent years, there has been a significant shift in pathology toward incorporating molecular and genetic methods in the diagnosis of tumors. The histomorphological diversity of kidney tumors is high, and the expression of immunohistochemical markers is often inconsistent, especially in the case of diagnostically challenging tumors. Therefore, genetic methods significantly improve the diagnosis of kidney tumors, which is highlighted in this work. At the same time, a detailed histomorphological examination is emphasized as the basis of diagnosis. The character of the workplace allowed to collect relatively rare kidney tumors. In our countries, there is a shortage of "expert" urogenital pathologists, which is why we consider the chosen topic to be current and relevant for diagnostic practice. In the theoretical part of the work, we would welcome comments on the future role of methylation profiling in the diagnosis of renal tumors.

Formal editing, methods.

The dissertation contains a total of 108 pages of text, including the full wording of the author's published articles. Seven articles are listed, two of which the applicant is the first author. For all

articles, the author provides separate comments, which are written without apparent stylistic or formal errors. All articles concern kidney tumors, therefore, a better title for the dissertation would be: Clinicopathological, morphological, immunohistochemical, and molecular biological features of renal tumors.

Results, Conclusion

Moanna Rogala, MD presented a precisely crafted work without significant formal or content-related errors, which builds upon a significant shift in pathologic diagnosis of renal tumors in recent years, with emphasis on the incorporation of genetic methods. Genetic methods have significantly influenced diagnostic pathology in the last decade, including the diagnosis of kidney tumors. Some kidney tumors are diagnosed specifically based on certain genetic changes. It would be advisable to comment on the limitations of genetic testing, including possible false positive and negative results, which could potentially significantly impact the accuracy of diagnosis and subsequent management of the patient with renal neoplasm.

Questions for the applicant

1. What are the clinical-pathological circumstances under which genetic testing should be incorporated into the diagnosis of renal tumors, given the high morphological diversity of genetically defined renal tumors that is not limited to younger age groups?
2. Is the diffuse strong CK7 positivity permissible in the diagnosis of clear cell RCC?
3. Are most of the tubulocystic carcinoma in fact missed FH deficient carcinomas?
4. What is the upper permissible percentage of RCC NOS diagnostic category?

Overall assessment, and significance of the work:

The work, which summarizes the author's publication activity, provided new insights into the histopathological diagnosis of selected renal tumors, defining several histomorphological, immunohistochemical, and genetic features that are helpful for pathologists in diagnosing kidney tumors, including some rare entities. The shortage of pathologists in our countries usually does not allow for "sub-specialization" of pathologists, but on the other hand, the availability of genetic methods in pathology is increasing. We consider the main contribution of the work to be the advancement of knowledge about kidney tumors and their diagnosis, which can be utilized in the routine work of general pathologists. The author demonstrated her ability to work independently and critically evaluate the results achieved. The goals of the work, as defined by the author, were fulfilled.

The submitted dissertation entitled "Clinicopathological, morphological, immunohistochemical and molecular biological features of tumors of the genitourinary tract" by Joanna Rogala, MD fulfills all requirements given in the official documents on the doctoral thesis. I recommend the dissertation for defense.

In Bratislava, 16.4.2023

Boris Rychlý, MD, Ph.D.

