

МЕДИЦИНСКИ УНИВЕРСИТЕТ
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To

The chairman of the scientific jury

Determined by Order № P – 1889/27.10.2020г.

Of the Rector Of Medical University

Plovdiv, „V. Aprilov” blvd. №15A

STANDPOINT

From Assoc. Prof. d-r Elena Gulubova Poriyazova-Markova, MD PhD

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Scientific speciality „Pathoanatomy and Cytopathology“, member of the scientific jury.

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Concerning: Defense of dissertation for acquisition of educational and scientific degree of
„Doctor”

from d-r Mariya Stoyanova Koleva-Ivanova

assistant in the Department of “General and Clinical Pathology” – MU – Plovdiv, Medical Faculty, for acquisition of educational and scientific degree of „Doctor” in the field of higher education 7. „Health and Sport”, professional field 7.1 „Medicine”, scientific speciality „Pathoanatomy and Cytopathology”,

On the topic: „ **Eosinophilic metaplasia in prostatic epithelium: main characteristics, morphology, morphogenesis**”

Supervisor: assoc.prof d-r Dorian Ivanchev Dikov, PhD

D-r **Mariya Stoyanova Koleva-Ivanova** was born on May 30 1984y. in Bourgas. She graduated English Language School „Geo Milev“ in Burgas. In 2009y. she has **master's degree of Medicine in MU-Plovdiv**. Since 2010y. she has been working as an assistant in the Department of General and Clinical Pathology at MU-Plovdiv. She acquired a speciality in „Pathoanatomy and cytopathology“ in 2017y. D-r **Koleva** is a member of BMS, National society of pathology, the Union of Scientists in Bulgaria and Confederation of Independent Trade Unions of Bulgaria, she is responsible for educational activities in the Department of general and clinical pathology and she is an administrative assistant.

D-r **Koleva** has 10 years of work experience as an assistant, **by teaching** students of medicine, dental students and pharmacy students **in general and clinical pathology in Bulgarian and English**. The study load of d-r **Koleva** during the last three academic years exceeds the norm for study load of a non-habilitated lecturer in MU-Plovdiv. She speaks English and has a certificate of proficiency in English, **level „B2“**.

Dissertation, submitted by d-r Koleva, is written on 165 pages and includes the following parts: introduction, literature review, aim and tasks, material and methods, results, discussion, conclusions, contributions and bibliography. The dissertation contains 28 tables, 75 pictures and 6 figures.

The introduction focuses on the main problems in prostate pathology. The first chapter of dissertation – literature review, is written on a total of 39 pages, and presents in-depth and detailed description of metaplasia as a general pathological process, with definition, nature, epidemiology, localization and morphological demonstration in various tissues. The types of prostate metaplasia are described, the greatest attention is paid to eosinophilic metaplasia (EM) and its morphological characteristics. The plenty of photographic material presents own photos and photos from immunohistochemistry and electron microscopy, made by the supervisor assoc. prof. Dikov (many photos are author's, from the archive of assoc. prof. Dikov), make a very good impression and prove that the problem has been investigated for a long time. Eosinophilic metaplasia has been related to other pathological changes, such as chronic inflammation and atrophy, and the differences have been reported. A differential morphological diagnosis is presented. The chapter ends with a summary of the literature data and with conclusions from the presented literature review. In this part of the dissertation, dr. Koleva emphasize the lack of specific data on the prevalence of EM, some qualitative features, biological significance, as well as in-depth ultrastructural research and connection with socially significant diseases.

In the chapter „Aim and tasks“ dr Koleva study the epidemiology, morphology and immunohistochemical phenotype of eosinophilic prostate metaplasia of TURP material, with clarification of the pathogenesis and general significance of the process. The six tasks described in detail fully meet the set aim.

The chapter „Material and methods“ presents in detail two groups of cases - 61 TURP-materials from the biopsy archive of University Multiprofile Hospital for Active Treatment „St. George“ EAD - Plovdiv and 62 TURP-materials from the biopsy archive of Service d'Anatomic et de cytologie pathologiques, Grand Hôpital de l'Est Francilien, Jossigny, France. In my opinion the small number of cases does not allow an epidemiological study with conclusions. Additionally, 19 autopsy prostates from the autopsy archive of two hospitals were used as a control group of the patients with the kind cooperation of the supervisor. The histological and immunohistochemical techniques, the ways of reporting the expression of the used markers, as well as the statistical methods of examination are described in detail.

The chapter „ Results “ describes in a volume of 114 pages the results obtained for each of the set tasks, as the first five tasks are well illustrated with many photos, figures and tables. It is necessary for the author to understand that EM of the prostate is a much more common change in the structure of the gland that has been defined so far in the known literature, as well as the finding that clinical manifestation in constellation with mean serum PSA do not reveal significant difference from these indicators in benign prostatic hyperplasia. The cytoplasmic granules diagnosed after histochemical staining, according to dr. Koleva and her supervisor assoc. prof. Dikov evolve either into lipochromic pigment or are phagocytosed. However, it has not been documented in how many patients this has been observed over time in repeated biopsy examinations. In one of the conclusions, these granules are defined as those of lysosomal nature and manifestation of exocrine function. Demonstration of the exocrine nature of EM was performed with the IHC markers PSA and MUC1, and of the lysosomal nature – with lysosomal markers, respectively a-1-ACT and Lamps. It is also good to mention the connection – similarity, identity or difference of these granules with those described by assoc. prof. Dikov in his dissertation as „ prostate lipofuscin pigment granules” , which is also the subject of scientific research. Interestingly, when using a laser technique to treat the prostate gland, changes similar to those in prostate EM are observed. The use of the marker MUC1 as a diagnostic IHC marker for EM indicates that it is not a form of mucinous metaplasia. EM is often observed in combination

with basal cell hyperplasia and Paneth cell changes, but is a pathological finding and does not occur in normal prostate and is often associated with prostatitis – IV, which was also the subject of scientific research by the supervisor assoc. prof. Dikov. It would be appropriate and elegant to separate previous, in-depth morphological findings of the supervisor from the current object of research, such as the prostate EM. In my opinion, in this way the dissertation would emphasize the independent research of dr. Koleva, in which I have no doubt.

In the chapter „Discussion“ dr. Koleva analyzes the data from the previous point and compares the results she found with the data in the literature. The chapter presents a detailed analysis and synthesis of the achieved results. At the end of the chapter the author complements the previous results and on their basis clarifies the pathogenesis and general pathological, biological and pathophysiological significance of EM, all of which are summarized in the chapter „Conclusion“.

The Dissertation ends with the chapters „Conclusions“ and „Contributions“, in which dr. Koleva presents seven conclusions, divided into scientific-theoretical and scientific-applied contributions, both original and confirmatory. In my opinion, the most significant is the scientific-applied contribution, which proves that apart from being a microscopic tissue phenomenon in benign prostatic epithelium, EM has diagnostic and differential-diagnostic value in relation to chronic prostate inflammation.

The dissertation ends with a „Bibliography“, containing 156 authors, of which 10 in Cyrillic and 146 in Latin.

Three publications related with the dissertation are presented, and all three are in peer-reviewed and indexed journals in the literature database.

The presented Abstract is written on a total of 63 pages and fully meets the requirements such as structure and content.

From our work I know dr. Koleva as an educated, patient and ambitious young colleague who works well in a team and constantly strives to improve both in her diagnostic work as a pathologist and in her research and teaching activities as an assistant. Consistently and diligently performs her professional duties.

I wish dr. Koleva to continue to work actively in the teaching, scientific and diagnostic fields of pathology.

In conclusion, the dissertation presents a high scientific and applied potential, and demonstrates the ability of dr. Mariya Koleva-Ivanova to present and summarize the data in the scientific literature. to look for possible relationships and to draw logical conclusions. I propose to the esteemed jury to award dr. Koleva the educational and scientific degree „Doctor”.



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Assoc. Prof. d-r Elena Poriyazova-Markova,

MD,PhD.

12.11.2020y.