

SUMMARY

The doctoral thesis MD. Liubov Kastnerova (previous name Kyrpychova) is focused on the histomorphological and molecular biologic features of selected cutaneous epithelial and nonepithelial tumors and is structured as a commentary to the 20 articles published during four years, representing the completed scientific projects in the Ph.D. course. In eight papers, the author of the thesis is the first author, whereas she coauthored in the remaining 12 papers. The thesis is composed of the commented files of authors own publications and it is divided into cutaneous epithelial and nonepithelial tumors.

The first section, «Cutaneous epithelial tumors», includes 14 articles that are subdivided into two parts: adnexal tumors (9 articles) and lesions of anogenital mammary-like glands (5 articles).

Of the nine articles on adnexal tumors, there are 5 articles focused on various benign and malignant adnexal lesions with apocrine or eccrine differentiation. Novel findings in this part include the identification of hitherto unreported alterations of the *MYBL1* gene in adenoid cystic carcinoma of the skin and lack of deletion of the 1p36 locus in this neoplasm; the lack of a correlation between cellular composition and the presence *CRTC1-MAML2* fusions in hidradenoma, the absence of *CRTC3-MAML2* fusions in this tumor, and new histopathological features and novel *NFIX-PKNI* translocation in primary cutaneous secretory carcinoma. Also, we performed a complex study including the HPV analysis and *HRAS* and *BRAF V600* mutations in syringocystadenoma papilliferum located in the anogenital area, which has never been a subject of such investigation in this location.

One of two articles on follicular tumors is a clinicopathological, immunohistochemical, and molecular biological study of 22 cases of basal cell carcinoma with matrical differentiation. The novel findings included the description of an atypical matrical component in 2 cases and the mutation spectrum in these rare variants. The second article is based on IHC study of BAP1 expression in trichoblastomas, both solitary sporadic and multiple ones occurring in the setting of multiple familial trichoepithelioma (MFT)/Brooke-Spiegler syndrome (BSS).

Two articles are focused on sebaceous neoplasms. One is the largest series of sebaceous lesions with so-called organoid patterns, namely the rippled, labyrinthine/sinusoidal, carcinoid-like and petaloid patterns. We confirmed the previously suggested proposition that all these patterns represent a variation of a single morphological spectrum. We established no association with Muir–Torre syndrome and detected no mismatched repair (MMR) deficiency in most cases, the new data. The second study on periocular sebaceous carcinoma reports new features that may be used as a differential diagnostic clue, namely cells with squared-off nuclei and so-called “appliqué” pattern (peritumoral subnecrosis of peripherally located neoplastic cells).

The subsection on the lesions of anogenital mammary-like glands includes five articles, which add new data regarding their normal histology, provide the detailed immunohistochemical profile of AGMLG, and demonstrate molecular changes in lesions arising from AGMLG comparing these to breast homologs. The novel data also includes the depth of adnexal involvement by neoplastic cells in extramammary Paget disease (EMPD) a large series, which provides practical treatment implications.

The second part, «Cutaneous nonepithelial tumors», includes five articles which are divided between 3 subcategories: lymphoproliferative disorders, mesenchymal tumors, and melanocytic tumors.

One of the three articles in the subgroup of lymphoproliferative disorders represents the largest series of cutaneous Hodgkin disease in which we provide the first description of so-called mummified cells in this condition in the skin. These cells are known in lymph node disease but have been overlooked in skin biopsies judging from the previously published articles. Their presence can serve as a clue to the diagnosis. Included were also two case reports. The first on an extraordinary clinicopathological course of a recently described variant of lymphomatoid papulosis, type E. The second article is an extraordinary case report of cutaneous primary effusion lymphoma (PEL) with an unusual intravascular presentation, combined with Kaposi sarcoma (KS) involving the skin, lung and gastrointestinal tract harboring a *FAM175A* germline mutation.

In the subsection of melanocytic tumors, there are two articles. In the first paper, the author presents a detailed pathological study on spitzoid lesions with *ROS1* fusion and novel fusions of this gene. The study also includes the extensive genetic investigation of other genes, with some novel data. The second article is an extraordinary case report which describes a case of a polypoid atypical Spitz tumor with a prominent fibrosclerotic stromal component, harboring a *CLIP2-BRAF* fusion, which has hitherto been not reported in melanocytic lesions.

As a representative entity of mesenchymal tumors, the authors describe a series of epithelioid fibrous histiocytomas in which new histopathological features and novel *ALK* gene fusions were found.