CURRENT MORPHOLOGICAL ACHIEVEMENTS IN UNDERSTANDING OF URINARY BLADDER PATHOLOGIES AND THEIR DETAILED ANALYSIS

E-mail: natavinnik091081@gmail.com

The paper presents the analysis of the current studies of the urinary bladder pathologies that occur in the clinical practice. The novel theories of the UB damage and the disorders of the urodynamics are impressive by its complexity and diversity. Understanding the causes and ways of the development of UB pathological process is crucial in the correct and timely diagnosis and further therapeutic management, resulting in the improving of patient’s quality of life. In particular, the analysis and study of some of the discoveries made by the scholars that form an understanding of the development of inflammatory, nonplastic and dysfunctional pathology of the bladder is presented. The paper highlighted the differential diagnosis of the inflammatory pseudotumor, pathogenesis of the overactive bladder, clinical and morphological picture of rare malignant tumors. The role of the advanced morphological studies in the diagnosis of the UB disease is emphasized.

Keywords: urinary bladder, urological pathology, overactive bladder, obstruction, inflammation, tumors, environmental pollution.

Generally, the pathology of the urinary bladder (UB) is often accompanied by its dysfunction and/or different types of complications. We have analyzed and described some of the discoveries made by the scientists, which contribute to understanding of the development of urinary bladder pathology. Inflammation of the UB is the common problem with the developed diagnostic and treatment protocols; however, the inflammatory process may have specific features. In this respect the case of inflammatory pseudotumor of the UB has been reported. The patient complained of the abdominal pain and hematuria. The CT and MRI showed the thickening of the wall of the organ, and cystoscopy test detected a neoplasm. After its removal the histological study showed proliferation of myofibroblastic spindle cells and mixed cellular infiltration (lymphocytes, neutrophils and eosinophils). Scientists emphasize the importance of the detailed differential...
diagnosis of this disease with the urothelial carcinoma, squamous cell carcinoma with manifestations of the secondary inflammation, leiomyoma, cystosomatosis, and tuberculosis, as the clinical picture of this pathology is ambiguous [1]. Being at any stage, the disorders of the medullar neuroregulation (CNS, spinal cord and peripheral ganglia) are accompanied by UB dysfunction. Therefore, injuries, chronic stresses, the imbalance between the neuropeptide receptors, inflammation or diseases of other organ affect the physiological innervation and coordination of the UB, resulting in the development of the overactive bladder syndrome. The authors emphasize on the importance of the expression of the kinin B1 and B2 receptors in the dysfunction of the detrusor traction and other urothelial neurotransmitters in the pathogenesis of this disease [2,3]. One of the first protective mechanisms, subjected to the impact of the stimuli in the urine, is the transitional epithelium, involving superficial sensory receptors (bradykinin receptors B1 and B2, p75NTR, TrkA, TrkB, NGF, BDNF, PACAP, purinoceptors, P2Y and P2X, adrenergic, transitory and cholinergic receptors, etc.) that participate in the afferent signaling [3-5]. The long-term impact of the various factors on the mucous membrane disintegrales the barriers, promotes the excessive expression of the receptors and activation of the neuronal hyperexcitability in the urothelium, as well as uncontrolled innervations of the smooth muscle cells of the detrusor with the subsequent development of reflex urination [2-4]. Medical practitioners are quite aware of this versatile problem, and for effective treatment it is necessary to establish a mechanism of its development in each individual case. Another problem related to violation of the urodynamic is the obstruction. The causes of such pathology are different: from the congenital to acquired with age [6]. In this way, disregarding the influence of other bodies on the bladder (prostate, urethra), the example is the consequences of the overactive UB, as changing the signal paths and excessive myogenic activity of the detrusor are complicated by its hypertrophy [5,7]. During the obstruction a mechanical stretching of the organ with deformation of detrusor myocytes, fibrosis and thickening of the wall occurs. It is also reported about the role of excess of estrogen and androgens, inducing the molecular mechanisms of damage. The histological and immunohistological examinations (ERα, PCNA and p-AKT) indicated the significant overgrowth of the smooth muscle fibers, a clear correlation between the excessive estrogen levels and expression of proliferating urothelial and fusiform cells of the UB and detrusor, along with the decrease in the thickness of the striate muscle layer of the proximal cross-muscular sphincter. It has been also demonstrated that induction of the estrogen is accompanied by hyperproliferation of the fibroblasts and destabilization of collagen III expression [6,7]. One of the most dangerous urological pathologies is the bladder cancer, which takes the 6th place in the United States by its incidence. Noteworthy, the risk for cancer in the male population is much higher than in females (7%:3%) [8]. Generally, the diagnosis of the type and malignancy of the tumor does not cause difficulties, but new statements with logical outcomes as for the difficulty of differentiation of neoplasia and its origin are reported quite often, with which medical professional almost never face worldwide. One of these discoveries is the case of extranodular marginal lymphoma associated with the urothelium. It is non-specific localization of this tumor in the UB, and not in the stomach, that led to additional examination (a bone marrow biopsy, endoscopic gastroduodenoscopy and CT diagnostics) and selection of the medical therapy [8]. Anaplastic large-cell lymphoma (T-cells) has the origin, similar to the primary tumor diseases with involvement of the UB, and the precise differentiation is possible only with the involvement of the panel of immunohistochemical antibodies [9,10]. It is the diffuse positive expression of CD30, ALK, EMA and vimentin and negative reaction from the AE1/AE3, CK7, CK20, CK5/6, P63, SMA, HMB-45, pan-Melan, S-100, Myo D1, synaptophysin, CD56, desmin, CD15, CD20, Pax-5, and CD3 that contributed to the confirmation of this rare pathology [10]. Usually, undifferentiated cancer without signs of keratinization and with lymphocytic infiltrate is specific to the nasopharynx; however, in cases of its localization in other organs it is considered as lymphoepithelioma-like carcinoma [11,12]. On the one hand, the histopathological manifestations of the tumor in the UB were characterized by muscular invasion, necrosis, inflammatory infiltration with predominance of lymphocytes, mitosis and scattered large epithelial cells, and on the other hand, by the signs, specific to non-invasive urothelial carcinoma. In such cases, the immunohistochemical differentiation of malignant lymphoma, small cell carcinoma and undifferentiated urothelial carcinoma with marked lymphocytic infiltration is carried out. The progress of such urological pathology is favorable; however, in conditions of poor identification the therapeutic management is ambiguous [12].

The cases of primary malignant melanoma with aggressive progress and mixed clinical symptoms are rarely reported [13]. This pathology deserves special attention of the practitioners, taking into account the complexity of the diagnosis and a precise differentiation between the primary lesion in this organ and metastatic highly malignant manifestation of melanoma of other organs (18% of affection), especially without previous clinical history [14-15]. Histological study of such neoplasms also impresses with its diversity of the morphological features without inner cytoplasmatic pigmentation of melanin, and it is immunohistochemical study, using the markers to Melan-A, S100, HMB45 and MITF, that is the most critical and informative in
confirmation of the diagnosis, as well as the p63, Desmin, Chromogranin, CD99 and Sytokeratin 34BE12 or AE1/AE3 to exclude other forms of carcinoma [14,16]. Interestingly, in the case of primary malignant melanoma the prevalence of local metastases in the pelvic organs reaches the high values and does not correspond to the nature of secondary metastatic manifestation [13-15].

The interesting cases of multiple malignancies that are developed in one person occur more often. The localization of multifocal primary tumors of different organs can be both within a single topographic area and at a considerable distance. In this way, UB neoplasia is often combined with cancer of the prostate, ureter, kidney, intestine, thyroid and mammary glands, stomach, lung, oral cavity, esophagus, larynx, etc. [17,18]. The case of double primary malignant neoplasm of UB in the form of invasive cancer and leiomyosarcoma is also reported [19]. Basically, the histogenesis of such tumors is specific to the affected organ, and the variants of immunohistochemical identification depend on the organs involved in the process, which is necessary to reject the dependence between their formations [17-19]. In addition, nowadays, a significant problem is the risk of UB cancer, associated with environmental pollution due to the development of the industry, urbanization and living conditions [20]. Currently, a clear etiological and pathological relationship between smoking, alcohol, chemical additives, and obesity is established; however, the authors critically emphasize the effect of aromatic amines and heavy metals [20-22].

Apparently, a danger of aromatic amines and salts of heavy metals is in their extreme toxicity and prevalence both in the environment, and possible contact with these substances while working in factories and plants. It has been discovered that the variable type of tumor depends on the type of metal, the boundaries of its toxicity and concentration [21-22]. It is known that the level of neoplasia of various organs, especially UB, is much higher in the locations with unfavorable environmental background. In addition to the evidenced role of environmental pollutants in cellular mutations and increasing incidence of UB tumors, they also contribute to the variability of differentiation and high aggressiveness of tumors, which greatly affects their diagnosis and treatment [20-23]. New reports regarding rare UB tumors are described and related to animals both in the simulated experimental study and in conditions of species habitat. Currently, enhanced understanding of pathogenesis of the UB tumors, their progression and treatment is the acute issue. That is why the scientists genetically simulate this disease in mice using specific chemical carcinogens that cause further display of different phenotypes or subtypes of cancer [24]. In turn, 4-hydroxybutyl (butyl) nitrosamine is used more often in simulation of tumors in rats with a further study of the effectiveness of chemical agents [25]. The case of fibrosarcoma of the UB in a cat greatly expands the idea on this issue [26]. The authors report, that this is the first documented case of such malignant tumor in these species, since the origin of the most neoplasia is epithelial (transitional cell carcinoma), and the other are represented by leiomyoma, leiomyosarcoma, fibroma, hemangiomia, hemangiosarcoma and lymphoma with proliferation of atypical mesenchymal cells among the membranes. Such moderate mixed cell infiltration and numerous mitoses often correspond to malignant mesenchymal tumor. Taking into account the uniqueness of this histologic picture the immunohistochemical diagnostics with antibodies to vimentin +, S-100 (+), glial fibrillar acidic (-), proteinsmooth actin (-) and desmin (-) has been carried out, which confirmed the diagnosis. Noteworthy, the tumors of the UB of the epithelial origin have been found in buffaloes that was caused by the bracken fern (Pteridium spp.), which grows on pastures and considered as the toxicant, immunosuppressor, mutagen and carcinogen. It has been also established that the agents, which the bracken fern is rich in, can enhance the effect of affection with the type 2 papillomavirus (BPV-2). The complex of these agents activates the PDGF β and Calpain 3 receptors with subsequent uncontrolled proliferation of the epithelium and its conversion into a malignant tumor [27].

The findings of similar studies conducted with the same etiological and pathological factors quite reasonably indicated the specific histological and immunohistochemical features (chronic inflammation of tumor stroma) of the bovine UB tumors exactly of the mesenchymal origin. In both cases, a low metastatic potential was observed. Consequently, it can be stated that our present-day life is not devoid of single rare clinical mysteries. In most cases, for the purpose of comparative oncogenesis the scientists use the complex of molecular studies that contribute to the exact final diagnosis. It is the outcomes of the correct timely diagnosis and understanding of the mechanisms of pathological processes in the UB that will influence on the therapeutic management, improving the patient’s quality of life.

### Conclusions

With the recent rapid scientific and research progress the number of theories on the ways and options for the development of multiple diseases of the bladder has significantly increased. Numerous lesions of the organ astonish with its variability of the outcomes, diversity and complexity of the progress, although remain poorly understood to date. Therefore, understanding the etiology, pathogenesis and therapeutic management of the diseases of the urinary bladder is the important and promising issue for contemporary urology.
References


Біохімія і антіоксидантна активність нанокристалічного диоксиду церію

О.С. Цехмістренко, С.І. Цехмістренко, В.С. Бітоцький, О.М. Мельничук, О.А. Олешко
Білоцерківський національний аграрний університет, м. Біла Церква

Проведений аналіз наукової літератури свідчить про широке застосування в біології та медицині наносполук диоксиду церію, які проявляють біометичну та антіоксидантну активність. Високий ступінь біосумісності, низька токсичність й каталітична активність нанодисперсного диоксиду церію дозволяє розглядати його як перспективний нанобіоматеріал для біомедичної застосування. Характеризується роль нанокристалічного диоксиду церію у захисті клітин від оксидативного стресу. Киснева нестехіометрія та пов'язана з нею можливість участі в окисно-відновних процесах у живій клітині, а також здатність до ауторегенерації збільшує високу ефективність застосування нанодисперсного диоксиду церію. Показано, що нанокерні може діяти як міметичні супероксиддисмутази, каталази, деяких оксидаз, оксидоредуктаз та фосфатаз, а також здатний брати участь у необхідних активних форм нітрогену.

Ключові слова: наночастики, діоксид церію, міметики, оксидативний стрес, супероксиддисмутаза.

Робота є фрагментом ЦНР “Розробка біотехнологій створення нових препаратів пробіотиків, біологічно активних речовин та наноматеріалів,” № державної реєстрації 0116U005824.

Церні (Ce) – рідкоземельний елемент (порядковий номер 58), який належить до лантаноїдів. Унікальність цернію (електронна конфігурація 4f⁵⁵d⁵⁶S⁵) обумовлена тим, що він може існувати у різних стабільних окисних станах (Ce³⁺ та Ce⁴⁺), на відміну від більшості інших рідкоземельних металів, які переважно існують у тривалентному стані [14, 25]. Сам церніє не має біологічного значення в фізіології ссавців, але розчинні солі Ce³⁺ традиційно використовуються в біомедичних цілях через їхню бактеріостатичну, бактерицидну, імуномодулюючу та протипухлинну активність [Ошбіка! Істочник ссылки не найден., 7]. Нанодисперсний діоксид цернію (НДЦ) широко застосовується в процесах механічного полірування, в розробці антикорозійних покриттів для металів і сплавів та каталізаторів окиснення дизельного палива [Ошбіка! Істочник ссылки не найден.]. Останнім часом спостерігається більш фундаментального та практичного інтересу до розробки та застосування наночастиц як потенційних каталітичних антіоксидантів у біології та медицині [6, 8, 9, 11, 19, 37]. Біологічна активність наночастиц діоксиду церніє визначається його кисневою нестехіометрією, яка залежить від розміру наночастиц і поверхневого лігангу [25]. Високий ступінь біосумісності, низька токсичність й каталітична активність нанодисперсного діоксиду церніє дозволяє розглядати його як перспективний наноматеріал для біомедичної застосування [Ошбіка! Істочник ссылки не найден., 15, 24, 29, 30, 32, 37]. Проте нині всі можливі механізми його біологічної активності є маловідомими.

Міметики (грец. mimetes – наслідувачі, імітатори, подібні) – речовини, схожі на природні синтезовані в організмі сполуки (медіатори, ферменти, гормони), які імітують діо інших субстанцій.