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Pathology of the urachus. History of the issue and current state of the problem

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Based on the analysis of literature sources, modern data are presented on the nosological structure of urachus diseases in adults and children, diagnostic methods, as well as treatment tactics for various anatomical variants of anomalies in the development of the urinary duct. A modern classification of urachal malformations caused by disorders of its obliteration is presented. Various modifications of the laparoscopic approach are considered for the most common types of this pathology. The reasons for the development of malignant neoplasms from the urachus tissue, including in the gender aspect, are described, and a comparative assessment of the methods of surgical treatment of urachus tumors is given.

Keywords: urachus; urachal cyst; urachal tumors; urachal malformations.

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Патология урахуса. История вопроса и современное состояние проблемы

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На основании анализа литературных источников приведены современные данные относительно нозологической структуры заболеваний урахуса у взрослых и детей, методов диагностики, а также лечебной тактики при различных анатомических вариантах аномалий развития мочевого протока. Представлена современная классификация пороков развития урахуса, обусловленных нарушениями его облитерации. Рассмотрены различные модификации лапароскопического доступа при наиболее распространенных видах указанной патологии. Описаны причины развития злокачественных новообразований из урахальной ткани, в том числе в гендерном аспекте, а также дана сравнительная оценка методов хирургического лечения пациентов с опухолями урахуса.

Ключевые слова: урахус; киста урахуса; опухоли урахуса; аномалии урахуса.

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ЭКО•ВЕКТОР

INTRODUCTION

Urachus pathology represents a significant problem in current clinical medicine [1]. It is characterized by polymorphic forms ranging from an incomplete fistula of the navel to malignant neoplasms from urachal tissues, and is a point of interest for doctors of various specialties. In most cases, diseases associated with the urinary duct manifest clinically in early childhood [2]. However, this does not make them a problem for pediatric practice only. In adults, the frequency of detection of urachus diseases decreases, but its malignant neoplasms are revealed more often. Moreover, the number of unresolved issues related to various aspects of the pathology under consideration, regardless of the age of the patients, remains significant.

Diagnosing urachus diseases is often a complicated process due to frequent asymptomatic course and variability of clinical manifestations caused by a range of morphological variants [3]. There are no universal algorithms for diagnosing urachus diseases. Errors are often registered at the preoperative stage, both as an incorrect assessment of the urachus pathology and as an incorrect differential diagnosis with other diseases of the urinary tract and abdominal organs [4].

The choice of treatment approach for diseases of the urachus is controversial ranging from conservative to radical removal of urachal tissues [5]. Furthermore, there is no algorithm to determine the nature surgical intervention that suits a particular indication (open or laparoscopic) [6]. In addition, there are no unequivocal opinions about the timing and methods of surgical procedures for complications (one-stage excision, puncture or minimally-invasive drainage followed by laparoscopic excision, or open intervention) [7].

The morphological presentation in urachus pathologies is still unclear. A number of publications describe the morphology of the cyst wall and fistula of the urachus in childhood: however, literature search on the analysis of the histological structure of the urachus in terms of prerequisites for neoplasms is sparse.

All these indicate the extreme complexity, the lack of unity and the presence of antagonistic opinions about urachus diseases, from its epidemiology to the choice of a treatment method.

In this work, we analyzed scientific publications from the Embase, Medline, Google Scholar, Scopus, and PubMed databases. Search keywords were “urachal abnormalities”, “urachal malformation”, “urachal cyst”, and “urachal adenocarcinoma.” Analysis was focused on original articles and studies, as well as descriptions of individual clinical cases.

Epidemiology

Urachus was first mentioned in 1550, when B. Cabriolus described an inflamed urachus in an 18-year-old woman. J.G. Walker in 1775 argued about the existence of a connection between the navel and the bladder throughout life. H. Luschka and J.B. Wutz independently presented works describing the histological structure of the urachus in 1862 and 1883, respectively [8, 9]. In 1906, J.F. Binni published the results of a study indicating age-related urachus reduction and its mechanisms [10]. In the early 20th century, R.C. Begg summarized data on the anatomy and blood supply of the urachus, while his study was based on 58 cases [11]. This was the first large-scale clinical study on urachus pathology.

The incidence of urachus pathology is controversial (Table 1). According to A.A. Gusev et al. [2], urachus pathology is often registered in childhood, accounting for 95% of cases of their total number, while urachus obliteration was detected in 30%–50% of newborns [2].

There are no guidelines regarding the incidence of urachus pathology in adults. B.L. Gami and S. Biswas [12] presented revealed 1 per 150,000 people to 1 per 5,000 people, while H.J. Jeong et al. [13] demonstrated 1 per 300,000 people. H.I. Rees [14] cites a study by O.W. Yoerg (1942), which revealed 3 cases of urachus abnormalities in 12,500 urological patients. M. Blichert-Toft and O.V. Nielsen [15] detected urachus pathologies in 8 out of 40,000 patients admitted to surgical departments. W.H. Risher et al. [16] described 41 cases of urachus pathology, and only 11 of them were over 18 years old. G.E. Schubert et al. [17] described characteristic tubular structures in the bladder in 32% of adult patients from autopsy reports.

Most authors agree that the incidence of urachus pathology in adults is lower than in children [16, 18–20]. The greatest prevalence is observed in young children. Choi et al. detected urachus pathology in children aged 1 day to 12 years (mean age of 3.9 years). Moreover, the authors indicated that the prevalence of this pathology is extremely low, regardless of age groups [21].

The incidence of urachus pathology is higher in males. B.L. Gami and S. Biswas indicate the ratio of males and females with urachus pathology as 3 : 1, while T.V. Mukaseev and Yu et al. indicate a 2 : 1 ratio [12, 22, 23]. However, other authors reveal that the prevalence of

Table 1. The incidence of urachus pathology in childhood

Таблица 1. Частота встречаемости патологии урахуса в детском возрасте

Author	Incidence, %	Sample size
T. Ueno [46]	1.6	3400
E.V. Dmitrieva et al. [28]	0.127	14094
J.M. Gleason et al. [25]	1.03	70000

Table 2. The structure of the pathology of the urachus
Таблица 2. Структура патологии урахуса

Author, year	Number of cases	Cyst	Fistula	Sinus	Diverticulum	Tumor
E.V. Dmitrieva et al. (2016) [28]	18	3	0	15	0	0
R.A. Ashley et al. (2007) [31]	176	–	–	–	–	66
B.G. Cilento, Jr. et al. (1998) [24]	45	16	7	22	0	0
B. Heuga et al. (2015) [30]	35	10	15	10	0	0
H.G. Mesrobian et al. (1997) [43]	21	9	2	9	1	0
J.H. Yiee et al. (2007) [27]	37	19	7	5	0	0
I. Sukhotnik et al. (2016) [26]	8	5	3	0	0	0
Total	340	62	34	61	1	66

males among patients with urachus pathology was not so pronounced. B.G. Cilento et al. [24] demonstrated a ratio of 8 : 7 in favor of males, and J.M. Gleason et al. [25] state that the disease is detected in male patients in 64% of cases.

Some authors specify the urachus cyst as the most frequent urachus pathology [26, 27], while others indicate the urachus sinus [28, 29] and urachus fistula [30]. R.A. Ashley et al. [31] demonstrated a high incidence of oncological diseases in urachus pathology (66 cases; 37.5%). The article presents a summary table on the incidence of various forms of urachus pathology (Table 2).

Diagnosis and clinical course

Diagnosing urachus pathology is also a subject of discussion. Due to frequent asymptomatic courses, urachus diseases are often detected accidentally in the course of various diagnostic procedures [32, 33]. A number of authors recount of frequent cases of manifestation of acute abdomen symptoms with inflammation of the urachus cysts [34, 35]. In 2000, C. Pesce et al. analyzed the data of 10 patients who had received treatment in the clinic for over 11 years. They noted that all patients had urachus cyst suppuration and one of them had cyst perforation into the abdominal cavity [35]. The most common complication of a urachus cyst was inflammation. J.S. Yu et al. [23] revealed that most cysts become inflamed prior to diagnosis. According to Yiee et al. [27], the clinical manifestation of the cyst occurs by 3.4 years of age, and the sinus/fistula manifest by 0.3 years of age. The most typical clinical manifestation of urachus inflammation is soreness of the umbilical region, hyperemia, and discharge from the umbilical fossa. With such manifestations in children, diagnostic errors are possible [1, 26]. Moreover, in the adult age group, this presentation is most characteristic for urachus pathology [36]. Some authors believe that urachus diseases are often manifested by hematuria [1]. Rare symptoms such as dyspareunia and chronic mucusuria are also possible [37, 38]. There are clinical manifestations that are not typical of childhood. An example is lithogenesis with the development of complications such as the cyst rupture and the calculus dislocation in the presence of an intestinal obstruction or acute urinary retention [19, 39]. S.L. Other studies have outlined urachus tuberculosis as well [7, 40]. In addition, rectourachal and sigmoidourachal fistulas could develop in the presence of the urachus inflammation [41, 42].

Table 3 presents the incidence of clinical manifestations of urachus diseases according to various authors.

According to some authors, the most preferred method for visualizing urachus pathology is ultrasound examination (US) because it is non-invasive, safe, and used to visualize superficial locations [23, 26]. In this regard, US is considered as the gold standard in the diagnosis of urachus pathology in childhood. Mukaseeva et al. described characteristic ultrasound findings in inflammation of the urachus cyst [22]. It often determines the nature of the pathology accurately [28]. However, there are a number of difficulties in diagnosing urachus diseases. These include the assessment of the fistula length, differential diagnosis of an inferiorly-located cyst and urachal diverticulum [23, 28], and clarification of the fistula nature [29, 43]. According to I. Sukhotnik et al. [26], computed tomography (CT) and magnetic resonance imaging (MRI) have the greatest diagnostic potential. However, their use is restricted in children These restrictions include the need for sedation and high radiation exposure. According to J.H. Yiee et al., CT should be used as an additional diagnostic method in case of insufficient US data. Most authors cite that cystography is inappropriate due to its low information capacity [44]. Some authors consider it necessary to perform fistulography and cystography when an urachus fistula is suspected [24, 43].

Multispiral CT (MSCT) is regarded as the gold standard in diagnosing urachus pathology [23, 36], and can access the relationship of the urachus with the surrounding

Table 3. The frequency of clinical manifestations of urachus diseases
Таблица 3. Частота клинических проявлений заболеваний урахуса

Author, year	Number of cases	Clinical manifestations, %				
		discharge from the navel	palpable lesion	pain syndrome	erythema	dysuria
I.V. Poddubny, Ya.A. Isaev (2015) [1]	Combined statistics	42–50	0–22	–	0–43	0–14
B.G. Cilento et al. (1998) [24]	45	42	33	22	22	2
M.O. McCollum et al. (2003) [32]	26	39	42	42	42	4
J.H. Yiee et al. (2007) [27]	37	54	22	30	30	14
J.M. Gleason et al. (2015) [25]	721	43	25	28	26	7

tissues. The need to use one of the high-precision imaging methods (MSCT and MRI) is also due to cancer alertness. Cilento et al. demonstrated a similarity of results with the ultrasound and CT in infected cysts and urachus carcinoma. According to some authors, the thickness of the anterior abdominal wall in adults restricts US visualization of some internal structures. Fistulography in adults is performed if urachus fistula is suspected, and has a high diagnostic value in this pathology [29, 43]. On the contrary, a number of authors are against its use, and they express the same opinion regarding the micturating cystourethrography [38, 43]. Other studies reveal the diagnostic value of cystoscopy in hematuria and suspected neoplasms of the urachus with invasion to the bladder wall [31, 38].

The choice of surgical approach in the treatment of urachus anomalies remains disputable. There are two opposing standpoints. On one hand, the most reliable surgical approach is indicated in relation to the risk of malignancy, as well as the development of purulent complications [31]. On the other hand, the recommendation of conservative management is due to the large number of asymptomatic forms, the relatively low frequency of purulent complications, and the risk of malignancy, as well as the possibility of the regression of disease [29, 45]. Elkbuli et al. indicated that 80% of urachus pathologies regress by the age of 2 years [5].

Nogueras-Ocaña et al. revealed that the spontaneous regression of urachus anomalies reaches 61.5% with an average median of 16.5 months. Two out of 13 patients required surgical treatment due to frequent relapses of the infectious and inflammatory process. In this regard, the authors concluded that it is advisable to manage patients as conservatively as possible with surgical intervention only in the case of recurrent infectious complications [45]. Dethlefs et al. also highlighted the need for the most conservative therapeutic approach in such patients, regardless of the form of pathology for up to 6 months of age, and the continuation of conservative management of patients with minimally pronounced symptoms [44]. Gleason et al. analyzed 721 case histories of children with urachus pathology, and they noticed that surgery was performed in only 61 patients [25]. Ueno et al. studied the anamnesis of 56 patients with urachus anomalies, who received conservative therapy and were under active case follow-up; the study revealed a regression of the anomaly in 30 cases (53.6%) [46]. In this regard, the need for dynamic monitoring of patients and narrowing of indications for surgical intervention is of utmost importance.

Contrary to the aforementioned constellations, Ashley et al. presented the results of a histological examination of the urachus tissue obtained during surgical intervention in adult patients [31]. and in 51% of cases, they revealed signs of cell atypia. Schubert et al. [17] revealed proliferative processes of the epithelium in 122 urachus biopsies in 43.6% of cases, signs of chronic inflammation in 23.1% of cases, and epithelial dysplasia in 7.7% of cases, which were considered as risk factors for the development of tumors in these tissues. Pinthus et al. [47] analyzed the results of histological examination of 23 preparations of urachus tissue, and revealed an abnormal epithelium in 26% of cases. Therefore, a conclusion was made about the need for preventive surgery in childhood.

Risher et al. [16] operated on all patients with urachus pathology, considering both the risk of suppuration and tumor transformation as indications for surgical treatment. The Campbell-Walsh Urology Atlas recommends active monitoring of patients with asymptomatic forms, and surgical intervention only in the presence of any clinical symptoms [48].

Treatment methods of urachus pathology used in the 1970s (opeing the cyst without excising the walls), were considered ineffective. In addition, treatment for festering cysts of the urachus remains controversial. Thus, most authors consider the need for staged treatment of these conditions. Due to the high efficiency of

antibacterial drugs, a number of authors indicate the absence of necessity for puncturing or draining of the cyst [5] or the need for drainage in the absence of the effect of antibiotic therapy [49]. Other authors consider it necessary to drain the cyst cavity with the use of antibiotic therapy, followed by excision of the cyst in the cold period [50–52]. Newman et al. suggested simultaneous excision of cysts in the phase of acute inflammation. Evseev et al. [36] demonstrated the possibility of laparoscopic excision of a festering urachus cyst complicated by peritonitis due to its perforation.

The laparoscopic excision of urachus anomalies due to the unsatisfactory results of open surgical interventions was the most widely used. Proponents of traditional approach motivate the need for open surgeries owing to the complexity of the most radical removal of urachus tissues by laparoscopic method.

The first report on the successful excision of the urachus cyst by the laparoscopic approach was published in 1993 by Trondsen et al. [54]. Since then, several studies have described the efficiency of this method in different age groups and various forms of urachus pathology. According to most authors, laparoscopic surgery is the gold standard in the treatment of patients with urachus pathology of any age group [55–58]. This is due to its low injury rate, great cosmetic results, and the fact that it is the final diagnostic method. There have also been publications describing the performance of robot-assisted surgeries in urachus pathology [59, 60]. We have not found the use of robotic systems in urachus surgery in Russian sources.

Despite the fact that most authors consider laparoscopic surgeries as the gold standard of surgical treatment for urachus pathology, the issue of radical excision of urachus tissues remains controversial. Although most authors agree on the need for complete excision of the urachus tissues; the need for excision of the fundus of the bladder remains a subject of debate. Thus, a number of authors believe that excision of the fundus of bladder is contraindicated due to an increase invasiveness, as well as an increase in the incidence of complications associated with the need for prolonged urine diversion from the bladder by means of a urethral catheter. However, other authors consider it necessary to excise the bladder fundus, regardless of the pathology form.

Laparoscopic surgery in urachus pathology remains a controversial topic [1, 58]. The points of location of trocars are discussed in the literature [1, 61]. Most authors use three trocars for approach, but the location points are different [36]. C.W. Cutting et al. and Kwok et al. used the technique with three ports located in the left mesogastrium and hypogastrium to ensure maximum view of the urachus, as well as to work at any level [50, 58]. Navarette et al. [61] used a three-port technique with trocars positioned slightly above the umbilicus medially, in the right mesogastrium, in the right iliac region. Some surgeons performed the intervention with the patient on the right side, and the operator positioned from the back, and three ports were installed as laterally as possible, linearly from the iliac region to the hypochondrium [62]. Bertozzi et al. proposed three trocar approaches with ports located in the right hypochondrium, left epigastrium and right mesogastrium [55, 56]. Cadeddu et al. installed four ports during laparoscopic surgeries, such that port 1 was above the navel along the midline, port 2 was in the right mesogastrium along the edge of the rectus abdominis muscle, port 3 was in the right iliac region along the edge of the rectus abdominis muscle, and port 4 was in the left mesogastrium along the edge of the rectus abdominis muscle [63].

From literature search, there is no evidence backing the advantages of the aforementioned surgical techniques, and a greater efficiency of using a 4-trocar approach over a 3-trocar one. At the moment, the 4-trocar approach is not optimal; in our opinion, the use of the 4-trocar is required only in cases of technical difficulties.

Urachus adenocarcinoma

Urachus adenocarcinoma was first described in 1863, and the first large-scale study of urachus tumors was conducted by Sheldon et al. in 1984 [64]. Patients over 50 years of age have the greatest risk of adenocarcinoma of the urachus, while cases of mucinous tumor of the urachus have been described in a 15-year-old girl. Yu.S. Tareev described a tumor of the urachus in an 18-year-old male patient. [65]. Similarly, Lee et al. described a case of urachus adenocarcinoma detection in a 32-year-old man [66].

The incidence of urachus malignancy is one case per 5,000,000, representing 0.35%–0.7% of all bladder tumors, with an increase of 0.55%–1.2% for the Mongoloid race [31, 65, 66]. According to Yu.S. Tareev, the incidence of urachus tumors is less than 0.015% in the general structure of oncopathology and about 1% of all tumors of the urinary bladder [65]. Urachus tumors are more common in males, accounting for 72% of all cases registered [67]. Due to the location of the urachus and late clinical manifestations of the disease, distant metastases are revealed in 20% of patients with urachus tumors [68].

The most common tumor of the urinary duct is adenocarcinoma of the urachus, and it accounts for 0.17%–0.34% of all tumors and 20%–39% of all adenocarcinomas of the urinary bladder; mucinous adenocarcinoma is less common, and transitional cell cancer is detected even less often. The predominance of adenocarcinoma, despite the presence of transitional epithelium, is due to metaplasia of the epithelium caused by chronic inflammation [69]. A major study by Wright et al., which summarized the data on 151 urachal adenocarcinomas

and 1374 non-urachal adenocarcinomas of the urinary bladder, showed a significantly more aggressive course of urachus adenocarcinomas [70]. Patients with urachal adenocarcinomas were younger (mean age 56 and 69 years, $p < 0.0001$) and were more often females compared to patients with non-urachal carcinomas (45 versus 36%, $p = 0.02$). Urachal adenocarcinomas were highly differentiated than non-urachal ones (35% versus 66%, $p < 0.001$). However, distant metastases were detected more (30% versus 15%, $p < 0.001$). Partial cystectomy was more common in urachus tumors (66 versus 16%, $p < 0.001$).

The most favorable type of urachus tumor is villous adenoma owing to its low recurrence rate after resection, but it requires accurate histological examination as it is frequently associated with adenocarcinoma and urothelial carcinoma, which have a poor prognosis.

There are two classifications of urachus tumors.

Classification by S. Sheldon et al. (1984) [64]:

- Stage I – the tumor is limited to the urachus and bladder;
- Stage II – the tumor propagates beyond the muscular layer of the bladder;
- Stage III – metastases in regional lymph nodes (in the pelvic cavity);
- Stage IV – metastases in non-regional lymph nodes or distant metastases.

Mayo Staging System classification [71]:

- Stage I – the tumor is limited to the mucous-muscular layer of the urachus and/or bladder;
- Stage II – the tumor propagates beyond the muscular layer of the urachus and/or bladder;
- Stage III – metastases in regional lymph nodes;
- Stage IV – metastases in non-regional lymph nodes or distant metastases.

Most authors have demonstrated that hematuria is the main and earliest clinical manifestation of urachus tumor [31, 64, 68, 72, 73]. Ghazizaben et al. [67] noted hematuria of varying intensity as the first symptom of urachus tumor in 71% of patients. F. Duan et al. [73] analyzed the treatment of 82 patients with urachus tumors and noted hematuria in 72.6% of cases, symptoms of the lower urinary tract in 12.9%, a palpable lesion in 22.6%, omphalorrhea/asymptomatic course in 3.2%. According to A. Ebrahim et al., the presence of hematuria indicates the invasion of the bladder wall, corresponding to stage III of the tumor and causes a poor prognosis. Zhao et al. described a case of urachus tumor metastasis to the mammary gland in a 42-year-old woman [74].

Diagnostic approaches in detecting urachus tumors differ from those in non-neoplastic lesions. If a tumor is suspected, CT and MRI are considered mandatory. To differentiate between a multilocular cyst of the urachus and a tumor, a percutaneous fine-needle or transurethral biopsy is performed.

According to most authors, radical surgery is the treatment of choice for urachus tumors, and partial cystectomy with excision of the urachal ligament, umbilicus, and dome of the bladder is recommended. In rare cases, with early diagnosis, organ-sparing surgery is possible. Ebrahim et al. demonstrated no advantage of cystoprostatectomy over resection in relation to the recurrence of symptoms. Moreover, the need of lymphadenectomy also remains controversial. Most authors consider the laparoscopic approach surgical treatment of choice for urachus tumors. Lee et al. suggested a cystoscopy with tattooing of the visible edge to determine the boundaries and increase the radicality of the intervention in some cases [66]. According to some authors, urachus adenocarcinoma is genetically similar to intestinal adenocarcinoma, causing a favorable response to systemic therapy in intestinal adenocarcinoma. Moreover, due to a low perfusion of the structures under study, cytostatic therapy is generally not advised [71]. During analysis, we did focus on the results of surgical treatment of patients with urachus tumors and the assessment of the postoperative pain syndrome index.

Table 4 presents the survival rate of patients according to various authors.

The high survival rate in the study by Pinthus et al. was due to early detection and high operational activity, (approaching 90%) [47]. According to Ghazizadeh et al., the average life expectancy from disease detection is about 17 months [67]. Chen et al. [68] demonstrated a relationship between survival rates and tumor stage. They showed that the rates were 6.2 years at stages I and II, and 1.8 years at stages III and IV.

Table 4. 5- and 10-year overall survival in patients with urachus tumors

Таблица 4. 5- и 10-летная общая выживаемость у пациентов с опухолями урахуса

Author, year	5-year survival rate, %	10-year survival rate, %
I.V. Poddubny, Ya.A. Isaev (2015) [1]	6	–
I. Efthimiou et al. (2008) [38]	34	–
R.A. Ashley et al. (2006) [72]	49	–
J.H. Pinthus et al. (2006) [47]	61.3	49.2
M. Ghazizadehet et al. (1983) [68]	6	–

CONCLUSION

Despite the relative rarity, urachus diseases can be manifested by the development of neoplasms and lead to severe complications. Thus, diagnosing, treating, and raising an awareness of urologists and doctors of related specialties regarding this disease is of utmost importance.

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