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Diagnosis and treatment of interstitial cystitis - literature review

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ABSTRACT

Interstitial cystitis (IC) also known as bladder pain syndrome (BPS) is the presence of chronic or recurrent pain, feelings of tightness or discomfort perceived as associated with the bladder, accompanied by at least one lower urinary tract symptom in the absence of infection or other identifiable causes [1]. These symptoms are pain or burning while urinating; frequent urination; feeling the need to urinate despite having an empty bladder; bloody urine; pressure or cramping in the groin or lower abdomen. There is no laboratory test to make a diagnosis, it is often a diagnosis based on the exclusion of other diseases, one of the diagnostic methods is cystoscopy with the collection of specimens from the bladder and their histopathological examination [2]. Currently there is no causal treatment, only symptomatic treatment is used, such as intravesical administration of hyaluronic acid or surgical methods.

KEY WORDS: interstitial cystitis (IC), bladder pain syndrome (BPS), diagnosis, treatment

INTRODUCTION

The results of epidemiological studies on the incidence of IC are ambiguous due to the lack of standardized criteria for diagnosis. IC is much more common in women than in men (10:1). The incidence is 52-500/100,000 in women compared to 8-41/100,000 in men. If a woman has a first-degree relative with IC, the incidence increases to 1,431/100,000, which may suggest a hereditary basis. The disease is most common in middle-aged people, but it can also occur in children [3]. The etiopathogenesis of painful bladder syndrome and interstitial cystitis is complicated and not fully understood. However, there are several theories that explain the

development of this disease: urothelium dysfunction associated with the glycosaminoglycan layer (GAG); neurogenic inflammation and mast cell activation, which release powerful inflammatory mediators; microcirculation disorders; neuronal hyperactivity; exogenous substances (ketamine). There is no evidence that infections contribute to IC, however, with recurrent urinary tract infections, there is increased transitional cell apoptosis and mast cell concentration, and decreased E-cadherin levels, which may contribute to hypersensitivity symptoms [4]. The lack of a tangible cause of this disease causes a number of difficulties in its diagnosis and treatment, IC confirmation is often delayed by several years and this causes a significant reduction in the quality of life of patients.

SYMPTOMS

Patients with IC are very diverse, and many of the symptoms overlap with other diseases of the urinary tract. They closely resemble the symptoms of common bacterial cystitis, but urine cultures are sterile and antibiotic therapy does not bring improvement. The most common symptoms reported by patients include: suprapubic pain, which increases with bladder filling and which subsides, at least partially after voiding, urinary urgency, pollakiuria - even several dozen voidings per day. These symptoms may initially suggest overactive bladder syndrome [5]. Besides, they often occur lower urinary tract symptoms: feeling of sudden pressure on the bladder; difficulty in stopping urination due to very strong urges; pain or burning sensation when urinating; difficulty starting to urinate; narrowing of the urine stream and weakening of its pressure; intermittent, pulsating stream of urine; increasing the time it takes to urinate; urination in drops; feeling of incomplete emptying of the bladder after urinating; urinary incontinence - involuntary leakage of urine. Due to the fact that some of the symptoms are related to the reproductive system (vulvodynia, dyspareunia), patients also go to gynecologists, but gynecological examination as well as vagina and cervix swab also show no abnormalities.

DIAGNOSIS

The diagnosis of IC is often based on the exclusion of other more common conditions with similar symptoms. National Institute of Arthritis, Diabetes, Digestive and Kidney Disease - the NIDDK has established exclusion criteria to facilitate the diagnosis of IC [6].

Criteria excluding the diagnosis of IC:
age under 18
urinating less than 8 times a day
symptoms lasting less than 9 months
not urinating at night
remission of the disease after the use of drugs antiseptic and antibacterial
vaginitis
diagnosis of bacterial inflammation of the urinary system in the last 3 months
bladder or ureter stones
diverticulum of the urethra
cancer of the urethra, uterus, cervix and vagina
radiation cystitis
urogenital herpes
tuberculous and chemical cystitis
detrusor overactivity
bladder cystometric volume above 350ml
urgency when filling the bladder over 150ml

Criteria excluding the diagnosis of IC in scientific practice [7].

At the beginning of the symptoms, basic tests such as urinalysis and urine culture should be performed, however normal urinalysis results and sterile urine cultures can often be misleading in the diagnostic process. A thorough physical examination, focusing on pain in the abdomen, pelvis, and genitals, may also be useful, the patient should also be advised to keep a voiding diary. Imaging diagnostics are usually not relevant. If at this stage we are unable to make a specific diagnosis and the symptoms are indicative of IC, cystoscopy should be considered.

Cystoscopy should be performed with a rigid cystoscope and glycine solution to allow clotting after biopsies. The height of the infusion should be 80 cm above the pubic symphysis, leakage through the urethra should be avoided, if necessary through a digital lock. The bladder is inflated until the infusion stops dripping, then the

bladder is held inflated for 3 minutes at maximum capacity before emptying begins. At this time, characteristic pathological changes in the bladder wall are sought. A second filling is then performed, but the bladder is not filled to its maximum capacity to optimize lesion vision and biopsy [8].

Classification of lesions visible in cystoscopy	
0	normal
I	petechiae in at least two quadrants
II	major submucosal haemorrhage
III	diffuse global submucosal haemorrhage
IV	mucosal rupture with or without bleeding

The results are divided into five grades: normal (0), petechiae in at least two quadrants (I), major submucosal haemorrhage (II), diffuse global submucosal haemorrhage (III) or mucosal rupture with or without bleeding (IV), performing an examination five areas of the bladder (anterior, posterior, lateral left and right, and lower) [9].

However, cystoscopy in most cases is normal, only in about 5-10% of patients it can show the presence of Hunner's lesion - an area of reddened bladder mucosa in which the structure of capillaries is abnormal. With Hunner's lesion, more severe clinical symptoms and lower bladder capacity can be expected, and its detection allows for the selection of the most optimal treatment [4]. It seems that a bladder biopsy is a greater value during a cystoscopic examination. Three separate zones can be distinguished in the biopsy. The peripheral zone of the inflammatory reaction presents a picture of infiltration from unequally sized mononuclear cells with nuclei of various sizes (histiocytes and monocytes). In the middle zone of the disease focus, there are reactive structural changes in the blood vessels that close as a result of the process of hyalinization and scarring. The inner zone of the disease focus is the central area of degenerative changes, often predisposing to the formation of fistulas. This area is hypocellular, showing complete obliteration of the anatomical structure of the urinary bladder [10].

TREATMENT

The treatment of IC is difficult because the cause of the disease has not yet been determined. The current guidelines divide the treatment into six stages, starting from the least invasive to complicated surgical treatment, almost all methods are symptomatic. The first-line (1) is based on lifestyle changes, the patient should be educated about the disease and its course. Diet is important, which foods exacerbate symptoms, and then try to eliminate them. One of the main triggers of pain and deterioration of the condition is stress, which is why every patient should avoid it. In addition, you can use bladder training and modify the amount of fluid intake. Second-line (2) treatment is mainly analgesic treatment using basic drugs (non-steroidal anti-inflammatory drugs), additionally amitriptyline, cimetidine, hydroxyzine, pentosan polysulfate, dimethyl sulfoxide, heparin or lidocaine may be included; it also includes manual physical therapy techniques that help reduce pain. Third-line treatment (3) should be initiated if previous methods prove insufficient. It includes cystoscopy, which will allow for a more accurate assessment of the bladder, if a Hunner's lesion is present, it should be removed immediately. Fourth-line treatment (4) is the implantation of a device for neuromodulation of the sacral nerves, the aim of which is to achieve the proper functioning of the bladder by restoring the correct balance between the conduction of nerve impulses from the bladder and the pelvic floor to the central centers controlling the micturition process and feedback. Fifth-line treatment (5) allows for two methods: oral administration of cyclosporin A or administration of intradetrusor botulinum toxin A, however, there is a risk of periodic self-catheterization after treatment. Sixth-line treatment (6) is surgical treatment, which includes methods such as (substitution cystoplasty, urinary diversion with or without cystectomy), but it should be remembered that sometimes even after surgery the pain does not stop. They can only be used when previous methods fail.

SUMMARY

In conclusion, IC is a very complex disease with an unexplained etiology, which causes many problems in the process of both diagnosis and treatment. Many people who suffer from IC are diagnosed with a very long delay, even several years, because the diagnosis of the disease is often made on the basis of exclusion of other similar diseases. The diagnostic process itself is not fully unified, moreover, the studies report that the NIDDK criteria are too restrictive to be used in everyday clinical practice as a diagnostic definition of interstitial cystitis [12]. Conservative treatment, unfortunately, does not always turn out to be effective, therefore, if it does not bring the expected improvement, cystoscopy with a biopsy of the bladder wall is recommended. During cystoscopy, we can remove Hunner's lesion, if present, or confirm interstitial inflammation in histopathological examination of

the biopsy. However, research is still being conducted in order to be able to learn the exact etiology in the future, and thus choose the best treatment methods.

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