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Review Article

Overview of Epididymitis

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Abstract

Introduction: Epididymitis, which is known as the inflammation of the epididymis, could attach both children and adults and is frequently encountered by clinicians in the outpatient setting. Epididymitis usually happens along with orchitis (which is the inflammation of testis); this syndrome is called epididymo-orchitis.

Aim of Work: In this review, we will discuss recent advances in the management and treatment of acute epididymitis.

Methodology: We did a systematic search for recent advances in the management and treatment of acute epididymitis using PubMed search engine (http://www.ncbi.nlm.nih.gov/) and Google Scholar search engine (https://scholar.google.com).

Conclusion: Predisposing factors for the development of epididymitis in most adult males include the presence of a history of urinary tract infections or a sexually transmitted disease, the presence of an anatomical abnormality, previous prostate or urinary tract surgical operations or instrumentation, and/or trauma. Acute epididymitis is generally considered to be a clinical diagnosis. A midstream urinalysis must be done to assess for the presence of an infectious cause. A urine culture must also be done for all pediatric patients as well as for adult males who get a positive urinalysis result. In patients who are fourteen years old or older, the administration of empiric antibiotics is generally recommended, and the choice of the antibiotic will be made based on the most likely underlying organism. Aims of management typically include treating the microbiologic infection and eradicating the organism; avoiding the spread of Neisseria gonorrhoeae or Chlamydia trachomatis infection to other sex partners; and avoiding the development of adverse events and complications that follow untreated cases of epididymitis, like permanent infertility or chronic pain.

Keywords: *Acute Epididymitis; Epididymis; Urinary Tract Infections*

Introduction

Epididymitis, which is known as the inflammation of the epididymis, could attach both children and adults and is frequently encountered by clinicians in the outpatient setting. Epididymitis usually happens along with orchitis (which is the inflammation of testis); this syndrome is called epididymo-orchitis [1,2]. In patients who develop acute epididymitis, both pain and scrotal swelling will be found for a period that is shorter than 6 weeks. On the other hand, chronic epididymitis will last for a period that is longer than 3 months and is often characterized by the presence of pain but the absence of swelling of the scrotum [3].

In this review, we will discuss recent advances in the management and treatment of acute epididymitis.

Methodology

We did a systematic search for recent advances in the management and treatment of acute epididymitis using PubMed search engine (http://www.ncbi.nlm.nih.gov/) and Google Scholar search engine (https://scholar.google.com). All relevant studies were retrieved and discussed. We only included full articles.

The terms used in the search were: acute epididymitis, epididymis, urinary tract infections.

Epidemiology

Annual incidence rates of acute epididymitis are about 1.2 per a thousand boys aged between two to thirteen years (with a mean of age eleven years) [4]; about a quarter of this subgroup shows recurrence within the first 5 years after the initial disease [4]. On the other hand, in adult males, forty-three percent of cases of epididymitis occur between twenty and thirty years of age [5]. A previously published series found that epididymitis happened with orchitis in a total of fifty-eight percent of patients.

Etiology and pathophysiology

Predisposing factors for the development of epididymitis in most adult males include the presence of a history of urinary tract infections or a sexually transmitted disease, the presence of an anatomical abnormality (like the presence of a bladder outlet obstruction), previous prostate or urinary tract surgical operations or instrumentation, sitting for long times, cycling, and/or trauma. Acute epididymitis usually presents as the development of a unilateral pain and inflammation within the scrotum. The etiology of epididymitis strongly depends on the age of the patient. For example, among boys who are younger than fourteen years, the etiology of epididymitis is unknown in most cases but can be associated with the presence of structural abnormalities which cause the presence of reflux of either infected urine or sterile urine to the ejaculatory ducts [4]. Epididymitis that occurs in this age group might also be a part of a medical syndrome, specifically following an infection with Mycoplasma pneumoniae, enteroviruses, and/or adenoviruses. Henoch-Schönlein purpura might also manifest as the development of an acute scrotum and bilateral vasculitic epididymitis in kids aged between two and eleven years [5].

On the other hand, infections with chlamydia trachomatis and Neisseria gonorrhoeae are considered to be the commonest etiologies among sexually active men aged between fourteen and thirty-five years old [1]. Whereas, in males older than thirty-five years, a case of acute epididymitis is most frequently caused by the presence of a retrograde flow of infected urine into the ejaculatory duct in the presence of a bladder outlet obstruction, often secondary to the underlying presence of prostatic hypertrophy [5]. Enteric bacteria should also be considered among males who practice anal sexual intercourse, regardless of their age [1]. Among patients who have an infection with human immunodeficiency virus (HIV), epididymitis cases could be a result of the presence of a concomitant infection, like from an infection with *Cytomegalovirus, Salmonella, Ureaplasma, Toxoplasmosis, Corynebacterium, Urealyticum, Mycoplasma,* or *Mycobacteria* [1].

Noninfectious acute epididymitis might result as a side effect to a certain drug or be caused by a reflux of sterile urine into the vas deferens as a result of the presence of a bladder outlet obstruction or any underlying systemic disease (like sarcoidosis or Behçet syndrome) [5].

Diagnosis; history and physical examination

Acute epididymitis usually manifests as a gradual onset pain of the posterior scrotum along with a swelling that develops within one to two days. There might be other clinical manifestations present like fever, blood in urine, pain with urination, and frequency of urination. In addition, the scrotal pain could radiate to reach the lower abdomen. On the other hand, testicular torsion or appendix testis (the presence of vestigial tissue along the testis) manifests as the development of a sudden severe unilateral pain that is usually linked to the manifestations like nausea and vomiting but without the development of fever or other urologic manifestations.

The presence of a past history of intermittent scrotal pain is not usually common among patients who have epididymitis or testicular torsion but might occur with intermittent testicular torsion [3]. Physical examination in patients with epididymitis will show the presence of tenderness of the epididymis which might extend to the near testis and scrotal swelling and/or scrotal inflammation. Elevation of the scrotum might relieve the pain (this is usually called as Prehn sign by clinicians). In contrast to cases of acute epididymitis with a structurally normal testis, testicular torsion normally present as a high-riding testis on one side which might lie in a transverse position in the scrotum with an anteriorly located epididymis. The absence of the cremasteric reflex indicates the presence of testicular torsion, while the presence of the cremasteric reflex in this clinical picture is suggestive of the presence of epididymitis [6]. Testicular torsion is typically linked to the presence of a blue-dot sign (a bluish discoloration of the scrotum directly on the torsed testis), suggesting the presence of an infarction or necrotic tissue [7].

It is essential to consider the presence of an inguinal hernia as it might also manifest as the development of swelling and/or tenderness of the scrotum. In cases of inguinal hernia, bowel sounds might be heard within the scrotum itself. Other etiologies like testicular cancer and testicular trauma might also be the cause of scrotal pain [8].

Diagnostic testing

Acute epididymitis is generally considered to be a clinical diagnosis. A midstream urinalysis must be done to assess for the presence of an infectious cause. A urine culture must also be done for all pediatric patients as well as for adult males who get a positive urinalysis result [9]. For patients who are sexually active and younger than thirty-five years old or those who have a new sexual partner, assessing for the presence of an infection with N. gonorrhoeae and C. trachomatis must be done [1]. If testicular torsion is thought to be present, color Doppler ultrasonography must be done as soon as possible. Findings like hyperemia, swelling, and elevated blood flow in the epididymis are frequently found on ultrasound in patients who have epididymitis, while there is a decreased or even an absent flow among those who have testicular torsion [10].

If color Doppler ultrasonography is not available to perform, assessment of the acute phase reactants can be beneficial and help in distinguishing between cases of epididymitis or testicular torsion. Epididymitis is usually linked to an increased C-reactive protein level [8].

Treatment

Among children aged between two years and fourteen years who do not show any systemic manifestations like fever, the use of antibiotics is usually restricted for only those who have positive urinalysis or urine culture results [9]. In patients who are fourteen years old or older, the administration of empiric antibiotics is generally recommended, and the choice of the antibiotic will be made based on the most likely underlying organism. Aims of management typically include treating the microbiologic infection and eradicating the organism; avoiding the spread of Neisseria gonorrhoeae or Chlamydia trachomatis infection to other sex partners; and avoiding the development of adverse events and complications that follow untreated cases of epididymitis, like permanent infertility or chronic pain [1].

To avoid the development of complications and side effects, and the spread of gonorrhea and chlamydia organisms, the CDC recommended administration of treatment before without waiting for laboratory investigations results, and making the choice of therapy based on the risk of chlamydia and gonorrhea or enteric organisms [1]. In certain settings where the presence of an underlying gonorrhea or chlamydia organism is found to be likely, the administration of intramuscular ceftriaxone (in a single 250-milligrams dose) along with oral doxycycline (100 milligrams two times a day for ten days) is the recommended protocol. In males who practice insertive sexual anal intercourse, the presence of an underlying enteric organism is considered to be likely present in addition to the presence of gonorrhea or chlamydia; in such cases, the administration of intramuscular ceftriaxone (a single 250-milligrams dose) plus either oral levofloxacin (like Levaquin; 500 milligrams one time a day for ten days) or oral ofloxacin (300 milligrams two times a day for ten days) is considered to be the recommended management protocol. On the other hand, when treating epididymitis patients who are older than thirty-five years, the presence of sexually transmitted infections is considered to be significantly less likely, and, thus, monotherapy with either levofloxacin or ofloxacin is usually enough to treat the likely present enteric organisms.

Because of the recent increase in chlamydia resistance rates, ciprofloxacin is no longer considered to be an adequate alternative fluoroquinolone to be used in the management of patients with epididymitis [1].

Supportive treatment can be used for patients with acute epididymitis and it includes analgesics, anti-inflammatories, and the elevation of the scrotum. Patients who have severe or intractable clinical manifestations or manifestations of a systemic infection might need to be hospitalized to receive sufficient management [5].

Initial management for patients who have idiopathic chronic epididymitis usually includes the administration of a two-week course of a non-steroidal anti-inflammatory medication with the application of scrotal icing and scrotal elevation. If clinical manifestations do not improve soon, the addition of a tricyclic antidepressant or a neuroleptic like gabapentin (Neurontin) might improve clinical picture. Similar to other chronic pain syndromes, the management of chronic epididymitis will likely need the use of a combination of modalities that is individualized to each patient [5].

Follow-up

Acute epididymitis could be often managed in the outpatient setting with a follow-up after a week to assess the clinical response to medications. In rare cases, hospital admission and intravenous antibiotics may be needed to improve systemic manifestations, abscess formation, or the presence of Fournier gangrene [11]. Epididymitis clinical manifestations usually improve after 2 or 3 days of initiating antibiotic treatment. However, residual pain might persist for up to several weeks [3].

Children who are younger than fourteen years old and who are treated for an underlying acute epididymitis must be also referred to a specialized urologist to assess for the possible presence of a structural abnormality [5]. Similarly, adult males who are older than fifty years must be assessed for the presence of a urinary tract obstruction because of an underlying prostatic hypertrophy. All patients who are being treated for an underlying sexually transmitted disease must inform their sexual partners to also be assessed and treated [3].

Etiology of epididymitis in children

As we mentioned earlier in this review, it is well known that most patients who have epididymitis and are sexually active developed their disease from a sexually transmitted organism. In contrast, among infants, acute epididymitis could be a systemic medical condition that is associated with other systemic diseases or resulting from an underlying abnormality in the genitourinary system [12]. On the other hand, the etiology of acute epididymitis among prepubertal males remains to be a debatable issue. There are many hypotheses that include the reflux of infected urine into the ejaculatory duct, the chemical irritation from sterile urine reflux or from pharmacological agents like amiodarone, hematogenously spread organism (either a virus or a bacteria) and direct viral etiologies [13].

In pediatric patients who have recurrent epididymitis, a genitourinary structural abnormality that was not detected previously must also be suspected to be present [14]. In their analysis, Bennett., *et al.* found a statistically significant increase in the frequency of acute epididymitis among children who are uncircumcised [15]. Their analysis included a total of seventy-nine boys who had acute epididymitis and demonstrated that only twenty-five percent of those patients had been circumcised while the expected circumcision rate in this specific population was about seventy percent. However, this paper is considered to be very old and authors assessed patients from different populations and did not use controlled groups. Despite these limitations, it is still the only paper that assessed the possible presence of an association between circumcision and acute epididymitis until this date. They explanation of their findings was that the foreskin could play a role in increasing the likelihood of developing a urinary tract infection.

A systematic review that included twelve 12 studies, of which only one was an RCT, and assessed the potential causative association between urinary tract infections (in general) and performing circumcision demonstrated that circumcision was associated with a significantly less risk of developing a urinary tract infection [16]. nevertheless, the same study showed that the number needed to prevent a single case of urinary tract infection was 111.

An important question that arises is how frequently the etiology of acute epididymitis in children is in fact a bacterial infection. Acute epididymitis among this population often arises following a direct spread of a bacterial urinary tract infection in the epididymis. The National Institute for Health and Care Excellence protocols for the management and treatment of urinary tract infections in the pediatrics population defined urinary tract infections as the combination of clinical manifestations of pathology of the urinary tract along with the presence of bacterial organisms in the urine; a positive urine culture is defined as the presence of a single bacterial organism in a high level, often more than 100,000 colony forming units per ml [17]. In several published studies, the proportion of a positive urinalysis among male children with acute epididymitis ranged between one percent to fifty-nine percent [11]. This wide variation could be explained by the different definitions of a positive urinalysis, that differs from the presence of a mild leucocyturia to positive culture in those papers. The likelihood of getting bacterial epididymitis without the presence of a urinary tract infection has been evaluated despite the fact that this clinical entity has not been shown in the pediatric population. In published literature, the epididymal aspirates cultures' results are strongly associated with those from urine specimens [18].

A potential explanation for the culture negative acute epididymitis cases could be an inflammatory phenomenon that follows another viral infection. Somekh., *et al*. assessed forty-four male children who had acute epididymitis [13]. They did both microbiological and serological assessments and compared their outcomes with a control group that included forty healthy male children. There was microbiological growth in about twenty percent of male children who had acute epididymitis and significantly increased titers to pathogens, indicating the presence of a recent infection. Comparing the 'epididymitis' group against the control group, high levels of titers were detected in fifty-three percent versus twenty percent for Mycoplasma pneumoniae, and sixty-three percent versus ten percent for enteroviruses and twenty percent versus zero percent for adenoviruses, respectively. This study provided solid evidence that epididymitis in male children could be a result by viruses probably following viremia or as a post-infectious inflammatory phenomenon.

This association has also been shown in several case reports of epididymitis in children that developed after acute Coxsackie B virus infections [19].

Despite that epididymitis in adult patients is strongly linked with the development of voiding dysfunctions, this is still a debatable issue among children with acute epididymitis. In a previous study that was conducted by Bukowski., *et al.* [20], voiding dysfunctions were was found in ten out of thirty-six children with acute epididymites using uro-flowmetry and post-void residual ultrasonography. The

commonest findings were the presence of high postvoid residual volumes and meatal stenosis.

Management of acute epididymitis in children

Systemic treatment with antibiotics is considered to be the best treatment for children who have acute epididymitis. nevertheless, some previous studies have challenged the necessity for routinely administrating antibiotics. In their study, Lau., *et al.* evaluated forty-eight male children with acute epididymitis prospectively and administrated anti-biotics only for those with pyuria; while the others received analgesia only [21]. During the follow-up period, there were no side effects or complications neither testicular atrophy among patients who only received supportive therapy and analgesics. Several other authors agree that antibiotics treatment must only be used for children who have pyuria, a positive urine culture or a known urogenital structural abnormality [18]. For other patients, management must be only supportive, and consisting of bed rest and analgesia.

Whether radiological imaging is important after a case of acute epididymitis is also considered to be controversial. The association between urogenital structural abnormalities and acute epididymitis is usually highest among infants [22]. in their study, Cappèle., *et al*. evaluated thirty-seven male children with acute epididymitis [22]. They demonstrated that only seven of included patients had a urogenital structural anomaly.

Conclusion

Predisposing factors for the development of epididymitis in most adult males include the presence of a history of urinary tract infections or a sexually transmitted disease, the presence of an anatomical abnormality, previous prostate or urinary tract surgical operations or instrumentation, and/or trauma. Acute epididymitis is generally considered to be a clinical diagnosis. A midstream urinalysis must be done to assess for the presence of an infectious cause. A urine culture must also be done for all pediatric patients as well as for adult males who get a positive urinalysis result. In patients who are fourteen years old or older, the administration of empiric antibiotics is generally recommended, and the choice of the antibiotic will be made based on the most likely underlying organism. Aims of management typically include treating the microbiologic infection and eradicating the organism; avoiding the spread of Neisseria gonorrhoeae or Chlamydia trachomatis infection to other sex partners; and avoiding the development of adverse events and complications that follow untreated cases of epididymitis, like permanent infertility or chronic pain. When dealing with a boy with an acute pain of the scrotum, the first priority is to rule out testicular torsion. There is no agreement in the medical literature for the need of imaging assessment for underlying structural abnormalities among children who develop acute epididymitis.

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