West of Scotland Sexual Health Managed Clinical Network

NHS Ayrshire & Arran | NHS Dumfries & Galloway | NHS Forth Valley | NHS Greater Glasgow and Clyde | NHS Lanarkshire

West of Scotland Protocol ***Approved January 2024***

EPIDIDYMO-ORCHITIS

What is New

Under investigations:
Testing a first pass urine for *M. genitalium* infection is included (previously considered)

Under treatment
When most probably due to Chlamydia or other non gonococcal sexually transmitted pathogen (eg where gonorrhoea has been ruled out by gram stain and no risk factors for gonorrhoea identified) ofloxacin has been removed as an alternative first line and is now 2nd line.

Advice on the use of fluoroquinolones antibiotics has been updated.

Introduction

Acute epididymo-orchitis is a clinical syndrome consisting of pain, swelling and inflammation of the epididymis +/- testes. The most common route of infection is local extension and is mainly due to infections spreading from the urethra (sexually transmitted pathogens) or the bladder (urinary pathogens).

Caution: EXCLUDE TORSION by careful clinical examination especially if sudden onset, young (<20yrs usually but can occur at any age): seek urgent urology opinion. This is a SURGICAL EMERGENCY – salvage of affected testis under 6 hours offers best outcome.

Aetiology

Bacterial

- Under 35 – most often a sexually transmitted pathogen such as *Chlamydia trachomatis* and *Neisseria gonorrhoeae.*
- Over 35 – most often a non sexually transmitted gram negative enteric organisms causing urinary tract infections. Particular risks include recent instrumentation (such as prostate biopsy and vasectomy) or catheterisation.
- There is cross over between these two groups and complete sexual history taking is imperative.
- Men who engage in insertive anal intercourse are at risk of epididymo-orchitis secondary to sexually transmitted enteric organisms.
- Abnormalities of the urinary tract are common in the group with gram negative enteric organisms.

- All patients with confirmed urinary tract pathogen should have further investigations of the urinary tract.
- Ureaplasma urealyticum is found in men with epididymo-orchitis but is often associated with *C. trachomatis and N. gonorrhoeae.* Evidence for its role in the development of epididymo-orchitis is lacking.
- *Mycoplasma genitalium* has been identified in some cases *of* epididymo-orchitis but evidence for its role in the development of epididymo-orchitis is so far lacking.

Viral

- Mumps – unilateral or bilateral orchitis can occur in up to 40% of post pubertal men who have mumps.

Granulamatous

- Tuberculosis - epididymo-orchitis is a rare presentation of TB (see BASHH).

Other Infective Causes

- Rare infective causes include Brucella, fungi such as candida and schistosomiasis.
    - Brucellosis – consider in the context of travel history to an endemic area, failure to respond to first line therapy and / or history of preceding fever, lethargy and night sweats.

Non Infective causes

- Behcet's Disease
- Adverse effect of amiodarone treatment
- Rare manifestation of Henoch–Schonlein purpura
- Other rare non-infective causes include Mediterranean fever and polyarthritis nodosa

Clinical Features

Symptoms

Often unilateral scrotal pain, swelling and erythema of relatively acute onset.

Patients may complain of symptoms or urethritis or urethral discharge but these symptoms may be absent, In addition there may be symptoms in keeping with a urinary tract infection such as fever, dysuria, frequency and urgency.

Testicular torsion is the most important differential diagnosis. This is a surgical emergency that should be considered first in all patients, particularly young men, as testicular salvage is required within six hours and success diminishes with time. The pain is typically sudden, occurring within hours and usually severe. The pain can radiate into the groin or lower abdomen and associated with nausea and vomiting. If there is any doubt as to the cause of an acutely painful and swollen testes, torsion should be considered until proven otherwise.

Signs

- Tenderness to palpation on the affected side
- Palpable swelling of the epididymis +/- involvement of the testicle
- There may also be urethral discharge, secondary hydrocoele, erythema and/or oedema of the scrotum on the affected side, pyrexia

Complications

More often seen on patients with uropathogen-related epididymo-orchitis

- Reactive hydrocele
- Abscess formation and infarction of the testicle – these are rare complications
- Infertility- there is a poorly understood relationship between epididymo-orchitis and infertility.

Investigations

Preliminary Investigations

- Gram stained urethral smear – **even if urethral symptoms are absent** – examined microscopically for the diagnosis of urethritis and presumptive diagnosis of gonorrhoea. Where facilities do not exist for immediate microscopy consideration may be given to referring patients to another centre.
- The presence of nitrite and leukocyte-esterase on dipstick testing may suggest a UTI in men with urinary symptoms but is is not diagnostic and its results should not preclude the other microbiological investigations above.

Laboratory Investigations

- Midstream urine specimen (MSU) for microscopy and culture.
- Urethral swab for *N. gonorrhoeae* culture.
- First pass urine for NAAT testing for *N.gonorrhoeae* and *C.trachomatis.*
- First pass urine for NAAT for *M. genitalium* infection.
- Screening for other STIs [syphilis and HIV testing (hepatitis testing based on sexual history)].
- White blood cell count, CRP and ESR can be elevated.

Further Investigations:

- Surgical exploration when torsion cannot be confidently excluded.
- If torsion not considered a possible diagnosis but diagnostic uncertainty remains seek advice from senior colleague.
- Ultrasound may help differentiate between epididymo-orchitis and other causes of testicular pain.
- Refer to BASHH when TB, Mumps or other rare infective or non infective cause is suspected.

Diagnosis

A clinical diagnosis presumptively made based on presenting history, risk of STIs, physical examination and preliminary investigations. A sexually transmitted cause should always be excluded.

Management

General

- Patients given advice on duration of symptoms, potential causes of epididymo-orchitis and possible long term consequences for themselves and their partners. This can reinforced by giving them a patient information leaflet 4236.pdf (bashh.org)
- Patients should be advised to abstain from sexual intercourse until they and their partner have completed treatment and follow up in those with confirmed and suspected STI.
- All patients with probable STI should be advised to attend a sexual health clinic for STI testing. When antimicrobilas are commenced in the non sexual health setting, a first void urine for *C. trachomatis* and *N. gonorrhoeae* NAAT testing, urethral swab for *N. gonorrhoeae culture* and MSU for culture should be taken.
- Rest, analgesia and scrotal support.
- An ultrasound of the testes if there is uncertainty about the clinical diagnosis or need to exclude associated complications

Treatment

Empirical treatment for epididymo-orchitis should be started in patients with objective swelling and tenderness on testicular examination.

Empirical treatment should be given to all patients with epididymo-orchitis at the time of the visit before culture/ NAAT results are available.

The antibiotic regimen chosen should be determined in light of the immediate tests. Age, history of insertive anal intercourse, recent prostrate biopsy, vasectomy, urinary tract instrumentation, or catheterisation or any known urinary tract abnormalities in the patient should be considered.

1. **For epididymo-orchitis most probably due to any sexually transmitted pathogen e.g.**
   younger patient
   high risk sexual history - a new sexual partner or more than one sexual partner in last 12 months
   contact of an STI
   no previous UTI
   urethral discharge present
   urine diplstick positive for leucocytes only

a. Most probably due to any STI

Ceftriaxone 1g IM single dose
PLUS
Doxycycline 100mg orally twice daily 14 days

b. Most probably due to Chlamydia or other non gonococcal sexually transmitted pathogen (eg where gonorrhoea has been ruled out by gram stain and no risk factors for gonorrhoea identified) could consider

First line: Doxycycline 100mg orally twice daily 14 days
Second Line: Ofloxacin* 200mg orally twice daily 14 days

2. **For epididymo-orchitis likely caused by sexually transmitted infections and enteric organisms consider eg STI risk factors in men who practice insertive anal sex**

Ceftriaxone 1g IM single dose
PLUS
Ofloxacin* 200mg orally twice daily 14 days

3. **Epididymo-orchitis most probably due to an enteric pathogen** e.g.
   older patient
   low risk sexual history
   previous urological procedures or urinary tract infections
   men who engage in insertive anal sex
   men with known abnormalities of the urinary tract
   no urethral discharge
   positive urine dipstick for leucocytes and nitrites

Ofloxacin* 200mg orally twice daily 14 days OR

Levofloxacin* 500mg once daily for 10 days OR

Amoxicillin/clavulanate 625mg orally three times daily for 10 days when quinonolones contraindicated

4. Where *mycoplasma genitalium* is identified treatment should guided to include an appropriate antibiotic for example:

Moxifloxacin* 400mg once daily for 14 days

*Flluoroquinolones must only be prescribed when other commonly recommended antibiotics are inappropriate. Refer to the full MHRA statement at https://www.gov.uk/government/news/mhra-introduces-new-restrictions-for-fluoroquinolone-antibiotics

Advice for healthcare professionals:

Fluoroquinolones can cause long-lasting (up to months or years), disabling and potentially irreversible side effects, sometimes affecting multiple body systems and senses.

Patients should be advised to stop fluoroquinolone treatment at the first signs of a serious adverse reaction such as tendinitis or tendon rupture, muscle pain, muscle weakness, joint pain, joint swelling, peripheral neuropathy and central nervous system effects, and to contact their doctor immediately.

Clinician should also

- Be alert to the risk of suicidal thoughts and behaviours with use of fluoroquinolone antibiotics.
- Avoid fluoroquinolone use in patients who have previously had serious adverse reactions with a quinolone antibiotic (for example, nalidixic acid) or a fluoroquinolone antibiotic
- Prescribe fluoroquinolones with special caution for people older than 60 years and for those with renal impairment or solid-organ transplants, because they are at a higher risk of tendon injury
- Avoid coadministration of a corticosteroid with a fluoroquinolone since this could exacerbate fluoroquinolone-induced tendinitis and tendon rupture

BASHH advises that fluoroquinolones are prescribed only when judged to be the most appropriate treatment for the patient's infection after considering factors such as likely causative organisms, antimicrobial resistance factors, the availability of alternative agents, and pharmacological considerations such as tissue penetration. www.bashh.org/resources/93/aemhra_statement

Advice for healthcare professionals to give to patients and caregivers:

Fluoroquinolone antibiotics have been reported to cause serious side effects involving tendons, muscles, joints, nerves, or mental health – in some patients, these side effects have caused long-lasting or permanent disability.

Stop taking your fluoroquinolone antibiotic and contact your doctor immediately if you have any of the following signs of a side effect:

- tendon pain or swelling – if this happens, rest the painful area until you can see your doctor
- pain in your joints or swelling in joints such as in the shoulders, arms, or legs
- abnormal pain or sensations (such as persistent pins and needles, tingling, tickling, numbness, or burning), weakness in the legs or arms, or difficulty walking
- severe tiredness, depressed mood, anxiety, problems with your memory or severe problems sleeping
- changes in your vision, taste, smell or hearing

Tell your doctor if you have had any of the above effects at any point while taking a fluoroquinolone – this means you should avoid them again in the future. An information sheet is available for patients in regular or large print.

In those with severe epididymo-orchitis or features suggestive of bacteraemia, inpatient management is required. Refer to BASHH for advice re antibiotic therapy.

If any of the recommended regimens are contraindicated – seek advice from senior colleague

If there is no improvement in the patient's condition by 72hrs, the diagnosis should be reassessed and therapy re evaluated.

Further follow up whether in person or by telephone is recommended at two weeks to:

- Assess compliance with treatment
- Ensure completion with partner notification
- Check for improvement of symptoms
- If patients tested positive for *N.gonorrhoea* arrange test of cure 2-3 weeks using NAAT after completion of antimicrobial therapy
- Test for HIV and syphilis at the end of relevant window period(s) from the contact of concern if indicated by sexual history.
- For patients with persisting symptoms arrangements made for clinical review. Swelling and tenderness can persist after microbiological therapy is complete but should have significantly improved. Where there is little improvement, further investigations such as an ultrasound scan or urological assessment should be considered. Differential diagnosis to consider in these circumstances are:
    - testicular tumour/abscess/infarction/ischemia/alternative infections such as TB and mumps or rarer non infective causes
- Uropathogen confirmed epidiymo-orchitis is an indication for urology referral to exclude structural abnormalities/urinary tract obstruction.

Partner Notification:

- All patients with likely sexually acquired epididymo-orchitis should be referred to an individual trained in Partner Notification
- Sexual partners potentially at risk should be tested for STIs and consideration given to provide treatment to cover *C.trachomatis* and *N.gonorrhoeae* if confirmed in the index patient
- The look back period is arbitrary. Four weeks is suggested on the basis of the current chlamydia guidelines and 2 weeks or their last partner if longer for gonorrhoea.

References

United Kingdom British Association for Sexual Health and HIV National Guideline for the Management of Epididymo-orchitis, 2020 [cited 25th January 2024] https://www.bashhguidelines.org/media/1291/eo-2020.pdf

Fluoroquinolone antibiotics: must now only be prescribed when other commonly recommended antibiotics are inappropriate [Internet]. Medicines and Healthcare products Regulatory Agency Published 22 January 2024 [cited 25th January 2024] available at https://www.gov.uk/government/news/mhra-introduces-new-restrictions-for-fluoroquinolone-antibiotics