Severe Sexually Transmitted Infections

Neurosyphilis, Mpox, and the Tubo-ovarian Abscess

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KEYWORDS

• Sexually transmitted infections (STIs) • Neurosyphilis • Penicillin • Mpox
• Tecovirimat • Tubo-ovarian abscess (TOA) • Pelvic inflammatory disease (PID)

KEY POINTS

- *Neurosyphilis* diagnosis is based on clinical suspicion and serology with confirmation through cerebrospinal fluid analysis.
- The treatment of choice for *neurosyphilis* remains intravenous penicillin. Data are limited for alternatives that include ceftriaxone and doxycycline.
- *Mpox* can be transmitted both via respiratory secretions and direct contact with skin lesions that appear similar to smallpox; however, the systemic disease is less severe.
- A serious complication of PID, TOA presents as an acute inflammatory process involving the fallopian tubes and the ovaries, usually of bacterial etiology
- *TOA* is managed conservatively with systemic antibiotics patients; transvaginal drainage and surgery are reserved for large abscesses and cases of antibiotic failure.

NEUROSYPHILIS

Introduction and Epidemiology

After a decline in the incidence of syphilis at the end of the twentieth century, for more than 2 decades, there has been a steady increase in the global incidence of syphilis. In the United States, between 2018 and 2022, the number of cases at all stages has almost doubled and vertically transmitted syphilis has almost tripled. Unfortunately, the current rates of neurosyphilis are not readily available, but it is estimated that 3% to 5% of all individuals with syphilis develop various forms of symptomatic neurologic involvement.[1]

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Abbreviations	
CDC	Centers for Disease Control and Prevention
CSF	cerebrospinal fluid
CT	computed tomography
FDA	Food and Drug Administration
HIV	human immunodeficiency virus
IV	intravenous
MSM	men who have sex with men
ND	no data
NTT	nontreponemal or lipoidal test
PCR	polymerase chain reaction
PID	pelvic inflammatory disease
PreP	pre-exposure prophylaxis
STIs	sexually transmitted infections
TOA	tubo-ovarian abscess
TT	treponemal tests
WHO	World Health Organization

Risk Factors

Syphilis is transmitted through vaginal, anal or oral sex, vertically during pregnancy through placenta, and through contact with infectious lesions. High-risk sexual behavior is associated with an increase in syphilis acquisition. Populations that are disproportionately affected by an increase in the incidence of syphilis are men who have sex with men, persons living with human immunodeficiency virus (HIV), Black, and Hispanics.

Clinical Picture

Neurosyphilis can present at any stage of treponemal infection. The range of presentations is wide, from asymptomatic involvement to symptomatology that may mimic stroke.

Early in the infection, evidence of neuroinvasion can be found in 30% of cases, but most of these cases are asymptomatic[2]; a minority present as acute meningitis, usually in the first year of infection. Usual symptoms include headache, neck stiffness, confusion, and vomiting. Cranial nerve abnormalities can be present. Typically, fever is absent.

Three syndromes can be identified in late neurosyphilis.

- *Late meningovascular* disease, with cerebral stroke and spinal infarcts: symptoms vary depending on location of the infarcted tissue, but may include aphasia, hemiparesis, seizures, pain, paresthesias, weakness of the lower extremities, hyperreflexia, and paraplegia.
- *Parenchymatous with general paresis:* early symptoms related to chronic meningoencephalitis include personality changes, poor memory, insomnia, and irritability. Paranoia, disorientation, depression, impaired judgment, delusions become more common later in disease. Slurred speech, tremors, seizures, and signs related to hydrocephalus can be found on examination.
- *Parenchymatous with tabes dorsalis:* symptoms are related to degeneration of spinal cord posterior column.

A particular form of neurosyphilis is a manifestation of tertiary, late syphilis: up to 40 years into infection patients can develop gummas, localized areas of granulomatous inflammation that can involve essentially any organ, including the brain and spinal cord. Manifestations depend on the location.

Otosyphilis and Ocular Syphilis

Both eye and ear involvement have been reported to be either independent from or as part of neurosyphilis. All cases of neurosyphilis should have a very careful formal hearing evaluation and eye examination to establish a baseline early in the treatment and to provide a reference point for follow-up.

- *Ocular syphilis*

Syphilis can cause both anterior and posterior uveitis and can mimic other infectious and inflammatory conditions. Especially in patients who present with exclusively ocular symptoms, syphilis serology should be part of the workup of uveitis. Anterior uveitis is most frequently bilateral, and panuveitis is the most common presentation.[3] Symptoms of anterior uveitis include redness, photophobia, and pain. Posterior uveitis findings include decreased vision and vision loss, floaters, scotomas, and decreased night vision. When diagnosis and treatment are delayed, permanent vision loss can occur. Other, less common presentations consist of scleritis, episcleritis, eyelid primary chancre, and optic neuritis. An uncommon but specific finding is the Argyll Robertson pupil: the light reflex is absent, but there is prompt constriction with near accommodation.

Differential diagnosis of ocular syphilis includes ocular tuberculosis, toxoplasmosis, cytomegalovirus retinitis, Lyme disease, and cat scratch disease. Significant challenges exist in differentiating among these conditions.

- *Otosyphilis*

Ear involvement can occur from treponemal invasion of the perilymph of the inner ear or as spread from the cerebrospinal fluid (CSF) as a result of neurosyphilis. Most individuals develop sensorineural hearing loss, which can be unilateral or bilateral. Tinnitus, vertigo, and loss of balance can also be found.[4]

Diagnosis of Neurosyphilis

While history and physical are very important, a combination of serologic tests is the cornerstone of diagnosis confirmation at all stages of syphilis except for the primary stage, during which antibodies have not developed yet and direct identification of treponemes is required, either by dark field microscopy or more recently by polymerase chain reaction (PCR), still not widely available.

Two categories of serologies exist: nontreponemal or lipoidal (NTT) and treponemal tests (TT). These are used in 2 different algorithm sequences. The traditional algorithm starts with an NTT (reflexed to a titer if positive, and confirmation with a treponemal test). This sequence provides simplicity and the reagents are relatively inexpensive but require significant human resources. In addition, the results can be subjective, and there is variability in titers between laboratories. Lastly, the NTTs can become negative in late syphilis, even in untreated individuals; they have lower sensitivity in early syphilis leading to false-negative tests, and there are many conditions that lead to false-positive NTTs. The algorithm is still used by small laboratories, and it is appropriate in populations with a high likelihood of previous syphilis. Larger laboratories use a reverse algorithm that starts with a screening treponemal test (enzyme immunoassay [EIA]) that can be done in large batches and involves much less tech time. If positive, this is reflexed to a nontreponemal test, which can also provide a titer if positive. This would confirm the diagnosis of syphilis. If the NTT is negative, then a second TT is performed, which can confirm or disprove the diagnosis. This algorithm provides higher sensitivity screening and allows larger number of tests to be run simultaneously.

CSF examination should be performed in all patients with suspected neurosyphilis: in an individual with compatible neurologic signs and symptoms and reactive serology; in tertiary syphilis (ie, cardiac syphilis or gummatous involvement of other sites); at treatment failure (lack of adequate serologic response—see later discussion for details on follow-up serology). Older Centers for Disease Control and Prevention (CDC) guidelines recommended a CSF examination in asymptomatic patients with HIV and a high serum rapid NTT, as well as in all cases of suspected ocular and otosyphilis, however, currently these recommendations were discontinued, since CSF analysis in these cases rarely changes the management.[5]

Any CSF abnormality including a high protein (>50 mg/dL), lymphocytic pleocytosis (>5 white blood cells/μL) or positive syphilis serology should be considered as consistent with neurosyphilis. A protein elevation is the least sensitive and specific out of all the listed parameters. The NTTs done from CSF are specific but not very sensitive, which is the opposite of the serum test characteristics. Some sources quote a 100% specificity of CSF Venereal Disease Research Laboratory (VDRL); however, a positive test should be interpreted with caution if it was performed in the setting of negative blood serology.[6] Consequently, CSF analysis for syphilis should not be performed if a patient does not carry a diagnosis of syphilis confirmed by blood serology.

Management

Treponema pallidum remains universally susceptible to penicillin, which is the drug of choice at all stages, including neurosyphilis. For years, injectable benzathine penicillin was successfully used for neurosyphilis, however, modern studies determined that the rate of failure is unacceptably high, and the current recommendation is to resort to intravenous (IV) aqueous penicillin G 18 to 24 million units per day for 10 to 14 days. Administration of IV penicillin in the outpatient setting requires either a computer-assisted or elastomeric pump for either continuous infusion or divided doses every 4 hours. Daily intramuscular procaine penicillin 2.4 million units along with oral probenecid 500 mg every 6 hours is an alternative to the relatively inconvenient IV formulation.[5]

When treating neurosyphilis as part of late syphilis, some clinicians may choose to add 1 dose of long-acting IM penicillin G as a supplement to the 10 to 14 days of IV penicillin. There is no evidence that such practice is required, and it is not recommended by the CDC guideline.[2]

In nonpregnant patients with an allergy to penicillin, ceftriaxone is an acceptable alternative to IV penicillin; however, pregnant patients with neurosyphilis should be desensitized and treated with IV penicillin. No recommendations exist for pregnant individuals with a history of penicillin reactions that are not amenable to desensitization (ie, drug reaction with eosinophilia and systemic symptoms [DRESS] and Stephens Johnson syndrome), and these rare cases should be managed by a multidisciplinary team including a consultation with an infectious diseases expert and with the input of an allergy specialist.

Although scant encouraging data exist on high dose (200 mg twice daily) doxycycline for the treatment of neurosyphilis, the CDC guideline does not recommend its use, due to the very small sample of patients studied.[2]

Follow-up and Prevention

In all cases of syphilis, serology must be repeated at regular intervals to ensure a 4 fold drop of the NTT titer in 1 year for early syphilis or in 24 months for late syphilis and in persons with HIV. Trending the titers is important, in order to avoid missing

reinfections in between very distant points of testing. Individuals who fail to respond to penicillin should be retreated and re-evaluated for HIV infection. Patients with neurologic symptoms should have a CSF evaluation.

All patients diagnosed with syphilis should be tested for HIV and if negative referred for pre-exposure prophylaxis (PreP). Sexually transmitted infection (STI) prophylaxis with doxycycline administered as a single 200 mg dose within 72 hours of a condomless sex was found to significantly reduce sexual transmission of syphilis and Chlamydia in men who have sex with men (MSM) and transgender women in a European study.[7] This prevention strategy is promising, but still to be proven effective in cisgender women (a study conducted in Africa failed to prove efficacy, thought to be related to poor adherence).

Summary

Neurosyphilis is an uncommon but serious complication of *T pallidum* infection. Incidence of syphilis overall has increased in the recent 2 decades. Diagnosis is based on clinical suspicion, neurologic findings as well as blood and CSF serology. Treatment is readily available but is associated with the practical challenge of short half-life of IV penicillin. Screening and prevention should be key in eradicating this infection that exclusively affects humans.

MPOX

Introduction

Mpox is a zoonotic viral infection caused by the mpox virus, previously named Monkeypox. The virus is an orthopoxvirus in the same genus as variola (smallpox virus).[8] Clinically, it presents with a rash similar to smallpox. Historic outbreaks were confined mainly to the Democratic Republic of Congo, Nigeria, in 2017, as well as some travel-related cases. In 2003, 71 human cases in the United States were related to the importation of exotic mammals. There have been a few travel-related cases in nonendemic countries in recent years. The global outbreak beginning around May 2022 has raised concern, given the community spread of a new mpox lineage. By November 2022, more than 78,000 cases in 100 countries had been reported.[8] On May 11, 2023, the World Health Organization (WHO) stated that mpox was no longer a public health emergency.[9] However, there is still low-level circulating Clade 2 mpox in the United States as of the most recent CDC update. The potential for future outbreaks warrants vigilance and provider awareness. In addition, outbreaks continue to arise on the African continent.

Virology and Epidemiology

Mpox belongs to the genus *Orthopoxvirus*, which belongs to the Poxviridae family. It is a large double-stranded DNA virus that replicates in the cytoplasm of the host cell.[10] The mpox virus is divided into 2 clades. Clade 1 is largely present in central Africa and the Congo Basin, while Clade 2 is found more in West Africa. Clade 2 has been noted to be less virulent than Clade 1 with a lower case fatality rate, about 0.1%.[8] A new lineage, B.1, classified as clade 2b, is responsible for the 2022 outbreak.[11] Historically, the mpox virus has had a low frequency of mutation because of its double-stranded DNA structure.[12] However, the 2022 mpox virus seems to have a much higher than expected mutation rate than a closely related 2018 to 2019 strain.[11,12] These mutations seem to be caused by (apolipoprotein B mRNA-editing catalytic polypeptide-like 3 [APOBEC3]) enzymes, proteins that are part of the human immune system. APOBEC3 enzymes are part of the host cellular defense mechanism,

introducing errors into the viral genome and blocking the replication of foreign viruses.[13] Many mutations are believed to coincide with significant human-to-human transmission.[8,12,14] The current cases have been noted in a younger population, in patients with no previous vaccine immunity or cross-immunity, and no exotic animal exposure or travel links to Africa.[14]

Transmission

Mpox can enter the body through respiratory or dermal routes. Respiratory transmission occurs when respiratory droplets deposit on mouth and nose mucus membranes.[3] Other modes of respiratory transmission include extended face-to-face contact or activities that suspend dried material in the air, like shaking of contaminated bedding. During the 2022 outbreak, the rapid spread of infection seemed to be secondary to direct contact with mpox lesions. This includes sexual transmission, where there are microabrasions in the recipient's skin or mucosa that occurs because of sexual activity.[8] There does seem to be a correlation between the viral load and tissue sample. Mpox DNA has been found in 60% to 70% of anus and throat samples, 50% of semen samples, and 20% of blood and urine samples.[8] Given the presence of viral DNA in semen, concern for sexual transmission was noted at the beginning of the outbreak. In addition, early case series showed almost one-third of those patients had evidence of a sexually transmitted coinfection.[15] There have also been some cases of transplacental transmission leading to congenital mpox.[8]

After gaining entry into the body, the virus targets lymphoid tissue. It has shown a tropism for other tissues, including ovaries, liver, pancreas, lungs, heart, salivary epithelium, kidney, and brain. Primary viremia leads to viral spread to local lymph nodes and causes lymphadenopathy. Secondary viremia is characterized by the spread of the virus through the circulation to other organs.

Clinical Presentation

Symptoms of mpox are very similar to those of smallpox, though not as severe. The incubation period in humans is typically 7 to 14 days, though it can range from 4 to 21 days.[16] During the 2022 outbreak, the incubation period was about 7 to 10 days. The shorter incubation period may be related to direct viral inoculation through sexual contact.[8] There has been a noted difference in the clinical manifestations between the most recent outbreak beginning in 2022 and previous outbreaks. The infection has 2 phases: a prodromal phase and a second phase marked by the appearance of a rash. Initial symptoms include headache, fatigue, fever, chills, sweats, sore throat, myalgia, and lymphadenopathy.[12] Rash develops a few days after the onset of fever and lymphadenopathy (1–5 days). The rash can last 2 to 3 weeks and progresses through several stages: it initially starts as small 2 to 5 mm macules that evolve into papules, followed by vesicles and finally pseudopustules.[8] The lesions are usually in the same stage of development. However, there are reports of simultaneous lesions in multiple stages[17] (**Fig. 1**A, B).

Similar to smallpox, the rash appears first on the face and trunk (centrifugal) and then involves the palmar and plantar surfaces. The phases, including macular, papular, and vesicular, last about 1 to 2 days, followed by the pseudopustular phase (containing solid debris rather than actual pus). Resolution occurs by umbilication, crusting, and scarring, taking 1 to 2 weeks.[11] The number of lesions can vary; historically, in endemic areas, patients presented with more than 100 lesions, while immunocompromised patients can present with over 1000 lesions.[8] However, this pattern appears to be different in the most recent outbreak, where anogenital and perioral lesions have predominated.[8,15] Most patients had less than 10 lesions, 73% had anogenital lesions, trunk,

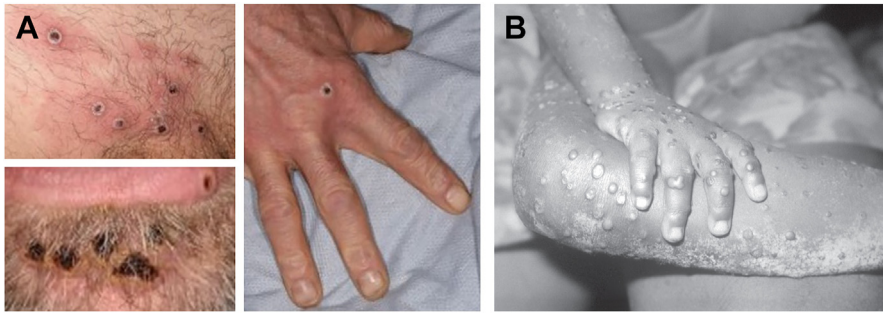

Fig. 1. (*A, B*) Individual mpox lesions. (Mpox: background information - GOV.UK. From: UK Health Security Agency. Published 8 September 2018. Contains public sector information licensed under the Open Government Licence v3.0.)

arms, and legs in 55%, face 25%, and palms and soles 10%.[15] Several patients only had a single genital or oral lesion or perianal lesion. The location of the lesion seems to coincide with the site of inoculation. In MSM who engaged in anal-receptive sex, proctitis was seen more frequently.[8,15,18] In comparison, MSM who engaged in oral receptive sex were more likely to have tonsilitis[8,11] (**Table 1**).

Given the location of the lesions, perianal, genital, and oral, the differential diagnosis includes several skin infections, other poxviruses as well as other sexually transmitted infections.

Varicella zoster, chicken pox, remains on the differential, though the notable difference would be lesions that develop in crops are in different stages of development and are fluid-filled. Another hallmark sign is that historically, mpox has had more significant lymphadenopathy, particularly submental, submandibular, cervical, and inguinal nodes.[17] During the 2022 outbreak, generalized lymphadenopathy has not been seen. Regional lymphadenopathy is more common and is seen in regional lymph nodes of the associated skin lesions.[8] Given the presence of either perioral or anal lesions, herpes simplex virus, syphilis, and other STIs have been part of the differential. One-third of patients in one case series had a coinfection with another STI, with about 9% of coinfections being syphilis.[15]

During the 2022 outbreak, most cases were mild and self-limiting. Hospital admissions were infrequent and occurred in 1% to 13% of cases. The most common reason for hospitalization was for pain management and treatment of secondary skin infections. Severe cases occurred in HIV infected and other immunocompromised patients.

Historically, complications have included bronchopneumonia and ocular infections (conjunctivitis, keratitis, and lesions on the eyelids). Rare instances of neurologic complications with encephalitis, seizures, and confusion have occurred.[11,17]

Diagnosis

Given the wide differential diagnosis, diagnosis based on clinical signs and symptoms alone has proved challenging. Patients with appropriate exposure history and clinical signs should be confirmed with laboratory testing. Viral culture, electron microscopy, and immunohistochemistry can be used to aid in diagnosis, but these methods are often limited by availability and expertise. Specific serology tests, such as immunoglobulin M and immunoglobulin G, are available. WHO does not recommend serology alone for diagnosis.[13] When using PCR, skin lesions have shown a clinical sensitivity of 91% to 100%. The sensitivity of oral, nasopharyngeal, and saliva has been reported between 69% and 100%, rectal swabs 78% to 97%, and seminal fluid 77.8% to

Table 1
Comparison of the clinical presentation in the 2022 outbreak with previous outbreaks

	2022 Outbreak	Previous Outbreaks
Population features		
Mean age	37–41 y	26–32 y
Smallpox vaccination in childhood	11%–18%	20%
Incubation period	6–7 d	12 d
Sex		
Male	97%–100%	53%–78%
Female	0%–3%	22%–47%
Systemic features		
Systemic symptoms	Fever (54%–72%), fatigue or myalgia (24%–81%), and headache (25%–53%)	Fever (45%–90%), fatigue or myalgia (73%–85%), and headache (48%–79%)
Lymphadenopathy	55%–87%, localized in the lymph catchment area of lesions	57%–87%, localized or generalized
Systemic symptoms start after rash	38%–52%	15%–66%
Clinical features of the rash		
More than 10 lesions	22%–36%	100%
More than 20 lesions	12%	46%
More than 100 lesions	0%–4%	20%–42%
Progression	Lesions present at different stages simultaneously; not all lesions progressed from one phase to another in order	Progression from one phase to another occurs in order
Distribution	Commonly localized to 1–3 body regions	Commonly disseminated to >3 body regions
Localization	Genitalia (55%–61%), perianal (34%–44%), oropharyngeal (14%–43%), trunk (25%–57%), arms and legs (50%–60%), face (20%–39%), and palms or soles (0%–10%)	Genitalia (67%–68%), perianal (not reported), oropharyngeal (38%), trunk (80%–93%), arms and legs (81%–91%), face (96%–98%), palms (28%–55%), and soles (10%–64%)

Outcome		
Complications	Rectal pain (14%–36%), sore throat (17%–36%), difficulty swallowing related to tonsillar or pharyngeal ulcer (5%–14%), penile edema (8%–16%), proctitis (11%–25%), secondary bacterial infection (3%–4%), and conjunctivitis (1%)	Secondary bacterial infection of skin lesions (19%), bronchopneumonia (12%), sepsis (1%), encephalitis (0.4%), keratitis (0.4%), and retropharyngeal abscess (0.4%)
Hospital admission	1%–13%	26%
Risk factors for severe disease	Unknown	Age (younger ages are more at risk), living with HIV and not being on antiretroviral therapy
Fatality rate	<0.1%	Clade 1 had 1%–12%, clade 2 had <0.1%
Sexual health		
Living with HIV	36%–67%	ND
Concomitant STI	16%–76%	ND
History of STI in past 12 mo	54%–55%	ND

Data were retrieved from published cohorts including 30 or more patients with mpox.
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100%.[18] Several point-of-care tests have been made available under the Food and Drug Administration (FDA) Emergency Use Authorization program.

Treatment

Management and treatment focus on supportive care, pain relief, and treatment of proctitis. Antibiotics have been prescribed for secondary bacterial infections related to extensive anogenital ulcers or abscesses. Antiviral therapy is available for those with severe illnesses, like eye infections, severe proctitis, encephalitis, or pharyngitis. Antiviral therapy is also available for those who are at risk of developing severe illnesses, like children aged under 8 years, pregnant people, nursing mothers, those with atopic dermatitis, and immunocompromised patients.[8] There are 3 antiviral agents that have shown efficacy in animal models or in limited data. These antivirals are cidofovir, brincidofovir, and tecovirimat, with tecovirimat being the preferred agent.[8] Cidofovir has only shown some efficacy in animal models, while there are limited case data for using brincidofovir.

Currently available antiviral agents for the treatment of human mpox virus infection (**Table 2**).

Tecovirimat was first approved in 2018 by the FDA to treat smallpox. A trial in those infected with mpox showed that tecovirimat taken at 600 mg twice a day for 14 days did not have significant side effects, with decreases in viral shedding and days of illness. Tecovirimat inhibits the spread of the virus in the body by preventing exocytosis from the cell, but it does not inhibit DNA or protein synthesis or formation of the mature cell.[19]

Vaccinia immunoglobulin was FDA approved to treat disseminated vaccinia related to smallpox vaccine complications. The CDC has allowed the use of Vaccinia immunoglobulin in an outbreak.[19] It is a prophylactic option in patients with severe T-cell immunodeficiency in whom smallpox vaccination is contraindicated after exposure.

Prevention

Avoidance of contact with individuals with mpox is recommended, avoiding close skin-to-skin contact, as well as with possible objects and materials. There is no specific vaccine against mpox. There is noted ability for antibodies made against one orthopoxvirus to cross-neutralize other species.[13] As such, other orthopoxviruses like horsepox virus and cowpox virus have been used as smallpox vaccines.[20]

Currently available vaccinia virus vaccines (**Table 3**).

The available second-generation and third-generation smallpox vaccines can be used to prevent infection in high-risk patients. They can also be used as postexposure prophylaxis, ideally within 4 days of exposure.[8] The second-generation vaccine ACAM2000 is a replication-competent attenuated vaccinia virus; it is contraindicated in immunocompromised patients.[11,21] The third-generation vaccine is a replication-deficient strain incapable of replicating in humans, making it safe for immunocompromised and pregnant people. JYNNEOS and IMVAMUNE (Bavarian Nordic, Denmark) are third-generation vaccines available for PreP and have replaced second-generation vaccines on the Advisory Committee on Immunization Practices recommendation.

Summary

While the mpox outbreak of 2022 is no longer a public health emergency, it remains present in the community at low levels. A proper clinical history including sexual history and possible exposures are key to making an accurate diagnosis along with PCR testing. Suspicion for mpox infection should also result in the screening of other STIs given the presence of coinfections as well as clinical mimickers.

Table 2
Currently available antiviral agents for the treatment of human mpox virus infection

Drug	Mechanism of Action	Indication	Dosage	Common Adverse Event(s)
Tecovirimat	Inhibits viral protein VP37, which mediates Golgi-derived lipid "envelopization" and exocytosis of intracellular orthopoxvirus particles	Treatment of smallpox in adults and children weighing ≥13 kg	600 mg orally twice daily for 14 d, or 200 mg IV every 12 h for 14 d	Headache and nausea
Cidofovir	Inhibits viral DNA polymerase	Not approved for treatment of orthopoxvirus infections	5 mg/kg IV weekly for 2 wk, followed by 5 mg/kg IV biweekly until symptom resolution	Nephrotoxicity, leukopenia, and thrombocytopenia
Brincidofovir	Inhibits viral DNA polymerase	Not approved for treatment of orthopoxvirus infections	200 mg orally, weekly, for 3 consecutive weeks	Gastrointestinal upset

Administered as intravenous (IV) dosing regimen of tecovirimat, based on recommendations from the FDA (https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/214518s000lbl.pdf) (From the source).

Source Elsayed S, Bondy L, Hanage WP. Monkeypox Virus Infections in Humans. Clin Microbiol Rev 2022;35(4):e0009222. https://doi.org/10.1128/cmr.00092-22. Epub 2022 Nov 14. PMID: 36374082; PMCID: PMC9769527.

Table 3
Currently available vaccinia virus vaccines

Product (Trade Name)	ACAM2000	JYNNEOS, IMVANEX, and IMVAMUNE
Formulation	Second-generation cell culture-based replication-competent attenuated vaccinia virus	Third-generation live, replication-deficient modified *Vaccinia* Ankara modified vaccinia ankara-bavarian nordic (MVA-BN)
Indication	Preexposure prophylaxis against smallpox and mpox	Pre-exposure prophylaxis against smallpox and mpox
Contraindications	Immunocompromise; eczema, infancy, pregnancy, breastfeeding, and cardiac disease; and allergy to vaccine component	Allergy to vaccine component
Dosing regimen and administration	One dose given subcutaneously using a bifurcated needle	Two doses given subcutaneously at days 0 and 28
Boosters	Every 3 y	Every 2 y
Efficacy	Limited data, although potentially comparable to that of Dryvax	Limited data, but potentially lower than that of ACAM2000 or Dryvax

Source Elsayed S, Bondy L, Hanage WP. Monkeypox Virus Infections in Humans. Clin Microbiol Rev 2022;35(4):e0009222. https://doi.org/10.1128/cmr.00092-22. Epub 2022 Nov 14. PMID: 36374082; PMCID: PMC9769527.

TUBO-OVARIAN ABSCESS

Introduction

A tubo-ovarian abscess (TOA) develops when an infection in the pelvic region advances to create a pus-filled mass involving the fallopian tubes and the ovaries. This condition is often a complication of untreated pelvic inflammatory disease (PID) that results from ascending genital tract infection.[22] TOA usually presents with abdominal/pelvic pain, vaginal discharge, fever with elevated inflammatory markers like leukocytosis, and radiological findings of adnexal mass. However, the presentations of TOA can vary significantly.

Etiology and Risk Factors

TOA results from untreated PID, typically originating in the vagina or endocervix, extending into the endometrium and adjacent adnexal structures. The majority of PID cases are caused by STIs, particularly chlamydia and gonorrhea cases.[21] In addition to these STIs, many bacteria, including anaerobes, gram-negative rods, streptococci, and mycoplasma have been isolated from the upper genital tracts of women with acute, symptomatic PID.[23]

Risk factors for developing TOA are similar to those associated with PID and include age below 25 years, having multiple sexual partners, and a history of prior PID.[24]

Clinical Presentation

The clinical presentation of TOA can vary significantly, ranging from acute and severe symptoms to more subtle, chronic complaints. Common symptoms include pain typically localized to the lower abdomen or pelvis and often described as dull and aching, as well as fever, abnormal vaginal discharge, and dyspareunia.

In some cases, patients may exhibit minimal symptoms or have atypical presentations, which can complicate the diagnostic process.

Diagnostic Approaches

The diagnosis of TOA requires a combination of clinical assessment and radiographic evaluation. Clinical suspicion, along with a physical examination revealing mucopurulent discharge and cervical motion tenderness, may suggest PID. Additionally, concomitant uterine or adnexal tenderness raises concern for TOA.[25]

Ultrasound and computed tomography (CT) are commonly utilized to evaluate TOA, with CT demonstrating greater sensitivity over ultrasound.[26] When CT is performed, it should include both oral and IV contrast. A study by Hiller and colleagues assessed the imaging characteristics of TOA on CT scan, revealing that the most frequent findings are thick, enhancing wall abscess, which may be multilocular. Other findings include bowel thickening and infiltration into pelvic fat.[27]

Management

Management of TOA has evolved; historically, it was managed surgically. However, with advancements in antimicrobials and drainage techniques, conservative management now achieves success rates of 16% to 95%, with most studies reporting a success rate of approximately 70%.[28] Current primary treatment involves antimicrobial therapy, while surgical interventions are preserved for cases with poor response to antimicrobials or ruptured abscesses.

In a study by Reed and Sweet[29] evaluating 119 patients with TOA, the success rate of conservative management was found to be 75%. The same study also indicated that patients with abscess sizes equal or greater than 10 cm had over 60% chance of requiring surgery, whereas those with abscess sizes between 4 and 6 cm had less than 20% chance of requiring surgical intervention. Despite these findings, the decision for surgical intervention should be guided by clinical presentation and the patient's response to antibiotic treatment.

Women exhibiting signs and symptoms of acute peritonitis should raise the suspicion for a ruptured TOA, which is considered a surgical emergency. A study done by Pedowitz and Bloomfield[30] found that before the introduction of broad-spectrum antibiotics in the 1950s, mortality rates from ruptured TOA reached 100%, following implantation of antibiotics therapy, these rates decreased significantly to 3.1%.

The selection of antimicrobials for TOA is guided by the common pathogens associated with this condition. The CDC recommendations for parenteral treatment of PID also apply to TOA, covering *Neisseria gonorrhoeae*, gram-negative and gram-positive aerobes, as well as anaerobes.[31] First-line treatment typically includes IV cefotetan or cefoxitin combined with doxycycline, or ceftriaxone plus doxycycline plus metronidazole.

It is recommended that women diagnosed with TOA should be hospitalized at the onset of treatment for monitoring purposes, including assessing the adequacy of the antibiotics response and identifying any potential complications such as ruptured abscess. Clinical response is generally indicated by the resolution of the patient's symptoms, including alleviation of pain, defervescence of fever, normalization of white blood cells, and a decrease in the abscess size observed on images.

In certain cases, antibiotics may need to be used in conjunction with source control, particularly for larger abscesses. Advances in radiological techniques have led to a greater reliance on percutaneous drainage of abscesses, sparing many patients more complex surgical procedures. Drainage can be performed via the abdomen,

vagina, or rectum. For low-lying pelvic abscesses, drainage through a posterior colpotomy can be effective.

A study conducted by Gjelland and Granberg[32] in 2005 reviewed 302 cases of women who received antibiotics along with transvaginal ultrasound-guided aspiration for TOA at Haukeland University Hospital in Norway between 1986 and 2003. The treatment was successful in 93.4% of cases, with 62.3% of patients experiencing complete resolution of their pain within 48 hours of the initial drainage procedure. Approximately 6% of women required surgical intervention. The study concluded that the combination of antibiotic therapy and transvaginal ultrasound-guided drainage is effective, safe, and associated with high success rates.

Summary

A TOA is a serious complication of untreated PID. Timely diagnosis and immediate initiation of antibiotic therapy are essential for effective management. Patients should be closely monitored for signs and symptoms indicative of acute peritonitis, which may suggest a ruptured abscess, which is a surgical emergency that requires immediate intervention.

Advancements in broad-spectrum antibiotics and the development of percutaneous drainage techniques have significantly improved outcomes for TOA. These interventions led to high success rates in managing this condition, allowing many to avoid more invasive surgical procedures.

CLINICS CARE POINTS

- Clinical recognition of neurosyphilis and ocular syphilis, prompt workup and administration of treatment can significantly improve outcomes, including preserving vision and preventing complications.
- Practitioners should familiarize themselves with the complexities of the various blood and CSF treponemal and nontreponemal serologies.
- New treatment modalities and vaccines for Mpox are currently availableNew treatment modalities and vaccines for Mpox are currently available.
- Antibiotics remain the cornerstone of tubo-ovarian abscess (TOA) treatment. Historically, surgical intervention was the primary approach, but with advances in radiological techniques, we can now combine medical therapy with percutaneous drainage for improved source control.
- A painful vesicular, pustular or nodular rash in a host with the appropriate exposures should raise the suspicion for Mpox.

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