Herpes Simplex Virus: Localized Disease

Background

1. Definition
    - Superficial localized infection caused by HSV
    - Primary infection:
        - Individuals w/no preexisting antibodies to HSV
    - Recurrent infection:
        - Individuals w/preexisting antibodies to HSV or prior hx of HSV infection
2. General information
    - HSV is a member of herpesvirus group
    - Dz in children comes in 2 distinct types
        - Localized
        - Cause of Neonatal sepsis
    - Occurs as 2 antigenic types- HSV1 and 2
        - HSV1 most commonly assoc w/infection of mucous membranes of mouth, lips, eyes
        - HSV2 most assoc w/localized genital infections but also can cause neonatal sepsis
    - All local herpes virus infections share characteristic of becoming latent after primary infection
        - Virus may subsequently reactivate periodically
    - Site of latency is dorsal root ganglia for both HSV1 and HSV2
    - Reactivation may occur from stimulus like fever, stress, UV light, other

Pathophysiology

1. Pathology of localized dz
    - Characteristic lesion is vesicle on skin or ulcer on mucous membrane
    - Usually involves only epidermis in superficial infections
    - Invaded epithelial cells are destroyed by virus and inflammatory response of host
        - Sparing an intact superficial cornified layer that covers vesicle
        - This layer is absent in ulcer
    - Cells invaded by virus
        - Coalesce to form multinucleated giant cells
        - Undergo nuclear degeneration
        - Ballooning and intranuclear inclusions
2. Incidence/ prevalence
    - Lifetime risk of HSV1 very high
    - HSV2: 20-30% in age group of 15-29 yo
3. Risk factors
    - Local dz
        - Race
            - Not directly related to race
            - Varies w/race d/t difference in prevalence of poverty, access to health
            - Higher among African Americans than Caucasians
        - Sex: infection rates of males = females

        - Age
            - 20% of children by age of 5 are seropositive for HSV1
            - HSV2 more prevalent in adolescent population
        - Lifetime risk for genital herpes directly correlated w/number of sexual partners
        - Incubation period for primary infection is 2-20 days w/average of 6 days
4. Morbidity/ mortality
    - Localized infections have 0% mortality
    - HSV infection of eyes can cause blindness
    - Herpetic ulcers
        - Expose dermis
        - Which then becomes a more ready surface to transmit or accept other sexually transmitted disease (if exposed)
        - Or become secondarily infected by bacteria

Diagnostics

1. History
    - Symptoms
        - Onset:
            - Usually acute h/o previous herpes infection
        - Location:
            - Oral mucosa, skin, eyes, perioral region, vagina, penis, anus are the most common sites
        - Duration:
            - Varies from 5-7 days for mild infections to 10-14 days for more severe infections
        - Associated symptoms:
            - Fever, irritability, anorexia, sore mouth, regional lymphadenitis, local pain
        - Asymptomatic shedding from other infected people usual mode of transmission
            - Those w/genital infection particularly benefit from hearing this
    - Past hx
        - Hx of previous herpes infection
        - Hx immunocompromise
    - Social hx: sexual hx for genital herpes
2. Physical exam
    - Herpetic Gingivostomatitis
        - Most common clinical presentation of first episode
        - Abrupt onset
        - Fever, listlessness
        - Inability to eat or drink
        - Gingivitis, gums maybe swollen, red, bleed easily
        - Occasional episodes of drooling
        - Vesicular lesions on tongue, buccal mucosa, palate, lips, face
        - Anterior cervical lymphadenitis maybe present

- Acute Herpetic Pharyngotonsillitis
  - In adolescents
  - Complain of fever, malaise, odynophagia, HA
  - Lesions on tonsils: vesiculoulcerative
- Herpes Labialis
  - Usually a reactivation
  - Localized pain, tingling, burning or itching as a prodrome followed by a vesicular rash
- Primary genital infections
  - Prodromal symptoms for initial infections incl
    - Possible fever
    - Malaise
    - Myalgias
    - Occasional headache
  - Followed by papules, vesicles and then erosions over a matter of hrs to days
  - Intial infections are usually more dramatic and prolonged versus recurrent infections
  - Symptoms may also incl: painful inguinal nodes, dysuria, vaginal discharge
  - Occasionally paresthesias of legs and perineum
- Recurrent genital infections
  - Vulvar irritation, maculopapular or vesicular lesions around vulva or on shaft of penis in males
    - Pain, itching, dysuria
- Infections in immunocompromised host
  - May begin as mouth sores which worsen w/pain, fever, odynophagia, drooling
- Other infections
  - Acute onset edema, erythema, localized pain and tenderness in the finger suggesting herpetic paronychia
  - Numerous cutaneous vesicles in children involved in wrestling: Herpes gladiatorum
  - HSV keratoconjunctivitis
    - Acute pain
    - Watery discharge
    - Itching
    - Blurred vision
    - Lid swelling
    - Conjunctival injection
    - Dendritic lesions on flourescein stain
    - Needs ophthalmologist

3. Diagnostic tests
   - Laboratory
     - Viral culture: best dx method, time taking
     - Viral PCR: often preferred initial method d/t quick results
     - Serology showing rise in antibody titers

        - Histological evidence of multinucleated giant cells and intranuclear inclusion bodies
        - Tzanck smear: low sensitivity
    - Other studies
        - Blood cultures
        - Urine culture
        - Fluid from eyes, nose and mucous membranes should be obtained if involved

Differential Diagnosis

1. Acute Herpetic Gingivostomatitis
    - Herpangina: coxsackie or enteroviruses most likely
    - Streptococcal pharyngitis
    - Thrush
2. Acute Herpetic Vulvovaginitis
    - Ammoniacal dermatitis w/secondary infection
    - Gonorrheal and monilial vulvovaginitis
    - Impetigo
    - Foreign body
    - Trichomonas
    - Vaginal candidiasis
3. Eczema Herpeticum
    - Eczema w/secondary bacterial infection
    - Varicella
    - Eczema vaccinatum
4. HSV skin lesions can be confused with Varicella Zoster infection
5. Acute Herpetic Keratoconjunctivitis
    - Conjunctivitis
        - Haemophilus
        - Pneumococci
        - Staphylococci
        - Adenovirus
        - Picorna virus
        - Influenza virus

Therapeutics

1. Mainly supportive care for mucocutaneous oral lesions
    - Avoid dehydration
    - Encourage fluid intake
2. Acyclovir
    - IV: 10mg/kg iv q8 hrs for extensive oral lesions maybe considered
    - PO: 15mg/kg 5x per day can be used if tolerated for children between 1-6 yrs to shorten duration
3. Tx of genital dz depends on if it is initial, recurrent or suppressive in intent
    - See individual drugs for details

4. For initial genital herpes in adolescents
    - Acyclovir 200mg five x/day OR
    - Valacyclovir 1000mg BID for 5 days OR
    - Famciclovir 250mg q8 hrs for 5 days
        - Valaciclovir and famicyclovir not recommended in children
5. Topical trifluridine for herpetic keratoconjunctivitis w/ophthalmology referral
    - Infants less than 1 month should receive IV acyclovir and close follow up
6. Other tx options w/less proven benefit may incl
    - L-Lysine and aspirin orally
    - Licorice root (glycyrrhiza glabra), lemon balm, aloe or zinc applied topically
7. Pts may well respond to an initial dx of genital herpes w/anger, disbelief or depression
    - It is useful to have printed educational materials to aid this discussion
    - Schedule a follow-up exam for discussion in near future

Prevention/ Screening

1. Avoid contact w/oral secretions of infected individual
2. Avoid sexual contact w/partner w/active genital herpes
3. Routine serological screening for HSV in asymptomatic adolescents and adults is not recommended

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