

Neonatal Herpes Simplex Virus (HSV) Infection

Background

1. Definition
 - Systemic infection caused by Herpes Simplex Virus
2. General information
 - HSV is a member of herpesviridae family
 - Occurs as two antigenic types: HSV1 and 2
 - Majority of neonatal sepsis from HSV is from HSV2 (70-85%)
3. Epidemiology
 - 1 in 3,000-20,000 live births

Pathophysiology

1. Pathology of dz
 - Vertically transmitted
 - Delayed T lymphocyte response to viral antigen likely reason for systemic spread in infants w/initial localized dz
 - Incl in utero, intrapartum or postnatal transmission w/majority of these transmissions intrapartum
 - May be localized, disseminated, meningoencephalitis or combination clinical pictures
2. Incidence/ prevalence
 - Neonatal HSV estimated at 1 in 3200 live births
3. Risk factors
 - Primary infection of mother in 3rd trimester carries 30% risk of neonatal infection
 - Preterm infants maybe at higher risk for disseminated dz
4. Morbidity/ mortality
 - Disseminated HSV has a mortality rate as high as 85% in untreated cases
 - Even w/tx, there is a high incidence of residual defects like
 - Seizures
 - Psychomotor retardation
 - Spasticity
 - Learning disabilities in HSV encephalitis

Diagnostics

1. History
 - Onset:
 - Initial symptoms usually start w/in first week of life for most common form of neonatal herpes, perinatally acquired
 - Characteristics and severity
 - Starts w/fever
 - May have vesicular skin or mucosal lesions
 - Usually causes severe systemic involvement unless promptly treated
 - Associated symptoms
 - Fever or hypothermia
 - Poor feeding
 - Anorexia

- Vomiting
 - Lethargy
 - Respiratory distress/ pneumonitis
 - Cyanosis
 - Icterus
 - Hepatosplenomegaly
 - High index of suspicion needed in scenario where infant manifests some of these characteristics
 - Duration:
 - Depends on immune status, time of dx and prompt tx
2. Physical exam
- May incl one or all of these features:
 - Vesicular skin lesions
 - Injection of eyes w/watering
 - Vesicular lesions in oropharynx
 - Encephalitis
 - Fever
 - Behavior changes
 - Seizures
 - Hemiparesis
 - Intracranial bleeding
 - Disseminated dz
 - Irritability
 - Poor feeding
 - Respiratory distress
 - Jaundice
 - Disseminated vesicular rash
 - Cough
 - Dyspnea (pneumonia)
3. Diagnostic tests
- Laboratory
 - Viral culture
 - Best dx method
 - Delays need for more immediate answers
 - Viral PCR
 - Often preferred initial method d/t quick results
 - Preferred method of dx for CNS infections
 - Should be done w/CSF
 - Serology showing rise in antibody titers
 - Histological evidence of multinucleated giant cells and intranuclear inclusion bodies
 - Tzanck smear from vesicular lesions
 - Low sensitivity
 - Imaging studies
 - CT or MRI brain may demonstrate focal abnormalities in suspected CNS infection
 - Also helps to rule out other causes

- Other studies
 - EEG may help dx seizure activity in pts w/HSV encephalitis
 - Blood Cultures, urine culture, fluids from eyes, nose and mucous membranes should be obtained

Differential Diagnosis

1. HSV Encephalitis
 - Vascular dz
 - Brain abscess
 - Other forms of viral encephalitis
 - Cryptococcal infection
 - Tumors
 - Toxoplasmosis
 - Bacterial meningitis
 - CNS hemorrhage
2. Cutaneous HSV
 - Vesicular erythema toxicum
 - Pustular melanosis
 - Disseminated candidiasis
3. Disseminated HSV
 - Bacterial sepsis/ pneumonia
 - Inborn error of metabolism
 - Congenital heart dz
 - Hypoglycemia

Therapeutics

1. Acyclovir
 - The only FDA approved medication for HSV in children
 - 60 mg/kg/day div q8hr IV for neonatal infection in term infants, or
 - 30 mg/kg/day div q8hr IV for all ages
2. Duration of tx is 14 days for superficial infections and 21 days for disseminated and CNS dz
3. Consider pediatric infectious dz consultation

Prevention

1. Hx of HSV infection should be obtained from women during first prenatal visit
 - Routine screening for HSV in asymptomatic pregnant women is not recommended
2. Treat pregnant women who develop primary or secondary genital herpes w/acyclovir
3. Any known or suspected maternal herpes during labor warrants delivery by cesarean section
4. Consider prophylactic Acyclovir for high risk women

References

1. Annunziato PW. Herpes Simplex Viral Infections. Gershon: Krugman's Infectious Diseases of Children, 11th ed. Philadelphia: Mosby; 2004. 259-276.
2. Alter S. Herpes Simplex Viral Infection. Available from <http://www.emedicine.com/ped/topic995.htm>. Accessed 3.9.2008.

3. Knezevic A, Martic J, Stanojevic M, Jankovic S, Nedeljkovic J, Nikolic L, et al. Disseminated neonatal herpes caused by herpes simplex virus types 1 and 2. *Emerg Infect Dis* [serial on the Internet]. 2007 Feb. Available from <http://www.cdc.gov/EID/content/13/2/302.htm> Accessed 3.9.2008
4. O'Riordan DP, Golden WC, Aucott SW. Herpes Simplex Virus Infections in Preterm Infants. *Pediatrics* 2006;118:e1612-e1620. DOI:10.1542/peds.2005-1228.
5. Genital Herpes. *Clinical Evidence*. BMJ Publishing Group. Accessed November 11, 2007, at <http://gateway.uk.ovid.com/gw1/ovidweb.cgi>
6. Rudnick CM, Hoekzema GS. Neonatal Herpes Simplex Virus Infections. *Am Fam Physician* 2002;65:1138-42,1143. <http://www.aafp.org/afp/20020315/1138.pdf>
7. Hollier L, Wendel GD. Third trimester therapy for preventing recurrent genital herpes at delivery. (Protocol) *Cochrane Database of Systematic Reviews* 2004, Issue 4. Art. No.: CD004946. DOI:10.1002/14651858.CD004946
8. Walker KS, Jones CA, Badawi N. Antiviral agents for treatment of herpes simplex virus infection in neonates. (Protocol) *Cochrane Database of Systematic Reviews* 2003, Issue 2. Art. No.: CD004206. DOI: 10.1002/14651858.CD004206.
9. Fatahzadeh M. Human herpes simplex virus infections: epidemiology, pathogenesis, symptomatology, diagnosis, and management - *J Am Acad Dermatol* - 01-NOV-2007; 57(5): 737-63; quiz 764-6

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