Short Review

Update on diagnosis of congenital infection

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ABSTRACT

Congenial infection is one of the greatest diagnostic challenges facing clinicians. The list pathogens related to intrauterine infections continues to grow with the identification of new etiologies and resurgence of others. Identification of a congenital infection as early as possible has both diagnostic and therapeutic advantages. This article will give an overview on common clinical findings in infants with congenital infection and a recommended clinical investigational approach for suspected congenital infection.

Keywords: Congenital infection, approach for diagnosis.

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The infant who is born with an infection acquired transplacentally during the first, second or early third trimester may have what is termed "congenital infection". Infection acquired in utero may result in abortion, still birth, developmental anomalies, intrauterine growth retardation (IUGR), clinical or asymptomatic infection with the risk of subsequent sequela of chronic postnatal infection.[1] The acronym TORCH [Toxoplasmosis, other agents, Rubella, Cytomegalovirus (CMV) and Herpes simplex virus (HSV)] was modified to STORCH to include syphilis, have been used for the last 2 decades to increase awareness for the common etiological agent in congenital infection.[2,3] The O in TORCH/ STORCH (other agents) include a list of pathogens that grows longer over time including not only varicella, Human immunodeficiency virus (HIV), hepatitis (B, C, E) parvovirus B_{19} and enterovirus but also newer pathogens (ie. Q fever, lymphocytic choriomeningitis virus), resurgence pathogens (ie tuberculosis, malaria) and rare pathogens (ie brucellosis).[4,5] Prenatal diagnosis is available for several organisms (Table 1), but only a few hospitals have the facility for this purpose.[6,7] The incidence of congenital infection in the fetus is high (0.5 - 2.5 percent) and a significant number of congenital infection in the infant relies on high index of suspicion, plus a combination of clinical evaluation and judicious microbiological evaluation. The maternal history including immunity, illness, exposure and travel during pregnancy may provide important information about congenital infection (Table 2).[1,6] Certain specific neonatal manifestation may provide helpful clues to strongly suspect specific etiologic agent in clinical grounds alone (Table 3).

The laboratory diagnostic approach to congenital infection has been tempered by the TORCH/ STORCH designation. TORCH titres have been frequently ordered by many clinicians to diagnose congenital infection. In most cases however, the test is used inappropriately and is non-diagnostic. It must be remembered that a single titer (serum) cannot be used to confirm the presence of one or a whole series of agent which can cause congenital infection. The STORCH battery of serologic tests has a poor diagnostic yield. Every effort should be made to isolate the organism from the neonate and to follow maternal and infant blood samples for several

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Table 1 - Pre-natal diagnosis of fetal infections.*

Organisms
Toxoplasma gondii
Rubella virus
Cytomegalovirus
Varicella-zoster virus
Parvovirus B_{19}
*Culture or polymerase chain reaction testing.

months. Negative maternal and neonatal serology generally excludes the possibility of fetal infection except in very recent and HIV infection.[4] Detection of specific Immunoglobulin G (IgG) antibody for etiologic agent in the newborn is not helpful because of passively transmitted antibodies from the mother. Serial titres taken postnatally that show a rise in titre at age 2 to 4 months or persistent titres at age 6 to 8 months, usually establish the diagnosis.

Exceptions are CMV antibody, which may also be peri - or postnatally acquired and HIV.[8,9] The demonstration of specific Immunoglobulin M (IgM) antibody in mother and neonate is unreliable except for rubella specific IgM and toxoplasmosis specific IgM. Total cord IgM level has been used as a screening test for congenital infections but lacks both sensitivity and specificity and its use is not recommended.[4,9] Recommended clinical, nonspecific and specific microbiological tests are described in Table 4 and 5.

In conclusion, diagnosis of congenital infection is one of the greatest challenges facing clinicians. Appropriate index of suspicion, oriented clinical evaluation and careful microbiological evaluation are the current best tools to identify infants with congenital infections early in life. Specific treatment for toxoplasmosis, syphilis, herpes simplex and HIV is predicted on accurate diagnosis and may reduce long term morbidity. The value and cost-effectiveness of prevention has been demonstrated in recent years through the use of rubella immunization, hepatitis B immunoprophylaxis and vaccine, zidovudine (AZT) treatment of HIV infected mothers, and diagnosis and treatment of maternal toxoplasmosis and syphilis. A suggested program for screening and preventive education for woman in pregnancy is described in Table 6.

Table 2 - Maternal history.

Illness	Infection
Mononucleosis like syndrome Lymphoadenopathy	CMV, Toxoplasmosis, HIV
Rash	Rubella, parvovirus B_{19} enterovirus, syphilis
Arthritis	Rubella, parvovirus B_{19}
Exposure/travel	
Contact with diapered children in day care household or school	CMV, parvovirus B_{19}
Handling or ingestion of raw meat that has never been frozen or kitten or cat feces in 21 days after animal's primary infection.	Toxoplasmosis
Exposure to person with tuberculosis or varicella	Tuberculosis - varicella
Malaria geographic region	Malaria
Immunity	Rubella, HBV

Table 3 - Common clinical findings in infants with congenital infections and their prevalence in certain infections.

Common clinical findings	Rubella	Toxoplasma Godii	CMV	Syphilis	HSV
Reticuloenothelial system					
Jaundice	+	++	+++	+++	-
Hepatitis	±	+	+++	+++	+
Hepatosplenomegally	+++	++	+++	+++	+
Anemia	+	+++	++	++++	-
Thrombocytopenia	++	±	+++	++	-
Disseminated intravascular coagulation	-	-	+++	++	-
Adenopathy	++	++	-	-	-
Dermal erythropoiesis	+	-	+	-	-
Skin rash	-	+	-	++	+++
Bone abnormalities	++	-	±	+++	-
Eye					
Cataracts	++	±	-	-	-
Retinopathy	++	+++	+	±	+++
Microphthalmia	+	±	-	-	+
Central Nervous System					
Microcephaly	+	+	++	-	++
Meningoencephalitis	++	±	+++	++	++
Brain calcification	+	+++	++	-	+
Hydrocephalus	-	++	±	±	+
Hearing defect	++	+	++	+	-
Pneumonitis	++	+	±	+	-
Cardivascular Myococaditis/CongenitalHeart disease	+	-	±	±	-

-None, +Rare, ++Less Common, +++Common, ++++Frequent

Table 4 - Clinical evaluation and non-specific investigations for suspected congenital infection.

Clinical evaluation of infant

Height, weight, head circumference
Skin rash
Opthalmological examination (pediatric opthalmologic preferred)
Cardiovascular examination
Liver/spleen sizes

Non-specific tests

Complete blood count with differential leukocytes and platelet count.
Liver function tests
Cerebrospinal fluid (CSF) examination (cells diff, protein, glucose culture/serology (see specific test).
Total serum immunoglobulin M
Maternal and infant serology for microbiology testing (see specific test).
Hold on blood sample for possible additional tests.
Roentgenogram of long bones (if rubella, syphilis likely)
Computed tomography scan of head with and without enhancement.
Placenta histopathology examination.

Table 5 - Specific tests for suspected congenital infection.

Tests	Interpretation
Viral culture	
-Throat, nasopharyngeal (NP), urine	- If positive, test is diagnostic for CMV (first 2-3 weeks of age). Rubella, HSV, enterovirus
-Blood	- If positive, test is diagnostic for CMV, HIV
-CSF	- If positive, test is diagnostic for HSV, CMV, enterovirus
Skin lesion/NP secretion (culture, dark-film of treponema pallidum)	- If positive, test is diagnostic for syphilis
Serology (etiologic agent of concern)	
A. Blood (IgG) (Mother and Infant)	- Negative maternal serology excludes infection. Serial infant serology identifies maternal antibody (falling titres), and active infection (titres higher in newborn or remain the same or rising during infancy).
IGm (Toxoplasma, Rubella)	- If positive, test is diagnostic of that infection
B. CSF Rubella specific IgM antibody VDRL	 - If positive, test is diagnostic for rubella - If positive, test is diagnostic for syphilis
Polymerse chain reaction (Blood) CMV HIV, Toxoplasma, Parvovirus B_{19}, HSV Trepenoma pallidum, enterovirus	- If positive, test is diagnostic for that infection
VDRL: Venereal Disease Research Laboratory Test	

Table 6 - Screening tests and prevention advice for pregnant woman.

Screening Tests

Hepatitis B and C infection
Rubella
Syphilis
HIV (with consent)
Brucella (if raw milk ingestion)

Prevention to reduce risk for infection

Toxoplasma Wash hands thoroughly after handling raw meat
Cook meat to 66°C or greater (previously frozen meat is safe)
Wash fruits and vegetables before consumption
Avoid contact with cat excrement

CMV No effective method of preventing uncommon complications of infection during pregnancy with CMV. For women handling respiratory secretions or diapers for young children she should wash hands after handling and may wish to be tested for CMV immunity

Burcellosis No raw milk ingestion

If exposed to tuberculosis, varicella, erythema infection (human parovirus B19) and mosquito bite (malaria region), inform physician promptly.

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