Targeted Screening for Congenital CMV

A guideline from the Colorado Chapter; American Academy of Pediattrics

Background

Congenital cytomegalovirus infection (cCMV) affects 0.5-0.7% of all newborns, and is the most common non-genetic cause of congenital hearing loss. Approximately 20% of congenital hearing loss is attributable to cCMV, and 20-25% of those born with cCMV will have hearing loss or developmental problems.

cCMV can be symptomatic or asymptomatic. Infants with symptomatic cCMV are defined as those with organ involvement other than hearing loss at birth, such as central nervous system damage, hepatitis, retinitis, bone marrow dysfunction, or rash. About 10% of all newborns with cCMV are symptomatic. Some newborns may appear asymptomatic, but will then be recognized as symptomatic after additional testing.

Risk factors for cCMV include:

1. Mother diagnosed with CMV infection during pregnancy
2. Small for gestational age: birth weight less than the 10th percentile
3. Microcephaly: head circumference less than the 10th percentile
4. Low birth weight or preterm: birth weight <2000 grams
5. Did not pass the newborn hearing screen (one or both ears)
6. Fetal hydrops or ascites, abdominal calcifications, or thickened bowel on prenatal ultrasound
7. Hepatomegaly, splenomegaly or elevated liver function tests (AST or ALT >100 U/L or direct bilirubin >1.0 mg/dL)
8. Abnormal brain imaging
9. Persistent thrombocytopenia (platelets <100,000/mm^3)
10. Petechial or “blueberry muffin” rash
11. Retinitis or other eye finding

The diagnosis of cCMV is frequently missed.

Reasons include a lack of awareness of risk factors and missed opportunities for timely testing. Postnatal CMV infection can occur as early as 3 weeks of life, so testing to identify congenital CMV infection must be done before day of life 21. Postnatal infection rarely causes problems except in those who are immunocompromised (including preterm infants).

Saliva PCR (DNA testing) is a sensitive, convenient, and cost-effective test for cCMV. Other commonly used tests include urine PCR and culture of saliva, urine, blood, or spinal fluid. Of note, a saliva PCR may reflect CMV in breast milk, so the saliva should be collected at least 2 hours after ingestion of breast milk. When saliva PCR is positive, urine PCR should be performed as a confirmatory test.

Early screening promotes timely testing and diagnosis of cCMV. Universal screening for cCMV, such as with a dried blood spot, is not technologically feasible or cost-effective at this point in time. Targeted screening of infants with risk factors, including all those with suspected congenital hearing loss, has been shown to improve the rate of detection of cCMV. Even though some infected children will be missed with targeted screening, many will be identified who would otherwise have gone undiagnosed.

Making the diagnosis of cCMV can change clinical care in these ways:

1. A pediatric infectious disease specialist can explain treatment options. In infants with symptomatic cCMV, valganciclovir improves hearing and speech development. Randomized trials of valganciclovir in infants with cCMV and hearing loss alone are underway.
2. Additional testing might show abnormal CNS imaging, bone marrow dysfunction or hepatitis.
3. A pediatric ophthalmologist can look for retinitis and plan for ongoing monitoring.
4. Repeated hearing testing can be scheduled, because hearing loss due to cCMV can be fluctuating or progressive.
5. Frequent monitoring for developmental delay can be provided, and referral to Early Intervention can be made.
6. The family can learn whether cCMV is the most likely cause of their child's hearing loss or other health complications, which may reduce the need for genetic testing and/or additional imaging.
7. The family can learn about the risk that hearing loss will progress and anticipate the possible need for hearing devices (e.g. hearing aids or cochlear implants) or language development support.
8. Contact with cCMV parent support groups can be provided to the family.

Action Plan: Improving detection of cCMV in hospital systems

These steps will help assure targeted screening for cCMV in every infant with risk factors, including all those who do not pass the newborn hearing screen:

1. Establish a work group on targeted screening for cCMV

A work group should engage all those parties needed for successful implementation of a system for detection of cCMV. This might include pediatric hospitalists, neonatologists, ENT physicians, pediatric infectious disease specialists, nurses and nurse educators in the newborn nursery and NICU, local primary care pediatricians, staff of the newborn hearing screening program, pediatric audiologists, and parent support groups for families of children with congenital hearing loss or cCMV. This hospital-specific work group should agree on a plan for targeted screening for cCMV. Responsibility for receiving and acting on all positive results for cCMV testing will need to be clearly defined; this might involve the lab calling every positive result to the hospitalist group, the NICU attending, a patient navigator, or other designated clinician.

Here is a simple flow diagram for targeted screening: Link.

2. Create a standing order to be added to the existing order set for newborns

Such a standing order might say:
If a newborn infant has any risk factors for cCMV, or has not passed the newborn hearing screen before discharge from the hospital, or not passed before 3 weeks of age:
1. Send saliva or urine PCR for CMV.
- Saliva should be collected with a sterile swab applicator tip flocked with nylon fiber at least 2 hours after ingestion of breast milk. Place in a vial of M6 viral transport media.
- Urine can be collected by bag, then transferred to a sterile leak-proof cup for transport.
- If hearing loss is suspected, send the samples with the diagnosis code H91.90- Unspecified hearing loss, unspecified ear.
- For other risk factors, use the relevant code.
2. Give parents the handout "Why is my baby being tested for CMV?" (English link, Spanish link). Explain that a test for CMV has been sent and the result is pending.
3. If hearing loss is suspected, tell the parents how to schedule an appointment with the pediatric audiologist.
4. Notify the infant's primary care provider about the pending test for CMV, and the reason for the testing.

3. Create a message to be added to the discharge summary

Such a message might say:
Problem: Screening for congenital CMV infection. This infant has been identified as having risk factors for congenital CMV infection, including _____.
A test for congenital CMV infection by saliva or urine PCR has been sent; the result is pending. If the test for CMV is positive, consult a pediatric infectious disease consultant. If only a saliva test for CMV was positive, send urine for CMV PCR as a confirmatory test. It is important that this test be done before 3 weeks of age.

4. Create a standing order for the place where outpatient hearing testing is done

Such a standing order might say:
If an infant fails the outpatient hearing test and has not yet been tested for CMV:
1. Send saliva or urine PCR for CMV. Saliva should be collected with a sterile swab applicator tip flocked with nylon fiber at least 2 hours after ingestion of breast milk. Place in a vial of M6 viral transport media. Urine can be collected by bag, then transferred to a sterile leak-proof cup for transport. Use the diagnosis code H91.90- Unspecified hearing loss, unspecified ear.
2. Give parents the handout "Why is my baby being tested for CMV?" (English link, Spanish link). Explain that a test for CMV has been sent and the result is pending.
3. Notify the infant's primary care provider about the failed hearing screen and the pending test for CMV.

5. Inform community pediatricians about the program

For more information, go to the cCMV resources section on the AAP-CO website, aapcolorado.org.