Title of case: “15 day old female with fever and nasal congestion”

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Date case created: 03/19/2022

Learning Objectives:

1. Apply the 2021 AAP Febrile Infant Guidelines for 8-21 day olds
2. Discuss the importance of laboratory tests for risk stratification
3. Choose appropriate testing/management based on infant’s risk of HSV infection

HPI: The patient is a 15 day old female who presented to the ED with acute onset of tactile fever that began this morning. She also has had nasal congestion and increased fussiness for 3 days. Her mom has tried nasal saline and bulb suctioning, but it does not seem to be helping and she noticed some dried blood in the patient’s nostril yesterday. Sick contacts include a 4 year old sister at home with nasal congestion. The patient has been breastfeeding approximately 15 minutes on each breast every 2-3 hours and has had an adequate amount of wet diapers.

Pertinent ROS: +tactile fever, +nasal congestion, +increased fussiness, -decreased appetite, -vomiting, -cough, -rash, -hematochezia, -eye redness/drainage, -lethargy, -seizures

Birth hx: 38 +5 GA via elective cesarean section due to repeat c/s. No complications. No NICU stay. Mom received prenatal care. Maternal Hx unremarkable, including GBS negative.

PMH: None

PSH: None

Meds: None currently (received Vitamin K and Erythromycin ointment after delivery)

All: NKDA

Imm: Up to date. Hepatitis B dose 1 received.

Dev: Appropriate for age. No concerns.

Social hx: Lives at home with mother, father and 4 y/o sister. 1 adult dog at home. No smoking in the household.

Family hx: PGF with HTN and CHF. Maternal aunt with hypothyroidism. Mother and sister healthy.

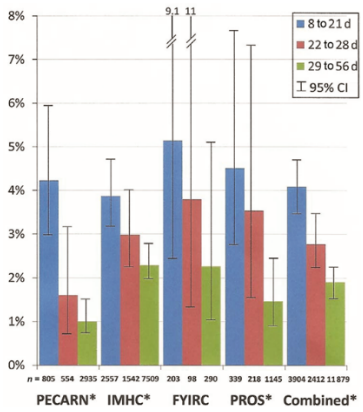
Vitals: temp 39.3^{o}C (rectal), HR 197 bpm, BP 90/61 mmHg, RR 42 rpm, Saturation 100% on RA, length 50cm (23.4%), weight 3.22kg (17.8%), weight-for-length 35.96%

PE (after antipyretics):

General: Appears well, alert, non-toxic and in NAD
Head: Normocephalic, without obvious abnormality, AFOF
Eyes: Normal inspection, PERRL, red reflex X2, no injected conjunctivae bilaterally
ENT: Normal TMs bilateral, normal pharynx, uvula midline, MMM, no thrush
Neck: Supple, no tracheal deviation, FROM, no clavicular crepitus noted
Heart: Regular rhythm and rate, no murmur, 2+ pulses throughout
Lung: No respiratory distress and lungs clear to auscultation, no wheezes/crackles/flaring/retractions
Abdomen: Soft, non-tender, no masses, normal bowel sounds, no apparent abdominal pain on palpation, no abdominal distention
Back: Normal inspection, Full range of motion
GU: Normal external female genitalia
Extremity: Normal inspection, normal ROM, no edema, moves all extremities freely
Skin: Skin color, texture, turgor normal. No rashes or lesions throughout body, capillary refill <2 seconds, no rash/blisters in palms/soles bilaterally, no petechiae/purpura
Neuro: No gross deficits and interacting appropriately for age, normal tone, suck, grasp; Normal Moro reflex symmetrical and bilateral

1) Which initial labs are absolutely indicated for this infant?
    a. Urinalysis (and urine cx), CBC, CRP
    b. Urinalysis, blood culture, CSF studies and CSF culture ←
    c. Urine culture, CBC, blood culture, CSF studies and CSF culture
    d. Urinalysis, blood culture, CSF studies and CSF culture , CRP

B is the correct answer. In the age group of 8-21 days, a urinalysis, blood culture, and lumbar puncture for CSF studies and culture (full sepsis workup) are always indicated as the initial workup. This is due to the higher prevalence of bacteremia in this age group, as indicated in the graph below, as well as a higher incidence of meningitis.



Continuing through the answer choices, a urine culture is not yet indicated. If the urinalysis shows evidence of infection, then a urine culture should be sent. In terms of the blood, a blood culture is important and should be sent regardless of what the basic blood tests show. A LP to obtain CSF studies, including a CSF culture, is indicated in this age group to rule out bacterial meningitis. Finally, a CRP or other inflammatory markers (IMs) are <u>not</u> absolutely necessary since it would not change the management in this age group. Some providers, however, may choose to send IMs as they may potentially guide ongoing clinical decisions.
Learning Goal: Learning objective #1, KAS 1, KAS 2, and KAS 4 addressed.

2) You decide to send inflammatory markers (IM) to help guide your clinical decision making. Which of the following is the most sensitive IM for an invasive bacterial infection?
    a. ESR
    b. Procalcitonin ←
    c. CRP
    d. ANC

B is the correct answer. Historically, C-reactive protein (C) had been used in the past as the IM of choice for prediction of bacterial infection, however <u>procalcitonin (B) has emerged more recently as the most sensitive IM for risk stratification.</u> It is expressed mainly by thyroid C cells and is produced rapidly in response to infection and other tissue injuries. It is more specific for bacterial infections than other IMs and rises more quickly to abnormal values.

As for ESR (A), it is an indirect measure of fibrinogen, a protein that is often elevated with inflammation, and fibrinogen has a much longer half-life than other IMs. This makes ESR helpful in monitoring chronic inflammatory conditions, but not as helpful for acute inflammatory conditions, such as acute infection.

Finally, markers such as WBC, ANC (D), or band count have become less useful due to *E. coli* replacing GBS as the most common bacterial pathogen in this age group.]
Learning Goal: Learning objective #2 and KAS 3 addressed.

3) The patient is started on antimicrobials and admitted to the hospital. Which of the following is a risk factor for HSV and would indicate further HSV testing and/or the addition of an antiviral to the empiric treatment regimen?
    a. Maternal hx of genital HSV lesions which resolved 1 week prior to delivery

b. Infant with fever
c. Decreased urinary output
d. Infant with thrombocytopenia ←

D is the correct answer. HSV should be considered when there is a maternal history of genital HSV lesions or fevers from 48 hours before to 48 hours after delivery (A) and in infants with vesicles, seizures, hypothermia (B), mucous membrane ulcers, CSF pleocytosis in the absence of a positive Gram stain result, leukopenia, thrombocytopenia (D), or elevated alanine aminotransferase levels. An infant's urinary output (C) is unrelated to the risk of HSV infection.
Learning Goal: Learning objective #3, KAS 4 and KAS 5 addressed.

Case resolution:

The patient's lab workup consisted of a normal WBC, Hgb, HCT, and platelet count on CBC. She had slight bandemia at 6% and an elevated CRP of 3.69 mg/dL. Her procalcitonin and UA were unremarkable. CSF studies consisted of a WBC count of 1 cell/mm3, RBC count of 234 cells/mm3, glucose normal at 48 mg/dL, and protein slightly elevated at 47 mg/dL. Her CSF meningitis/encephalitis panel resulted positive for enterovirus, in addition to her Respiratory Pathogen Panel (RPP) resulting positive for rhinovirus/enterovirus. She was admitted to the hospital on IV ampicillin and gentamicin. The patient did not have any of the risk factors for HSV and thus was not placed on empiric IV acyclovir. She remained stable and afebrile throughout the admission and was discharged home after 24 hours of her blood, urine, and CSF cultures remaining negative.

Citations:

Litao, M. K. S., Search for more papers by this author, Kamat, D., & Al., E. (2014, September 24). *Erythrocyte sedimentation rate and C-reactive protein: How best to use them in clinical practice*. Pediatric Annals. Retrieved March 20, 2022, from https://journals.healio.com/doi/abs/10.3928/00904481-20140924-10

Pantell, Robert H., et al. "Clinical Practice Guideline: Evaluation and Management of Well-Appearing Febrile Infants 8 to 60 Days Old." *American Academy of Pediatrics*, Oxford University Press, 1 Aug. 2021, https://publications.aap.org/pediatrics/article/148/2/e2021052228/179783/Clinical-Practice-Guideline-Evaluation-and.