A rash with a twist

Mfed Mosely.,MD.,FAAP.,FRCP(C)
Consultant Neonatologist & Pediatrician
Medeor 24*7 International Hospital
Al-Ain UAE

Presentation

A 3-week-old, 3650grams neonate was admitted from the ER with parental report of 24 hours of fever, lethargy, and witnessed seizure activity.

Presentation

Female 3450grams, AGA, 40 wks,NSVD,
APGAR (9,9 at 1&5m),

Mom:

Healthy 24 years old G2P1
+Prenatal care
Negative serologic,GBS, and Hep B
Rubella immune
Group A positive .
No consanguinity.

Maternal TORCH,:

- Treponema pallidum Ab negative;
- CMV IgG positive & IgM negative;
- Parvovirus IgG positive & IgM negative
- Toxoplasmosis IgG positive & IgM negative
- HSV-1 IgG negative & IgM negative
- HSV-2 IgG negative & IgM negative

Maternal Hx C/u

➢There was no maternal history of vulvovaginal candidiasis.
➢She was regularly in the presence of her sister's cat, but never touched the cat
➢She had a prior history of chickenpox, but not during the pregnancy.

Infant hx

Breast feeding well,

2 days prior to presentation noted to be

- Febrile with temperatures up 37.9ºC.

The following day

i. Lethargic
ii. Experienced a 1-minute episode of right upper extremity shaking.

Still not sure NICU

History was negative:

1-Respiratory infection,

2-Emesis

3-Changes in voiding and stooling patterns.

However

1- 1 week earlier sibling was reportedly ill with a rhinovirus infection

2- 2 weeks earlier a cousin who was visitin had fever up to 40 degrees associated with refusal of drinking and a pustular rash on his buttocks as well as his fingers resembling the rash that showed up on the baby near the umbilical area which lasted for 3 days during that time mom had wiped it up with alcohol swabs causing it to clear up and leave a current marks.

Progression NICU

Her examination:

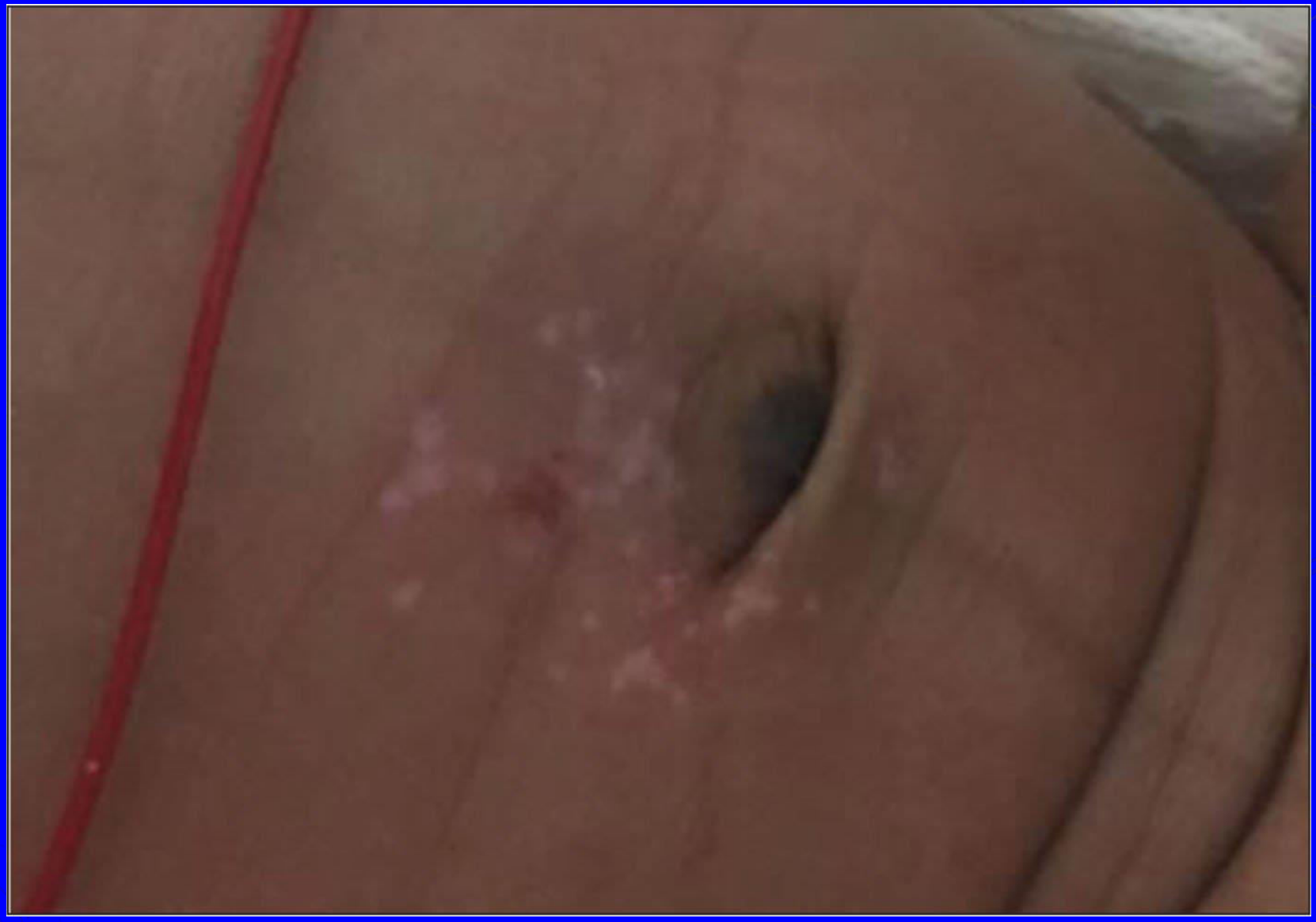
+++ Fever of 38.6 C & lethargy+++

+

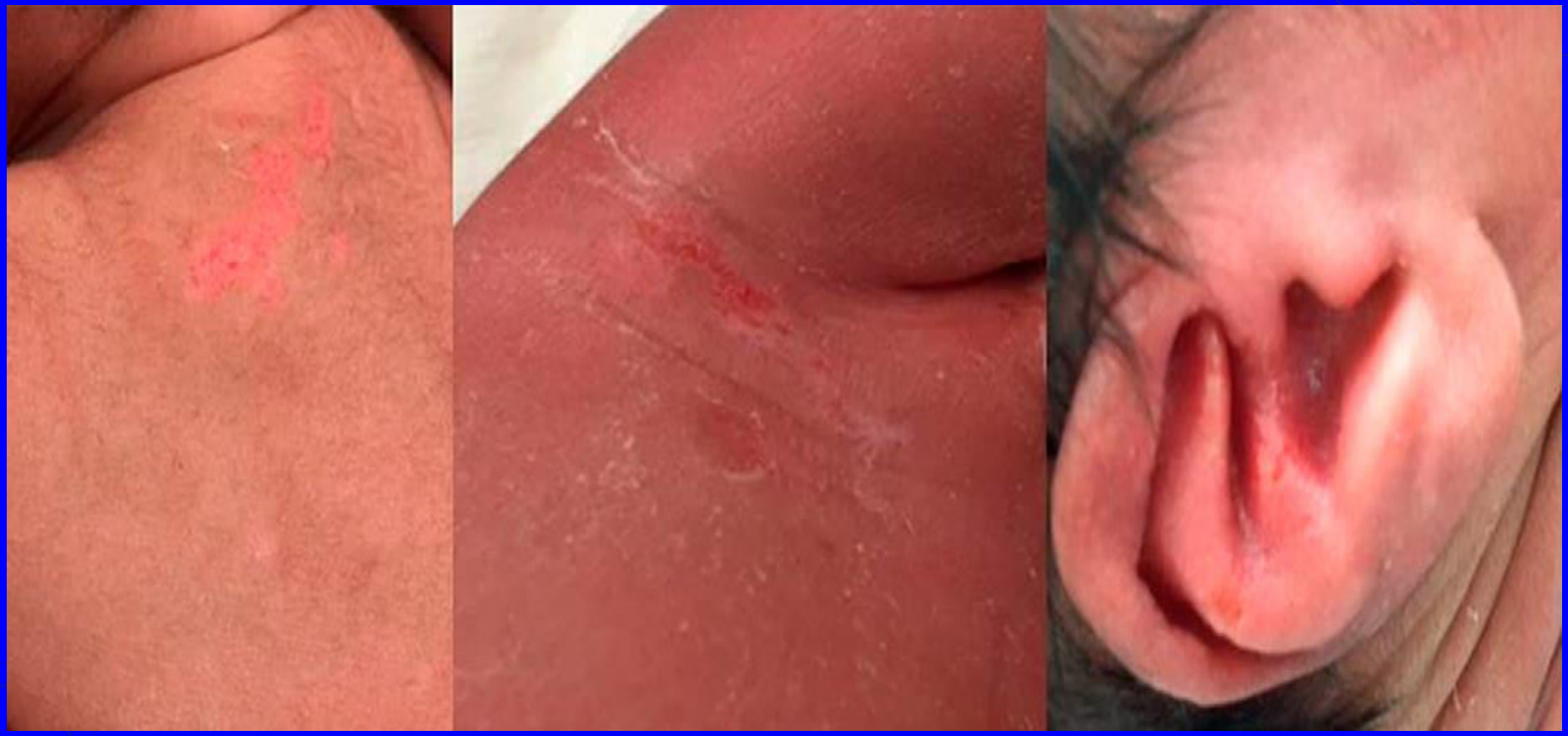
1-A fading rash around the umbilicus area that was in the process of healing was not blistering or purulent and the area was minimally red but slightly thickened and the cord had already fallen off, no oozing was noted and no discharge.

2- Multiple, diffusely scattered, maculopapular crusted lesions in various stages of healing, vesicular lesions, an area of active liquefaction over the right hip (without evidence of crusting), and an area of desquamation of skin on the digits (fingers > toes)

Hypopigmented periumbilical macules noted at time of presentation.



Skin lesions in various stages.



NICU course

Initial NICU:
Brief episode of seizure-like activity consisting of right upper extremity shaking that was self-limited.

Neonatal sepsis testing was initiated:
CBC: (WBC) of 18.7 k (differential unavailable).
CRP 0.5 mg/dL (4.76 nmol/L)

(CSF)

WBC 33 cells: 18% neutrophils, 76% lymphocytes, and 6% monocytes.
RBC 48 cells
Glucose 47 mg/dL , protein of 141 mg/dL.
Blood, urine, and CSF cultures were collected,
Ampicilin & Gentamicin started

NICU Course

8 hours of NICU still febrile up to 38.8 ºC

Intermittently apneic with desaturations to 88%.

Lethargic, anterior fontanelle full but not tense,+exaggerated Moro.

.

Labs NICU

A serum HSV DNA PCR, surface HSV DNA PCRs (conjunctivae, oropharynx, and rectum).

Empiric intravenous acyclovir was added.

Seizure activity so EEG showed evidence of spikes in the left temporal and occipital lobes without epileptiform discharges.

High flow nasal cannula was required due to mild hypoxia and brief periods of apnea (possible pneumonitis).

CT & MRI

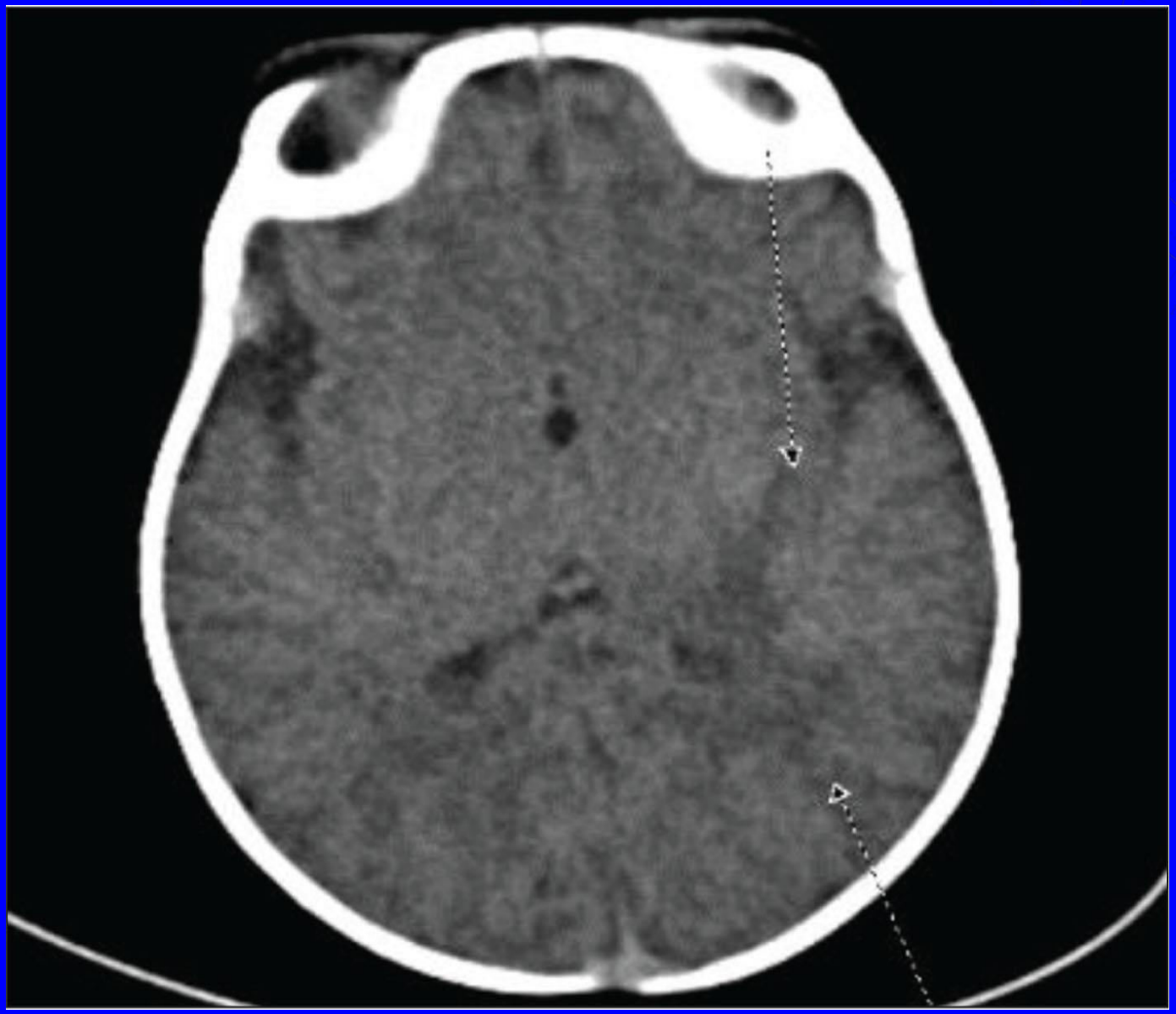
(CT) without contrast

Hypoattenuation within the left temporal and occipital lobes.

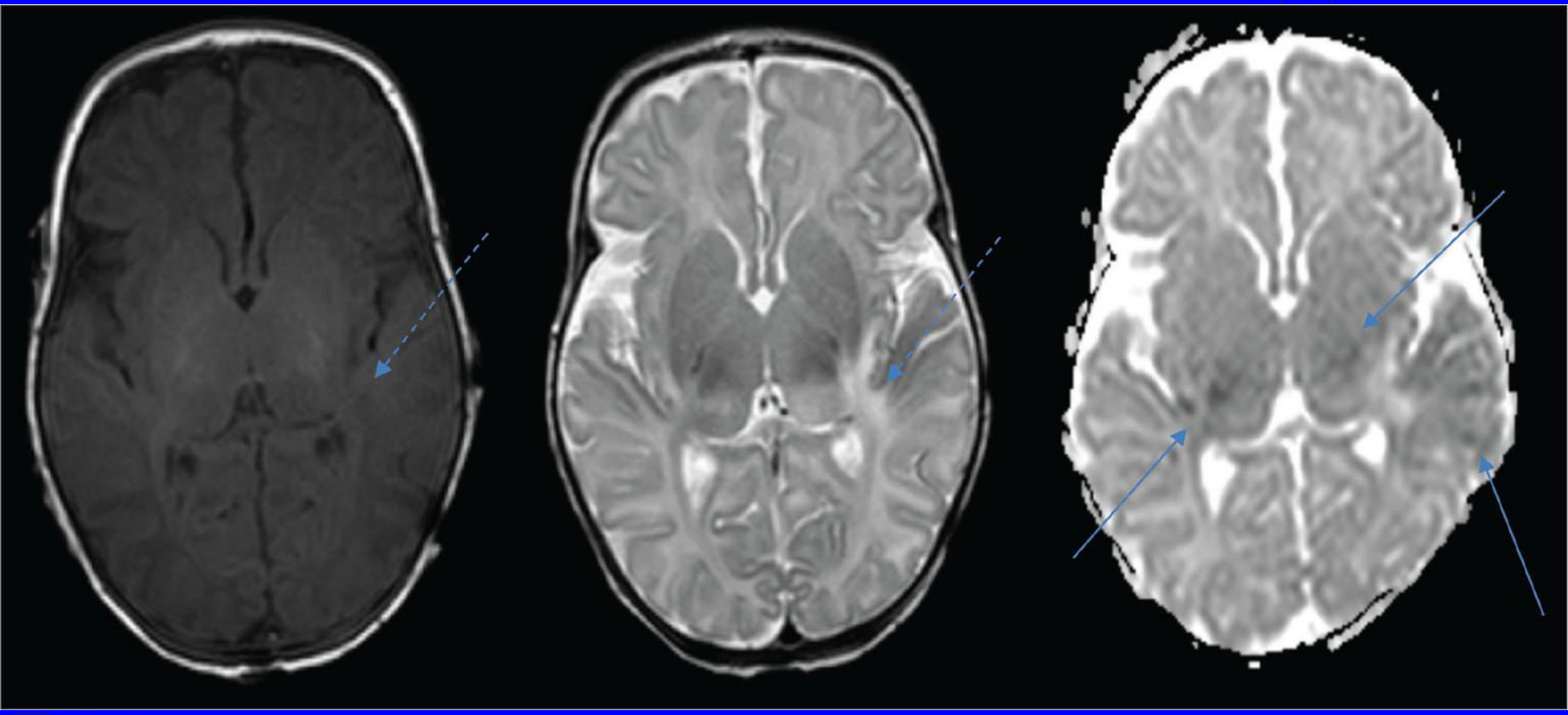
(MRI)

Diffusion restriction + edema affecting the left temporal, parietal,occipital lobes, the thalamus and insula, suggestive of encephalitis.

Computed tomography of the head, demonstrating hypoattenuation in the left temporal and occipital lobes (arrows).



A magnetic resonance image of the brain showing (from left-to-right) T1-weighted, T2-weighted, and reverse-diffusion weighted images consistent with viral encephalitis. Restricted diffusion (solid arrows) as well as edema (dashed arrows) are seen in the left temporal lobe, parietal lobe, occipital lobe, thalamus, and insula.



NICU

48 hours NICU
O2 discontinued, (remained febrile with T 38.6).

HSV DNA PCR of MM & CSF (initial CSF 48h) negative

Acyclovir C/u Why:
her history, clinical presentation, and radiologic findings.

DIFFERENTIAL DIAGNOSIS

Neonatal Bacterial sepsis
Enteroviral sepsis
Congenital icthyosis syndromes
Cutaneous candidiasis
Epidermolysis bullosa
Herpes simplex virus infection
Incontinentia pigmenti
Varicella zoster

Not negative until I say so

Day 9 PCR was positive for HSV-2:Dx confirmed

Clinically: fever and lethargy improved SO complete the remainder of the 21days course.
Six months of suppressive oral acyclovir was recommended with close observation

Discussion

A Serious Infection

✓HSV types 1 and 2 are enveloped DNA viruses:
✓("fever blisters" & meningoencephalitis)

✓Latency after primary infection : recurrent disease and/or asymptomatic shedding.[1]

✓Early recognition & Rx:

1. Better outcome
2. Prevent progression to disseminated disease, (Mortality54%)
3. Antiviral : disseminated disease from 50% to 23%

Dx & Rx:

✓The recognition of specific clinical manifestations,
✓The use of correct lab
✓The prompt Rx pending lab results

Discussion

Incidence of Neonatal HSV

1 in 3,000 to 1 in 20,000 live births
1,500 United States.

Transmission

Mainly perinatal route:	85%.[1]
Postnatally direct contact	10%
Intrauterine transmission:	>5% (rare)[1]

Risk of transmission.[1]

Mothers (primary HSV)	25% to 60%
Mothers (recurrent infection)	<2%.[5]

>75%

Infants are born to mothers asymptomatic or unaware having HSV

Discussion

Neonatal HSV disease can manifest in several ways:

(1) Skin, Eye, Mouth (SEM) 1st & 2nd week **(45%)**
(2) Central nervous system (CNS) : 2nd& 3rd week **(3%)**
(3) disseminated disease; 1st & 2nd week **(25%)**

2/3 dissemi/CNS= skin lesions, = diagnosis extremely challenging.1

Most neonatal HSV shows = 6 weeks but all first month.

Seizures, focal neurologic deficits, and CSF abnormalities: **CNS**
(important in late autumn and winter when enteroviruses)

Vesicular rash areas of trauma (fetal scalp electrode) **SEM regardless how well**

Fever, hepatitis, respiratory distress, and coagulopathy, especially in the absence of a bacteriologic diagnosis.1 : **Disseminated HSV**

Considerations in Diagnosis

Lab

Viral culture, gold standard
Direct Immunofluorescent Assay (DFA). (out of favor.)
Less sensitive than culture,
No advantage over the PCR assay

HSV DNA PCR assay increased use

Serologic : maternal antibodies = confound factor

Guidelines for labs testing

Current guidelines :

(1) surface swabs of mouth, nasopharynx, conjunctivae, and anus for HSV culture plus an optional PCR assay;

(2) skin specimens of vesicles for HSV culture plus an optional PCR assay;

(3) CSF sample for PCR assay;

(4) whole blood sample for PCR assay.1
12 to 24 hours (risk for contamination)

Viral culture remains the preferred method for surface
PCR surface assay remains a widely (paucity of data).

PCR assay on CSF is a sensitive (75%-100%) and specific (71%-100%) preferred test for CSF

The HSV DNA CSF PCR as early as 1 day
A negative (when performed early during illness) does not rule out

So

Retesting when high clinical suspicion

Similarly,

PCR assay of whole blood or plasma is critical Dx;
Plasma HSV PCR was positive
78% (SEM),
64% CNS,
100% disseminated disease.
oftentimes be the only positive test.
The blood HSV PCR assay was the
First positive test in 19% (n = 4/21)
Only positive test in 10% (n = 2/21).

The importance of thorough specimen collection
despite the high sensitivity and specificity of PCR assays.

Treatment and Sequelae

1- Nature of neonatal HSV : high morbidity and mortality
So Doubt parenteral acyclovir 20 mg/kg Q 8 hr (Pending results of culture)

Once the diagnosis is confirmed, acyclovir should be continued for a total of
14 days in the case of SEM disease and for a minimum of
21 days in CNS or disseminated disease.
No data to supporting oral agents for neonatal HSV disease.
Regardless type:
1- Ophthalmologic examination
2- Neuroimaging : MRI, CT, or ultrasound
3- Proven CNS dictates a repeat lumbar puncture performed near the end of the initial treatment period to document clearance of HSV DNA from the CSF.

Although extremely rare, should the PCR remain positive, treatment should be extended for 1 additional week with reassessment of the CSF toward the end of the extended course. treatment course.[1,7]

The prognosis

Depends on the type of disease.

SEM	mortality 0%, morbidity 5%
CNS	mortality 15% morbidity 54%,
Disseminated	morality 54% morbidity 38%

Presence of seizures at the initiation of antiviral therapy was correlated with abnormal developmental at age 12 months.[7]

Completion of initial parenteral therapy is followed by suppressive therapy with oral acyclovir for 6 months regardless of disease type, shown to improve neurodevelopmental outcomes as well as prevent recurrent skin lesions. Kimberlin et al.[13]

Prognosis

Dosing of acyclovir is 300 mg/m2 3 times daily, weight-adjusted monthly for growth.

Neutropenia is a major side effect of acyclovir and typically occurs early during treatment, so absolute neutrophil count monitoring is recommended at 2 and 4 weeks after initiation of therapy, then continued monthly during the

CONCLUSION

1- Neonates presenting with vesicular skin lesions, focal neurologic deficits, and/or clinical sepsis with evidence of multisystem organ involvement in the absence of a bacteriologic diagnosis should prompt providers to strongly consider neonatal HSV disease as an etiology.

2-Untreated SEM disease progresses to meningoencephalitis and/or disseminated infection in approximately 75% of neonates.

3- Given the relatively high rates of morbidity and mortality associated with this condition, initiating parenteral acyclovir therapy pending further investigation is imperative.

4- Clinical manifestations, in addition to multisite PCR assays to assess for the presence of HSV DNA, assist in disease classification and diagnosis that ultimately determine duration of therapy as well as overall prognosis.

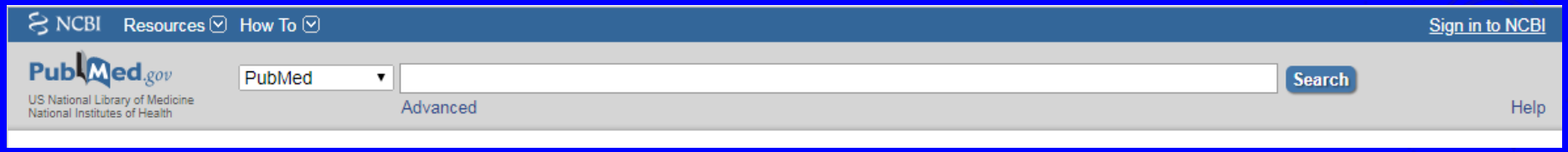
5- Given the demonstrated finding of improved neurodevelopmental outcomes and skin recurrences, all survivors of neonatal HSV should receive 6 months of suppressive oral acyclovir therapy after completion of parenteral therapy with close clinical monitoring.

SHOULD WE CHANGE OUR PROTOCOL?

J Emerg Med. 2018 Feb;54(2):261-265. doi: 10.1016/j.jemermed.2017.10.016. Epub 2017 Dec 1.

During the Emergency Department Evaluation of a Well-Appearing Neonate with Fever, Should Empiric Acyclovir Be Initiated?

Bruno E[1], Pillus D[1], Cheng D[2], Vilke G[3], Pokrajac N[3].



CONCLUSION

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Neonatal HSV infection carries significant morbidity and mortality if left untreated. High-quality clinical evidence on when to evaluate and treat for possible HSV infection is lacking. Based on available research, HSV infection in the febrile neonate should be strongly considered if age is < 21 days, or if presenting with concerning clinical features. If testing is performed, empiric treatment with high-dose acyclovir should be initiated. Additional research is needed to further clarify which cases mandate evaluation and treatment for HSV, and to better define treatment protocols.

Objectives

1-Know the epidemiology, prevention, and pathogenesis of perinatal infections with herpes 1, herpes 2, Neonatal sepsis, bacterial omphalitis, Entervirus infection manifestations

2-Know the clinical manifestations, diagnostic features, management, and complications of perinatal infections with herpes 1, herpes 2.

3-Know the cutaneous manifestations of herpes simplex

4-A call to rethink the protocol

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