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Fever and Rash in a 2-Month-Old Female

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Case report

A previously healthy, full-term female infant presents to an emergency department with a 3-week history of a persistent diaper rash that has now spread to her abdomen and extremities. The patient is noted to be increasingly agitated at home but without fevers, weight loss, neurological changes or changes to urine or stool output. She has been seen by her PCP who prescribed oral dexamethasone 1 week prior to the emergency department visit, which the patient was taking nightly. Mom was also given Lotrimin cream for the rash, but does not think either medication has made a difference.

On initial exam, patient was pale, fussy, and ill-appearing. She was tachycardic with normal heart sounds. No hepatosplenomegaly noted. There was swelling and erythema of the labia and perianal area with several scattered, non-draining pustules. There is associated maculopapular lesions over the hands and feet along with desquamating lesions on her palms and abdomen as demonstrated in (**Figures 1-3).**

Laboratory evaluation shows a normocytic anemia with a hemoglobin of 5.0 g/dL, reticulocyte count of 2.7%, RBC count at 1.7 M/ul, and no abnormalities of platelets or leukocytes. Electrolyte and hepatic function panels are largely unremarkable. Urinalysis is normal and a blood culture is pending. There was concern for Langerhans Cell Histiocytosis based on the skin lesions, so a skeletal survey was ordered which revealed multiple lytic lesions, specifically, left acromion and left distal radius lesions and a possible left distal humerus lesion as seen in Figures 4-5. Additional findings include a healing fracture of left distal tibial metaphysis, along with an L4 compression fracture. The patient is admitted for further workup and management. She quickly becomes febrile on the floor resulting in a more complete septic workup, including cerebrospinal fluid analysis.

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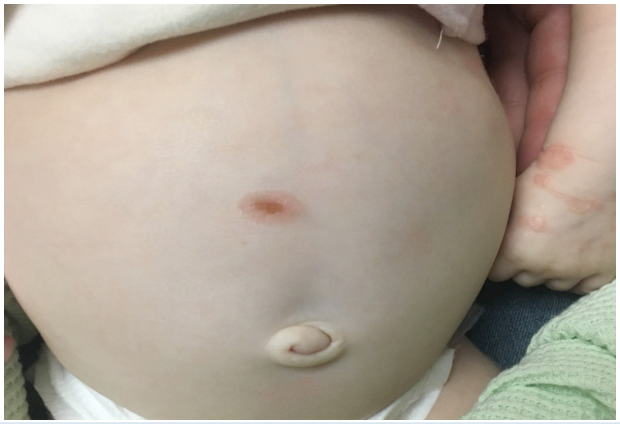

Figure 1

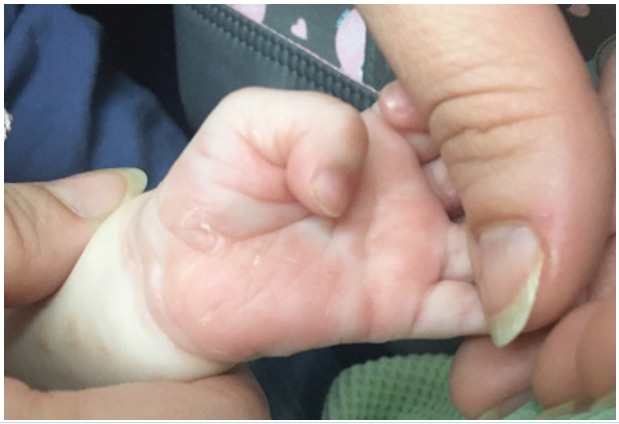

Figure 2

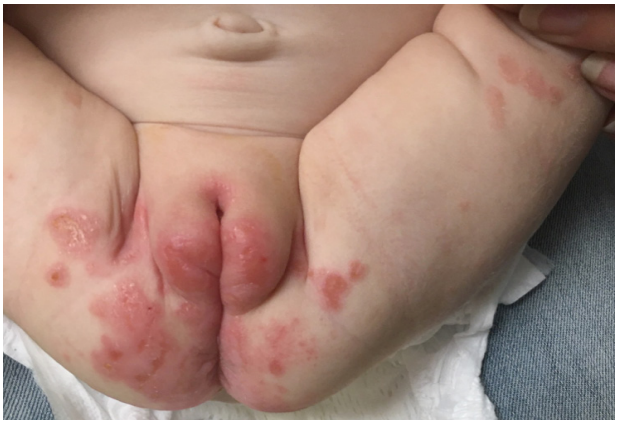

Figure 3

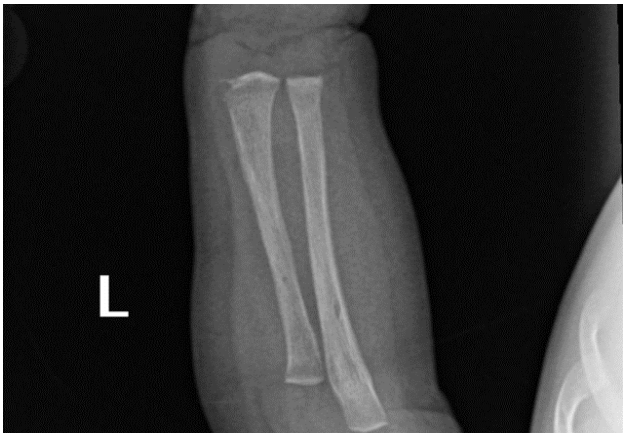

Figure 4

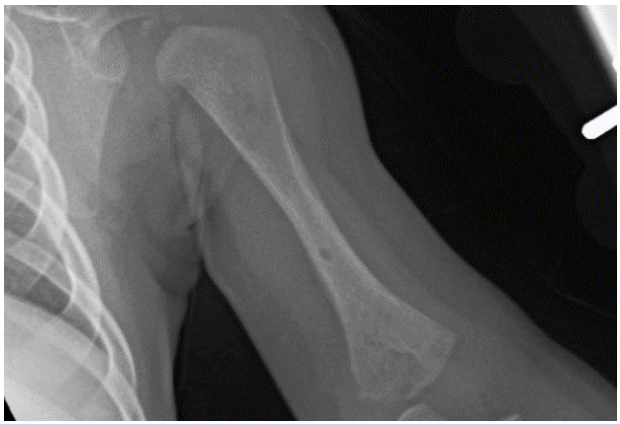

Figure 5

Hospital course

For this patient, her RPR drawn in the ED returns positive at 1:128 (normal: non-reactive, low: <1:8), along with confirmatory testing using fluorescent treponemal antibody absorption (FTA-ABS). The CSF was positive with a VDRL 1:32. Subsequently, numerous spirochete organisms are identified on skin biopsy. The diagnosis of congenital neurosyphilis is made. Upon further review, the mother disclosed having a genital rash and limited prenatal care not allowing for standard of care infectious testing at the end of pregnancy (mother's early pregnancy RPR was non-reactive). With the confirmation of congenital syphilis, the patient completed a 14-day course of penicillin. The skin manifestation improved quickly and significantly. Follow up 2 months after treatment revealed an RPR of 1:32 with no further clinical signs of syphilis infection. In this case, late identification of seroconversion during pregnancy resulted in this infant's disease. Fortunately, this infant responded well to therapy and continues to follow in ID clinic.

Final diagnosis

Congenital Syphilis

Discussion

Fever and rash as presenting symptoms in a child is one of the most encountered problems in pediatrics. The differential includes a large host of infectious etiologies, and an equally large number of non-infectious etiologies. Exhaustive history taking and ardent physical examination is crucial to help differentiate amongst the diagnoses.

Lytic bone lesions are not commonly encountered and have a fairly limited differential [1]. Benign bone lesions such as bone infarction, osteogenic lipomas, and bone cysts are often found incidentally. Osteomyelitis is another cause, although this is an uncommon presentation. Primary bone malignancies along with metastases from elsewhere can present in a similar fashion; as can congenital fibrotic bone lesions such as McCune-Albright syndrome. However, in the case presented above the clinical picture of anemia, fever, rash, and lytic lesions can narrow down the differential to two primary diseases: congenital syphilis and Langerhans Cell Histiocytosis (LCH). LCH is a clonal proliferation of myeloid dendritic cell precursors that can be an uncommon cause of fever, anemia, persistent rashes and bone lesions in children. Occurrence in infancy is exceedingly rare, however multiple reports have been made [2-4].

Congenital syphilis is an infection of the fetus or neonate when Treponema pallidum is passed from the mother to her

baby during pregnancy. Our relationship with this organism tracks back hundreds of years with evidence of vertical transmission occurring as early as the 14th century [5]. The great imitator, as it is often known, can present with a host of symptoms. Early congenital syphilis can easily be confused for other diseases, as demonstrated in Table 1 [1, 6]. The most common presenting symptoms tend to be hepatosplenomegaly, syphilitic rash, and desquamation. Petechiae and anemia can also be found on presentation but are rare. In our case, lytic lesions have already developed and are not typically seen on presentation. If left untreated, congenital syphilis will invariably result in intellectual disability, deafness, skeletal abnormalities, abnormal facial features along with a multitude of other symptoms. Initiation of treatment prior to development of symptoms of late congenital syphilis is crucial, as symptoms are largely irreversible.

Throughout history, syphilis has been treated with a myriad of medications, with some more spurious than others, such as mercury, arsenic derivatives, and even coinfection with malaria. Since the discovery of penicillin, this has become preferred to previous options. The treatment of choice for congenital syphilis is a 14-day course of IV penicillin with close follow-up with infectious disease physicians.

As the saying goes, an ounce of prevention is worth a pound of cure, and consistent with this, congenital syphilis can be prevented with penicillin-based antibiotic treatment of the mother during pregnancy. Sadly, reports show that cases of congenital syphilis have risen every year since 2013, and, more specifically, data from the Centers for Disease Control and Prevention (CDC) shows a 291.1% increase in congenital syphilis between 2015-2018 [7]. The most up to date data is from 2019 as syphilis cases from 2020 are still being collected and analyzed. The majority of cases of congenital syphilis do appear to localize to a few states; however, it is important to recognize that 43 states as well as the District of Columbia reported at least one case in 2019. The standard of care includes initial screening at the first obstetrics visit and is to be repeated near the end of the pregnancy for high-risk populations and areas of high rates of syphilis [8]. It is important to recognize the growing rates of syphilis and congenital syphilis in the United States and keep the diagnosis on the differential when assessing complex infantile/neonatal cases [8]

Missed opportunities for syphilis prevention appear to fall into one of four categories, according to Centers for Disease Control and Prevention 2018 data; these four categories include lack of adequate prenatal treatment despite timely syphilis diagnosis during pregnancy, lack of timely syphilis testing and treatment, late identification of seroconversion during pregnancy, and lack of syphilis testing despite appropriate prenatal care [7]. The most common missed opportunity for cases of treating congenital syphilis in 2019 was lack of adequate prenatal treatment despite timely syphilis diagnosis during pregnancy at 40.2%. The national rate of congenital syphilis in 2019 was 48.5 cases per 100,000 live births.

Conclusion

Congenital syphilis is a preventable sexually transmitted disease affecting nearly 2,000 infants nationally. Congenital syphilis can have such varied presentations which allows for mimicry of several other diseases, including malignancies such as LCH. It is important to include a wide differential of diagnoses when evaluating an infant with a rash. Cases of congenital syphilis have risen dramatically between 2013-2019 and have affected the majority of US states. The CDC recognized four major categories involved in missed cases of congenital syphilis: lack of adequate prenatal treatment despite timely syphilis diagnosis during pregnancy, lack of timely syphilis testing and treatment, late identification of seroconversion during pregnancy, and lack of syphilis testing despite appropriate prenatal care.

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