Congenital syphilis on the rise: testing and recognition are key

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Abstract:

Congenital syphilis has reappeared; more frequent antenatal testing and recognition of the features in infants are crucial to prevent morbidity and mortality.

The incidence of congenital syphilis (CS) is increasing in Australia as a result of the dramatic increase of infectious syphilis in pregnancy. CS can occur following negative maternal antenatal screening and absence of identified maternal risk factors. Clinicians need to be familiar with updated guidelines that recommend frequent antenatal testing in particular risk groups. CS should be considered in any critically unwell infant - diagnosis can be made via clinical examination, parallel infant and maternal rapid plasma reagin (RPR), infant IgM and placental PCR. Management includes 10 days of intravenous benzylpenicillin and follow-up serology at 3, 6 and 12 months of age or until RPR is nonreactive.

Clinical Record

A 3-month-old infant was admitted to paediatric intensive care with clinical sepsis, hepatosplenomegaly, severe anaemia, transaminitis, high lactate and coagulopathy. He was born at 37 weeks gestation via emergency caesarean section for fetal bradycardia following an uncomplicated pregnancy.

Leukemia with sepsis was suspected. As part of extended sepsis screening, syphilis serology was performed on day 5 of admission and revealed a rapid plasma reagin (RPR) of 1:128, reactive treponema pallidum particle agglutination (TPPA), positive blood syphilis polymerase chain reaction (PCR) and subsequently reactive enzyme immunoassay for immunoglobulin M (EIA IgM) antibodies to syphilis. Further assessment revealed hepatosplenomegaly with infiltrates, mottled retinal pigmentation (Fig.1) and vitreous opacities, osteopenia, periostitis, metaphyseal erosions and positive Wimberger sign (Fig.1) - all typical features of congenital syphilis. Cerebrospinal fluid (CSF) analysis revealed normal cell count and chemistry and was non-reactive for venereal disease research laboratory test (VDRL) and *T. pallidum* DNA was not detected by PCR. Audiology was normal. The infant was treated with intravenous (IV) benzylpenicillin 60mg/kg 6 hourly for 10 days. He responded well and was discharged home after a total of 18 days in hospital. At one year of age, he had normal development and vision despite persistent retinopathy on fundoscopy.

Subsequent parental serology revealed a maternal RPR of 1:32 and a paternal RPR of 1:64. The mother was a non-Aboriginal woman who had a negative single antenatal syphilis serology performed at 12 weeks' gestation. The father was an Aboriginal man. Neither parent described skin lesions consistent with a chancre, but the mother had developed a rash on her abdomen and backs of legs at around 30 weeks gestation, which persisted until the end of her pregnancy. The father also had a rash on his chest at around the same time.

Discussion

Congenital syphilis is a vertically transmitted bacterial infection caused by *Treponema pallidum,* and is associated with serious perinatal consequences such as premature birth, intrauterine growth restriction, miscarriage, stillbirth and perinatal death(1) and is entirely preventable with appropriate antenatal screening and penicillin treatment of infected pregnant women.

Despite the 2007 launch of a World Health Organisation global initiative to eliminate congenital syphilis, there remains a persistent increase in rates of congenital syphilis in high-income countries which is related to increased rates of infectious syphilis, particularly in pregnancy. Factors contributing to the worldwide re-emergence of this infection include an increase in higher-risk sexual activities, increased travel and migration and social and economic conditions that limit healthcare access in some populations(1). National data for Australia reveals that infectious syphilis notifications are increasing significantly in all States except Tasmania. Between 2009 and 2019 there was a fourfold increase in the rate from 5.9 to 23.2 per 100,000. This increase is was most marked in the Northern Territory which had an 8.6-fold increase from 16.8 to 138.6 notifications per 100,000 (2).

Rates of infectious syphilis notifications are up to 300 times higher in Aboriginal and Torres Strait Islander peoples, with up to 70% of infections among those aged between 15 and 29. Roughly equal numbers of males and females are affected(3). By contrast, infections in non-Indigenous Australians prior to 2014 were largely confined to men who have sex with men with more recent trends showing increasing infections in heterosexual persons with a concomitant increase in incidence among young women of child-bearing age. This case highlights the need for clinicians to be aware of the increasing incidence of congenital syphilis and to consider this as a possibility in critically unwell infants presenting with non-specific symptoms. The prominence of anaemia and thrombocytopaenia in this case is reflected in other published literature, with congenital syphilis gaining recognition as a mimicker for haematological and oncological disease(4) Other common features of congenital syphilis include hepatosplenomegaly, fever and rash, but there are a wide range of diverse presentations which vary in nature, age at onset, and severity.

Penicillin remains the only recommended treatment in pregnancy, with adequacy of treatment defined by a fourfold reduction in RPR titre over 6-12 months and completion of treatment course at least 30 days prior to delivery of infant(5). As such, mothers treated for infectious syphilis in pregnancy should have monthly serology until delivery to monitor response to treatment and to exclude reinfection. A further critical aspect of adequate maternal treatment is ensuring that all current sexual partners and their contacts are tested and treated to prevent re-infection. Infants with confirmed congenital syphilis should receive 10 days of IV benzylpenicillin.

Additionally, infants born to mothers treated for syphilis during pregnancy, should have follow-up serology at 3, 6 and 12 months of age (until RPR remains nonreactive) even if initial assessment for congenital syphilis at birth is negative(5).

This case also demonstrates that congenital syphilis can occur following syphilis infection in women who have negative antenatal testing and who have no specific risk factors for syphilis infection identified during pregnancy. The case described also demonstrates insufficient retesting of women with specific risk factors – in this case, an Aboriginal partner. These specific risk factors are comprehensively listed in the recently published Queensland Syphilis in Pregnancy guideline(5) and include Aboriginal and/or Torres Strait Islander woman or partner, migrants/refugees from high prevalence countries, adolescent pregnancy, woman or partner with sexual practices resulting in increased risk, women with late or no antenatal care, unwanted pregnancy

and substance use. All women should be tested at first antenatal visit, preferably before ten weeks gestation and again if risk of exposure occurs or if symptomatic. However higher risk women should have up to 5 tests during pregnancy; early first trimester, 16-26 weeks, 26-28 weeks, 34-36 weeks gestation and again at birth in particular situations(5). One of the challenges is to identify potential risk factors during pregnancy and this requires a clinical context and specific skills in history taking, including taking sexual histories. Screening intervals could also be considered for the general population in areas of increasing transmission, accepting that multiple factors would need to be balanced. Further discussion of the merits and risks of a second test later in pregnancy for all women is warranted

Lessons from Practice

- The incidence of congenital syphilis is on the rise in Australia and it can occur in the setting of negative maternal antenatal screening
- Congenital syphilis is an important differential to consider in any critically unwell infant and symptoms may include non-specific signs such as anaemia, thrombocytopaenia, hepatosplenomegaly, fever and rash.
- A diagnosis of congenital syphilis can be made through clinical findings and parallel testing of infant and maternal rapid plasma reagin (RPR), infant antibodies to syphilis via enzyme immunoassay for immunoglobulin M (EIA IgM) and placental syphilis polymerase chain reaction (PCR).
- Treatment of congenital syphilis involves 10 days of intravenous benzylpenicillin and follow-up serology at 3, 6 and 12 months of age or until RPR is nonreactive to ensure treatment is effective.

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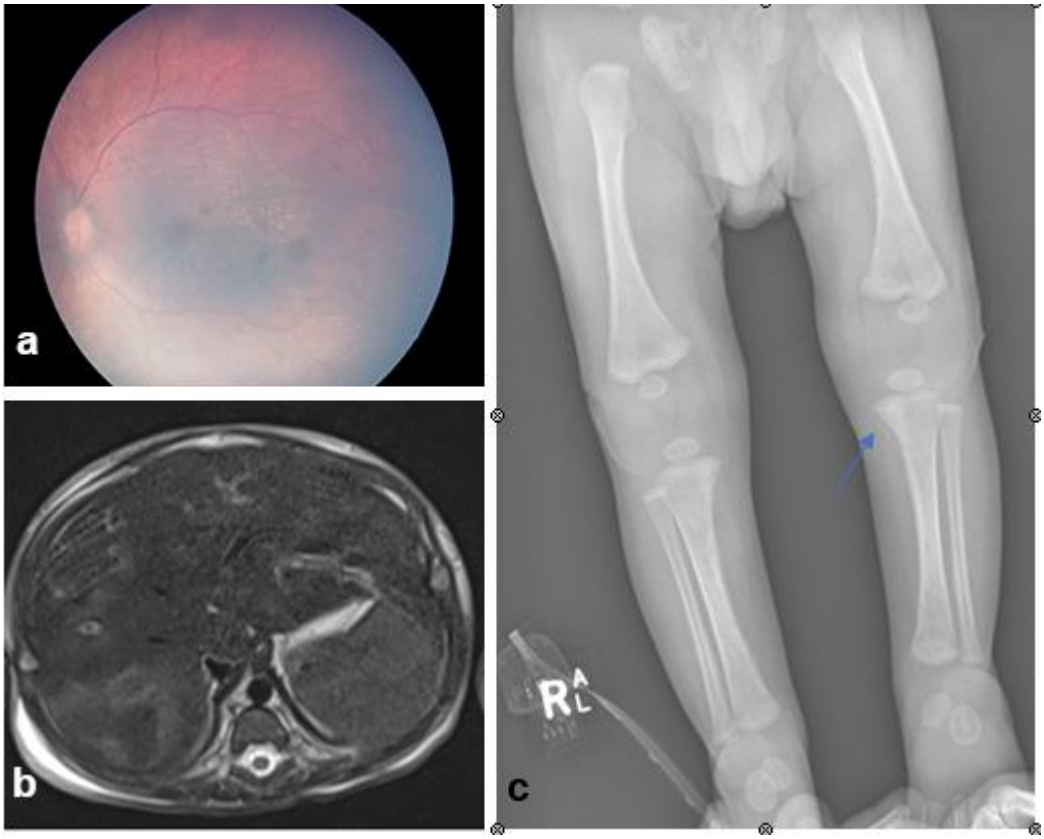

Figure 1: Clinical features of syphilis in case described

a Mottled ‘salt and pepper’ pigmentary retinal changes consistent with chorioretinitis on fundoscopy

b CT abdomen reveals markedly heterogeneously enlarged liver

c Long bone X-ray reveals generalised periostitis, with early erosions of mid metaphysis distal femora and of medial proximal tibia (Wimberger’s sign – see arrow)