

NEONATAL VARICELLA DESPITE MATERNAL IMMUNITY – A CASE REPORT AND WHAT CAN BE LEARNT

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ABSTRACT

A 20-day-old previously well neonate presented with a 3-day vesiculopapular rash and was admitted to the paediatrics ward. He received extensive workup and treatment with IV acyclovir. The disease ran a mild, uncomplicated course, and recovery. His mother was found to be immune to varicella, having had the disease as a child. However, her immunity had not transferred to the neonate, which was unexpected. A literature review revealed that maternal varicella antibodies do not necessarily prevent infection but may help the infant avoid severe or complicated disease. A review of the management of neonatal varicella in both the immune and the non-immune mother which put the child at risk is also done. Vaccination of all susceptible young females prior to pregnancy will help to reduce the incidence of neonatal varicella in infants and is strongly encouraged. Vaccination of household contacts especially siblings, is also encouraged. Family Physicians should remain open to the diagnosis of neonatal varicella, even when the mother has a history having chickenpox as a child.

Keywords: Neonatal varicella; Maternal immunity;

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INTRODUCTION

Neonatal varicella is caused by transmission of varicella-zoster virus (VZV) from mother to foetus in utero, or acquired from exposure to the virus postnatally. The latter is uncommon, occurring primarily in infants born to non-immune mothers. Mothers who are immune to VZV transfer protective maternal immunoglobulins to the virus transplacentally to the foetus.¹ This provides infants with passive immunity during the early months of life, while their innate immunity is still maturing. There have been a few reports previously of neonatal varicella occurring in full-term infants born to mothers immune to VZV.

We report a case of neonatal varicella occurring in a full-term infant, born to a mother immune to VZV, review existing literature for similar cases, and discuss current management.

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DETAILS OF THE CASE

A 20-day-old fully breast-fed neonate, born full term with birth weight of 3.3kg (7.3lb), developed a generalized three-day vesicular rash predominantly over his face and trunk. This was a typical varicella rash, with crusting of early lesions. There was no history of fever, decreased oral intake, abnormal sensorium or behaviour, and physical examination was also unremarkable for complications. He had required a short course of phototherapy inpatient for exaggerated physiological jaundice, but otherwise had an unremarkable birth history.

There was no known history of exposure to varicella. His mother had no illness or rash during the antenatal or peripartum periods, and no household contacts had illnesses. The potential sources of exposure were nosocomial while in hospital following his birth, and during visits to the paediatrics clinic in the government hospital for jaundice follow-up, though no specific sick contact was identified. The child had at other times been at home with no visitors.

His mother reported having varicella as a child and no previous varicella vaccination. Her antibody levels during pregnancy were not known. Her serum was tested and found to be immune – VZV IgG antibody level was 238mU/mL. IgM antibodies were undetected, indicating no recent infection.

GAINING INSIGHT: WHAT ARE THE ISSUES?

1. Why would an infant born to a mother immune to VZV still acquire neonatal varicella?
2. How many such cases have been reported in the literature? Do we know what is the expected clinical course of such infants?
3. Do such infants require inpatient admission, acyclovir therapy, and invasive studies like lumbar puncture?
4. Would the treatment be any different if the mother is non-immune?
5. What is important for family physicians to know and advise our patients regarding risks of neonatal varicella and its prevention?

STUDY THE MANAGEMENT: HOW DO WE APPLY THE INSIGHTS IN OUR CLINICAL PRACTICE?

1. Neonatal varicella despite maternal immunity

It is widely understood that in-utero transfer of maternal antibodies transplacentally protects neonates from varicella.² Transfer of antibodies occurs primarily in the third trimester, and so preterm infants are more vulnerable with lower IgG concentrations,³ both because of less transfer time, and lower innate immunity. In a healthy term infant, serum IgG should

be equal to, or even surpass maternal serum IgG levels,¹ providing essential protection for the neonate till their own immunity develops. In this case study, maternal immunity did not protect the infant from neonatal varicella.

2. Similar cases in the literature

A PubMed literature search yielded 4 case reports of similar cases. Two cases were reported by Readett and McRibbon,⁴ where the neonates developed postnatally acquired neonatal varicella around 2 weeks of age following exposure to an infected sibling, though both mothers were found to be immune but the titres were not reported. Another 2 cases were reported by Bendig et al,⁵ also with exposure to an infected sibling. Baba et al⁶ reported 5 cases occurring in infants 27 days to 2 months old – all with pre-existing known VZV antibody, but with low titres, in an outbreak in a domiciliary institute for infants in Japan, the clinical course of the disease was mild and the infants recovered uneventfully. A fourth case reported by Jackson and Aitken in 2011,⁷ describes a 17-day-old child presenting with a 2-day rash and his mother's booking blood sample was VZV IgG positive. There was a contact with of the neonate at day 2 of life, with a cousin who subsequently developed chickenpox.

The maternal titre has been shown in studies to be the single most important predictive factor of neonatal VZV-IgG titres.⁸ As such, the presence of maternal antibodies does not necessitate immunity. In our case, the maternal IgG level was 238mIU/mL; it may even have been lower prenatally as levels were measured after the mother had been exposed to the infected neonate and presumably would have had a boost in antibody levels from the exposure. A comparable situation is seen in case reports of adults with proven varicella immunity who still developed breakthrough varicella.^{9,10} Martin et al in 1994¹¹ noted that the criteria of protective. VZV remained ill defined. It is still so today.

The presence of maternal antibodies, albeit low, seems to provide some protection against the development of severe disseminated disease. In all of the reported cases, the neonates had mild and uncomplicated disease courses with full recovery. In contrast, if the mother is non-immune, the infected child is at risk of high morbidity.

3. Management of the patient in this case report

The child was admitted to the paediatric general ward. A clinical diagnosis of primary varicella infection in the neonate was made. VZV DNA was detected in his blood and vesicular swabs via polymerase chain reaction (PCR). Cerebrospinal fluid studies were normal with no VZV DNA detected. This was done to exclude any central nervous system involvement in view of his young age, though the infant was clinically well. He was treated with intravenous acyclovir therapy for 10 days, and had an uneventful and mild clinical course. All lesions had crusted over on discharge, following completion of acyclovir therapy. His 2-year-old brother received vaccination against VZV.

A literature review provided the information for the management of exposure to and varicella in neonates born to immune mothers shown in Table 1.

Table 1. Management of Exposure to and Varicella in Neonates Born to Immune Mothers⁷

1-Neonate first 7 days of life, exposed to a family member other than the mother	If mother is immune, no rash in baby no intervention is required. Watch for occurrence of rash.
2-Neonate less than one month old who develop chickenpox	Immune status of mother confirmed Treat with IV Acyclovir to reduce risk of severe disease regardless of use of VZIG or not.
3-Chickenpox in healthy children between 1 month and 12 years.	Disease is usually mild, and antiviral treatment is not usually required.
4-Neonate born before 28 weeks or less 1 kg. Baby would not have received adequate maternal antibodies.	Irrespective of immune status of mother Give VZIG routinely IV Acyclovir X 7 days Treat any secondary skin infection

4. The situation of the non-immune mother

Table 2 summarises the treatment principles for infants where the mothers are non-immune to chickenpox. Risks to the foetus or neonate from maternal chickenpox are related to the time of infection in the mother.

Table 2. Management of Neonatal Varicella Where Mothers were Non-immune

Stage of gestation and duration of rash in mother	Evidence of outcome from case studies	Recommendations to reduce risk to neonate
1-Last 3 weeks of gestation – 1 day of rash in mother	2 reported cases successfully treated: delivery was delayed and the increasing maternal IgG crossing placentally protected the child. ^{12,13} Treatment with VZIG may not be essential. This was recommended but the parents refused and this was not given in the case study by Noce et al and patient was well.	Postpone labour 4 days or more to allow for maternal IgG to cross placenta to the neonate. Oral acyclovir to mother for 7 days – to protect against maternal viral pneumonitis and reduce infection risk to foetus. Treatment with VZIG may not be essential.
2-Last 3 weeks of gestation – appearance of rash 7 days before delivery to 7 days of delivery (particularly within 5 days before and 2 days after delivery)	Half of neonates exposed to maternal varicella will develop chickenpox despite the administration of VZIG. Mortality prior to VZIG was 30%; this is reduced with introduction of VZIG ⁷ . VZIG may prolong the incubation period for up to 28 days so neonates must be monitored for symptoms during this time. Note that VZIG is not enough during incubation period and the disease can still progress to viral pneumonia ¹⁴ . The learning point is to monitor the child after VZIG and treat early with IV acyclovir. Illustrative case studies emphasizing the importance of IV acyclovir with onset of rash: □ Kongthavonsakul & Pruksachatkun ¹⁵ , 2012 Thakur and Sahay ¹⁶ , 2010 □ Pattanasu ¹⁷ , 2008 □ Isaacs ¹⁸ , 2000 □ Narkeviciute ¹⁹ , 2007	Treat with VZIG post-exposure prophylaxis (250 IU i.m.). Monitor the child for onset of rash. With onset of rash, treat with IV acyclovir 10-20 mg/kg 8H for at least 7 days. Note that oral absorption is poorly absorbed with bioavailability of only 10-20%.
3-Neonates less than a month old, who develop chickenpox	Need to reduce the risk of severe disease, regardless of maternal immune function and the use of VZIG. ^{20,21,22}	IV Acyclovir X 7 days at 30-60 mg/kg divided into 8H for 7 – 10 days) if child is unwell
4-Neonates born before 28 weeks	Baby would not have received adequate maternal antibodies transplacentally.	IV Acyclovir X 7 – 10 days.
5-Chickenpox in healthy children between 1 month and 12 years	As described by Jackson & Aitken ⁷ , the disease is usually mild and can occur in susceptibles at early age. The preventive action to take is to encourage immunization. ²³	Antiviral treatment is not usually required. In Singapore, due to high risk of infection at young age, chickenpox vaccine is given at 12 months and 15 months.

5. What is important for the family physician to know and to advise

Non-immune females of reproductive age could be advised to be vaccinated against VZV before pregnancy occurs, to reduce risk of morbidity to neonates. This would be an additional incentive towards encouraging vaccination. As it is a live vaccine, females should wait until 1 month after the vaccination before getting pregnant.²³

In addition, exposure to an infected sibling is a common source of infection. Vaccination should be encouraged in all children from 12 months of age to protect both themselves and their siblings. Parents need routine advice to isolate infected persons from the neonates, even if maternal immunity had been present.

DISCUSSION

What is new in this case report? Neonatal varicella may occur despite maternal immunity, but morbidity tends to be lower in such neonates. Maternal antibodies seem to provide some protection against severe disseminated disease. Table 1 shows the principles of treatment for infants of immune mothers.

What is known?

VZV infection in pregnancy is damaging to the foetus: it causes the fetal varicella syndrome in infections up to 28 weeks gestation,²⁴ and neonatal varicella in the infant born within 3 weeks of maternal infection in late pregnancy. The most vulnerable period for the foetus is the window of maternal infection 5 days before delivery to 2 days post-delivery.²⁵

Limitations of this case report.

The evidence used in the discussion of this report is based on cases reported in PubMed and also only from papers written in English.

Recommendations for further action?

Immunisation against VZV for all women of reproductive age group will limit the number of newborns having primary varicella infection in the neonatal period. Immunisation of other household members, such as siblings, is recommended as well.

CONCLUSION

The lessons that may be learnt from this case study are: Maternal varicella antibodies do not necessarily prevent infection in neonates especially if titres are low but may help neonates avoid severe or complicated disease. Family physicians seeing neonates in the community should remain open to the diagnosis of neonatal varicella even if maternal immunity is known to be present and give routine advice to isolate infected persons from neonates. Vaccination against VZV for females prior to pregnancy, and for siblings, should be encouraged.

DECLARATION OF INTEREST

The authors declare that they have no conflict of interest in relation to this article.

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