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Vesicular rashes in neonates are challenging in terms of diagnosis and management. Herpes infection is an important diagnostic consideration. We report two illustrative neonatal cases of herpesvirus infections with vesicular rashes. Such babies may be remarkably asymptomatic. A high index of suspicion leading to a prompt diagnosis, timely quarantine measures, and institution of antiviral treatment are pivotal for desirable outcomes.

Case reports

Case 1

An afebrile and asymptomatic neonate with 39 weeks and 6 days of gestation received a 5-day course of intravenous penicillin and gentamicin, because of prolonged rupture of maternal membranes and a slightly elevated plasma C-reactive protein level (14.6 mg/L; reference level, <10 mg/L). He developed a vesicular rash on day 12 of life, initially involving the face and forehead that subsequently spread to the entire body. Spontaneous rupture of the vesicles yielded yellow non-purulent fluid. He was admitted to a newborn unit (Fig 1), and cared for in a cubicle. The mother had childhood chickenpox, and developed some vesicles (which became crusted) on the dorsum of her right hand and arm 2 days before delivery. As chickenpox is an air-borne infection, the neonate was immediately transferred to an isolation room. He was treated as having herpes or a bacterial skin infection with acyclovir plus intravenous ampicillin and cloxacillin, and remained asymptomatic. Immunofluorescence staining of vesicular fluid confirmed the presence of varicella-zoster virus (VZV). Consequently, one cubicle of the newborn unit (involving 12 babies and their parents) was quarantined. The mothers of seven of these babies had unknown chickenpox immune status. They tested anti-VZV immunoglobulin G positive and were regarded as immune. The remaining five mothers reported a definitive history of chickenpox. The nursing and medical staff involved was all known to be immune.

Case 2

A boy of 34 weeks and 6 days of gestation was delivered vaginally. His 37-year-old mother from Mainland China had received intrapartum antibiotics for a febrile illness (37.7°C) and prolonged rupture of membranes (42 hours). Shortly after birth, the afebrile neonate developed tachycardia (172 beats/min) and tachypnoea (55 breaths/min). He received intravenous antibiotics and continuous positive airway pressure support with supplemental oxygen (fraction of inspired oxygen=0.23). He rapidly became asymptomatic and oral feeding was commenced the next day. Eight days later, he developed one vesicle (4 mm) on the chest, followed by another on the right earlobe, and then the lower back and the right periumbilical area. The patient was treated as bacterial skin infection with intravenous ampicillin and cloxacillin. Three days later, the infant temperature increased to 37.8°C. A cluster of vesicles was noted on the left anterior chest wall (Fig 2). The mother gave no history of vaginal herpes or cold sore. The boy was quarantined; his vesicular and cerebrospinal fluid (CSF) tested by polymerase chain reaction (PCR) confirmed the presence of herpes simplex virus type 2 DNA. The CSF yielded a white cell count of 382×10^6 /L with 60% polymorphs, and a red cell count of 75×10^6 /L. The patient was treated with a 3-week course of intravenous acyclovir and made an uneventful recovery.

Key words

Herpes genitalis; Herpes simplex;
Herpesvirus 2, human; Infant, newborns

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Discussion

Vesicular rashes in the neonates are challenging in terms of diagnosis and management. Herpesvirus infections are important diagnostic considerations.¹⁻⁷ These two cases highlight the importance of a contact history with herpes infections, but this is often

unavailable.^{2,4} For case 1 (chickenpox), regrettably the nature of the vesicles found on the dorsum of mother's right hand and arm 2 days before delivery could not be confirmed. If these lesions were zoster, they could have been the source of infection via direct contact after delivery. A typical presentation of recurrent chickenpox or zoster in the mother may be absent, making the identification of high-risk newborns difficult. Alternatively, the newborn could have acquired air-borne infection, which is often more difficult to identify. Although chickenpox is one of the most contagious airborne diseases, neonatal chickenpox acquired soon after birth is rare.^{2,4,5} The period of infectivity is between 10 days after first exposure and 21 days after last exposure. Potentially, admission of an infected neonate to a newborn unit could cause an outbreak. It is a policy of our newborn unit to document the immune status of all staff. Nevertheless, all other neonates and parents in the same cubicle as our patient 1 had to be quarantined and the mothers' status was evaluated. Varicella-zoster immunoglobulin (VZIG) may be administered for the non-immune. Frontline staff should be vigilant not to admit neonates with chickenpox to the neonatal unit, in order to avoid putting other non-immune infants at risk and the subsequent tedious quarantine measures.

Herpes simplex is a sexually transmitted disease that may result in serious and fatal neonatal infection.^{1,3-5,7} The mother might not give any contact history. The vesicular rash at the time could be scanty and indistinct. Symptomatology of neonatal herpes meningitis may be absent, as occurred in one of our patients. Nevertheless, the diagnosis must not be delayed, as early treatment with prompt institution of intravenous acyclovir is life-saving. It is important to pursue prompt laboratory investigation of any suspicious vesicular lesions in neonates. Molecular approach by conventional or real-time PCR is the method of choice, because of its high sensitivity and specificity, and rapid turn-around time. However, the reality in most Hong Kong public hospitals is that these molecular tests are not available or are not undertaken at a frequency high enough to meet the clinical need. The second option for rapid diagnosis of vesicular lesions is immunofluorescence staining of lesion scrapings. However, the sensitivity of this technique relies heavily on the quality of specimens. The early stage of herpetic lesions in neonates is often too small to yield good-quality specimens.

The differential diagnosis of a neonatal vesicular rash also includes *Staphylococcus aureus* and enterovirus infections, but timely isolation and institution of specific antiviral therapy for herpes must not be delayed.^{2,3,6} Between 2008 and 2010, only one neonatal case of VZV and one of herpes simplex virus type 1 were recorded in Hong Kong. Proven neonatal herpes infections were likely

新生兒疱疹病毒感染：何所學？

為新生兒診斷及醫治水疱皮疹是一項挑戰，迅速作出疱疹病毒感染的診斷相當重要。本文報告兩宗新生兒感染疱疹病毒並出現水疱皮疹的病例，這些受感染的新生兒可能完全沒有其他症狀。要有效迅速地醫治病人，醫生必須對此病有高度警覺性、及時採取隔離措施及為病人施以抗病毒治療。



FIG 1. Case 1: neonatal chickenpox



FIG 2. Case 2: neonatal herpes simplex: a cluster of vesicles on the anterior chest wall medial to the left nipple

to be exceedingly rare in our locality. Perinatal-transplacentally acquired varicella (as occurred in the neonate born to the mother with a rash between days 2 and 5 after the birth) has a mortality of up to 30%.²⁴ This condition should be recognised and promptly treated. Varicella-zoster immunoglobulin prophylaxis is indicated for the neonate within 10 days of initial exposure if (1) perinatally a maternal varicella/chickenpox rash is present, and (2) the VZV antibody status of the mother or infant is negative.

Rarely, fatal cases have been reported despite VZIG prophylaxis in mothers with an onset of chickenpox in the perinatal period. Early treatment with intravenous acyclovir is recommended at the first sign of illness.

In summary, effective antiviral treatment is available for herpes infections. Physicians caring for neonates with a vesicular rash must be vigilant to ensure prompt isolation and ensure that appropriate treatment is administered without delay.

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