

## Delivery Management in Maternal Varicella Peripartum Infection with Vulvar Lesions: A Case Report

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### 2. Key words

Varicella Zoster Virus, Infections in pregnancy, Vulvar lesions, Preterm premature rupture of membranes (pPROM).

### 1. Abstract

**1.1. Introduction:** Maternal varicella near term carries the risk of neonatal varicella. Transmission is usually transplacental, cases of maternal genital lesions near delivery have never been described.

**1.2. Case Presentation:** Our patient presented at 36th week with primary varicella with vulvar vesicles. The day following the rash development she ruptured membranes. We decided for an urgent cesarean section and the newborn was not infected and did not present complications due to prematurity. VZV specific immunoglobulins were administered to the newborn after collection of cord blood. Molecular virology studies confirmed VZV presence in vulvar vesicles and that the newborn was uninfected, with negative PCR on cord blood, throat swab and urine. The virus was found in amnio-chorial membranes. At 28 days of life the infant developed uncomplicated varicella after exposure to her older brother who was infected.

**1.3. Discussion:** In absence of specific guideline on this scenario and in absence of similar cases in literature, we suggest a cesarean section should be performed in case of maternal varicella with genital lesions. In case of rupture of membranes performing it as soon as possible might be recommendable to avoid ascending transmission. Rapid confirmation of VZV in vulvar lesions is valuable.

### 3. Introduction

Varicella-zoster virus (VZV) is one of eight herpesviruses known to cause human infection worldwide [1]. In Italy incidence of varicella in pregnancy is of 1.21 to 6 cases/10,000 but vaccination coverage in seronegative adult women is poor [2].

VZV, like other herpesviruses, is fully capable of infecting placental cells and transmitting vertically from the mother to the fetus [3]. Embriopathy followed by fetal death is described and fetopathy followed by congenital varicella syndrome, although devastating in terms of postnatal mortality and disability, is rare [4]. A much more frequent issue is peripartum Varicella. VZV exposure, whether prenatal with transplacental passage of the virus to fetal blood or postnatal, in a newborn lacking humoral immunity to the

virus may have a dramatic course, as it has in immunocompromised patients. It is even more serious in preterm and low birth weight infants. Maternal VZV-IgG are synthesized soon after infection and actively transferred across the placenta to the fetus, but fetal titer becomes significant only after a few days of active transport, as demonstrated by Brunnel [5]. Newborns born from mothers who develop a rash from 7 days before to 7 days after delivery are considered high risk for a complicated infection. Historically, mortality for this condition has been reported as high as 31% in infants born from mothers who developed rash in the last 4 days before delivery. The state of art of neonatal treatment with preventive administration of VZIG and oral or intravenous Acyclovir has substantially changed this data. VZIG passive immune prophylaxis modifies the disease, and, even if it does not prevent infection,

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reduces its severity. It is recommended for perinatal varicella in newborns of mothers who develop a rash 5 days before to 48 hours after delivery [6].

In Varicella, genital vesicles are not common and have never been described in a pregnant woman near delivery, instead of Herpes simplex viruses (HSV) lesions, which are frequent causes of genital infection. We present a case of a woman with peripartum varicella and genital lesions, her delivery management and neonatal outcome.

#### 4. Case Report

A 34 years old woman, 6 gravida 2 para, with a spontaneous pregnancy, was admitted to our emergency department at 35 week of gestational age (WGA)+2days for fever and rash. Her previous pregnancy history was unremarkable, except for maternal smoke (6-7 cigarettes a day) and upper respiratory tract infection with fever in the third trimester, treated with amoxicillin. First, mid, third trimester ultrasound, and a fetal heart ultrasound were normal. She had an history of exposure to VZV (a son with chickenpox) and tested VZV IgG and IgM that were negative at 34 WGA+6days. She developed fever at 35 WGA+1day. The day after admission, at first clinical examination a vesicular rash was observed on head and trunk and a clinical diagnosis of varicella was made. A few hours later she had a preterm premature rupture of membranes (pPROM) and the fetus was cephalic and extra-pelvic. Antiviral therapy with intravenous Acyclovir 750mg three times a day was started, and isolation was disposed. Complete blood count revealed neutrophilia and liver and kidney function tests were normal. At obstetrical examination vesicular vulvar lesions were noted. Delivery management was evaluated collegially. A cesarean section was performed, and a female was born without any obstetric complication. About 4 hours passed from rupture of membranes to delivery for anesthesiologic indication. Birth weight was 2900g and cardiorespiratory adaptation was good. Placental pathology showed intraparenchymal infarcts, villous agglutination and intramural fibrin deposition, of unspecific significance. Scrapings from the basis of a maternal vulvar vesicle was analyzed for VZV genome detection by PCR, which was positive. Furthermore, VZV-PCR was positive on an amnio-chorial membrane sample. VZV-PCR was performed on cord blood after delivery, on neonatal throat swab on the third day of life and on neonatal urine on the fourth day of life and were negative. Specific anti-VZV immunoglobulins (VZIG) were administrated in the first day of life. The newborn was isolated and observed in Neonatal Intensive Care Unit (NICU) for one week and did not develop infection. Both mother and newborn had negative VZV IgG and IgM. The mother was isolated and

discharged on the third day after delivery and did not develop any complication. At time of discharge, all lesions were crusted, and breastfeeding was encouraged. In the first month of life the infant was exposed to her brother who had varicella and at 28 days of life developed varicella, which had a benign course with no complications and no need for hospitalization. At last follow-up at 4 months the infant was in good health, the mother had repeated VZV serology and had positive VZV-IgG.

#### 6. Discussion

We present a case of an unvaccinated pregnant woman infected with VZV in the third trimester from her unvaccinated son. For pPROM and varicella with vulvar lesions a cesarean section was performed at 36th WGA, in 4 hours from rupture of membranes, and the newborn was uninfected and in good health.

Primary VZV infection in the third trimester represents a substantial risk for both the mother and the infant. The mother was at high risk for VZV pneumonia, also for smoking, Acyclovir treatment was initiated in 24h from rash development, as recommended [7], and the infection had a benign course.

Perinatal vertical transplacental transmission rate for varicella is substantially lower than for horizontal airborne plus contact transmission rate, being of 20 to 50% compared to the about 90% risk for non-immune households contact of a contagious varicella infected patient [8]. Bloodborne transplacental transmission is relatively inefficient, with studies on VZIG reporting about one infant in two with infection [9] compared to the primary natural ways of spreading of the virus. VZV, indeed, is present in cell-free highly infective enveloped virions concentrated in vesicle fluid, from where it is liberated and efficiently transmitted by contact or aerosolized [10].

Thus, we considered passage in the channel of delivery at maximum risk of infection for a non-immune fetus who had a theoretical risk of 20-50% of transplacentally acquired infection. Genital lesions in varicella are rare, and we found no specific guideline on this issue. Only one case was reported in literature about genital zoster in near term pregnancy in 2020 [11] but in that case report the patient was treated with Valacyclovir from 38 weeks until delivery, no lesion was visible at clinical examination during labor and a cesarean section was performed for other obstetric reasons.

Our case report is in fact the first case reported in literature of pPROM in a patient with genital varicella lesion. Based on these considerations and on the experience on HSV genital infection around delivery in case of pPROM, we performed a cesarean section.

When congenital infection is a concern, it is important to delay

delivery to allow for IgG transport, however in the setting of ruptured membranes we had to balance this advantage against the risk of colonization of amniotic cavity and ascending transmission [6]. In our case, positivity of membranes and placenta with uninfected newborn testifies ascending colonization of amniotic cavity is possible and might have represented a considerable risk of infection for the uninfected fetus. The newborn had no contact with the virus from the mother and did not start active synthesis of protective VZV-IgG, since at the end of the first month of life, when presumably the passive immunity given by the VZIG administered after birth waned, she developed uncomplicated varicella when exposed to a household contact.

It is worth noting that in our patient serology was negative with a positive molecular isolation, which is a more sensitive technique. IgM positivity is not detected in a substantial minority of patients, so clinical diagnosis is essential [12], especially in the onset of illness.

Even if rare during pregnancy, in literature cases of unexpected VZV genital lesions are reported in male and female [13]. In a study from Birch et al 2003, in a population of 6210 adults with suspected genital herpes, VZV was detected in 2.9 % [14].

In current guidelines of management of herpes and varicella during pregnancy, the presence of genital lesion of VZV is not considered. It is possible that genital zoster infection is not recognized, since HSV and VZV lesions are very similar, but VZV should be considered as a differential diagnosis of genital herpes-like lesions mostly in pregnancy.

In conclusion, for our experience, we recommend cesarean section in varicella with vulvar lesions, even in the setting of pPROM. Rapid confirmation of VZV in vesicles by PCR is advisable.

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