Varicella in a peripartum woman with serological evidence of previous infection, and subsequent neonatal infection

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ABSTRACT
Chickenpox or primary varicella is a common childhood exanthem. Adult primary varicella is a serious but rare infection because lifelong immunity is typically acquired after childhood exposure. There are, however, case reports of clinical re-infection in the literature. Varicella in pregnancy may have multiple complications for both the mother and fetus. This is a case report of a pregnant woman who developed clinical varicella in the peripartum period despite serological evidence of previous infection. Her baby subsequently developed neonatal varicella two weeks after delivery and discharge. This report discusses the phenomenon of varicella re-infection and highlights the need to maintain a high index of suspicion for varicella in at-risk populations.

CASE
Patient consent for case report obtained verbally.

A 30-year-old gravida 2 para 1 woman at 39 weeks gestation by dating ultrasound scan presented to the delivery suite with painful regular contractions. She was assessed to be in the active phase of stage 1 labour by the midwife. The midwife noted a generalised rash which progressed over several hours and requested an obstetric review.

The patient recalled that the rash started one day ago around her upper chest. She was intending to visit her family doctor but presented to the delivery suite due to her painful contractions. She had experienced mild subjective fevers overnight but felt well. She did not have any coryzal or conjunctival symptoms, and did not complain of pruritus. There was no recollection of any sick contacts in the previous two to three weeks. She stated that she had varicella as a child and this was corroborated by her mother. She had one daughter who was 4 years old and had been immunized against varicella. The daughter was well and had no sick contacts at pre-school.

On examination, the patient had erythematous macules which were well circumscribed with diameters of approximately 2mm. Some of the macules had central nodular components surrounded by erythema. On closer inspection there were one or two possibly fluid-filled vesicular lesions. The rash was scattered and bilateral, located primarily on the face (with additional scalp and post-auricular involvement), neck, chest and proximal upper limbs. Lesions crossed the midline with no dermatomal distribution.

The physical examination was otherwise unremarkable and her vital signs were normal.

A blood sample to test for serum varicella IgG was immediately sent to assess immunity. Based on the clinical picture at this time, it was thought that she was unlikely to have varicella zoster virus (VZV) infection or reactivation. Labour progressed normally with delivery of a healthy baby girl with a rash which was erythematous and macular with sporadic pustules. This was thought to be erythema toxicum and not varicella.

On clinical review the following morning, ten hours later, the woman had developed more lesions, with some of the previously nodular lesions becoming vesicular. There was an increased concern for varicella, the patient was placed into an isolation room away from other maternity patients and several vesicles were swabbed and sent off for VZV DNA PCR testing. Contact tracing within the hospital was conducted by an infection control nurse specialist.

The paediatrician discussed the case with a paediatric infectious diseases specialist and the baby was given an empirical dose of varicella zoster immunoglobulin and observed over 24 hours. During this time the progression of the rash in the mother slowed and she was subjectively and objectively well. The baby developed no vesicular lesions or features suggestive of varicella. Her vitals were within normal parameters. They were discharged and the mother advised to return should the baby become unwell or develop a new rash.

Several days following discharge, serum varicella IgG returned positive, signifying previous VZV infection and theoretical immunity. The PCR swabs of the vesicular lesions also tested positive for VZV DNA. Although there was no history of contact with an infected individual, this presentation...
was thought to be a VZV re-infection rather than a disseminated herpes zoster re-activation because the rash was generalised with no clear dermatomal preference or distribution.

Two weeks after discharge, the baby developed crops of vesicular lesions on the face, head, feet and bottom, and re-presented to the hospital. She was otherwise well with feeds, not irritable, and not dyspnoeic. She was diagnosed with neonatal varicella, and was discharged after 48 hours of clinical observation with no indication of needing further varicella zoster immunoglobulin.

**DISCUSSION**

Primary VZV infection, commonly known as chickenpox or varicella, is a common childhood viral exanthem caused by human herpes virus. Varicella has a classic generalised rash which transitions from erythematous papules, to fluid-filled vesicles, then to pustules. Adult varicella has a greater morbidity than childhood varicella, with a common complication being viral pneumonitis. A group at risk of further morbidity to varicella are pregnant women. The phenomenon of varicella re-infection is rare, more commonly the virus re-activates as herpes zoster; also known as shingles.

Varicella is a highly contagious illness with high transmission rates. It has two key methods of transmission: either direct contact with fluid from vesicular lesions, or inhalation of aerosolized vesicular fluid or respiratory secretions. Patients are infective from one to two days prior to the onset of the rash, until all the skin lesions are crusted over. Patients should be isolated in a closed room until they are non-infective. The room should be equipped with negative pressure ventilation to prevent airborne transmission of the virus. Contact precautions for healthcare workers involving gown and gloves should be undertaken, and all staff looking after the patient should have evidence of immunity to varicella. Due to confusion about the diagnosis of varicella in the above case, there was a delay in implementing airborne and isolation precautions for the patient until subsequent clinical review. While all maternity rooms in the hospital were single rooms, there was still a transmission risk as the room is in direct contact with the corridor which was a shared space. However, the patient did not have a significant number of vesicular lesions nor coryzal symptoms, therefore her infectivity was probably lower than a primary varicella infection. Nevertheless, there was still a possibility of a varicella outbreak in a high risk obstetric population due to delays in diagnosis.

Prior to the availability of the varicella vaccine, most children were expected to have been infected before adolescence, providing them with immunity against re-infection. However, an American surveillance study found that 9.5% of paediatric patients diagnosed with varicella had a previous diagnosis of varicella by a physician or a recollection of a rash with features typical of varicella.[3]

Re-infection in adulthood after childhood exposure or vaccination is rare but there are case reports of immunocompetent patients who experience a subclinical response,[3] or clinical re-infection.[4,5] Most case reports of varicella re-infection feature healthcare workers because they have evidence of previous infection with documented levels of serum varicella IgG. The test for serum varicella IgG is predominantly used by healthcare workers to show immunity to varicella as part of their job requirement. This test is not routinely used by the general population, which makes documenting varicella re-infection in the community almost impossible. Cases of re-infection may be misdiagnosed as primary varicella. Varicella re-infection may be less rare than classically considered but this will be difficult to prove.

Historically varicella in pregnancy was a condition with a high mortality of up to 36%,[6] however the RCOG guidelines suggest that the rate is now lower due to advancing medical care.[11] Complications in pregnant women infected by varicella include pneumonia, hepatitis and encephalitis. The fetus is also at risk of congenital anomalies if the mother is infected in the first trimester. Lastly, peripartum maternal infection leads to neonatal varicella which is associated with high mortality. Due to the possible complications, varicella in pregnancy should be treated as outlined in the RCOG guidelines.[11]

Re-infection by VZV in pregnancy has not been well researched. Martin et al, published a case series of four pregnant women with serological evidence of previous varicella exposure, who had contact with an infected individual and subsequently developed clinical features suggestive of varicella with an accompanying increase in IgG titres.[7,8] In two patients, the infection was described as mild. One of them had approximately 50 lesions as opposed to the classically expected hundreds of lesions. All four patients delivered healthy normal babies. Similar to this case, all of the women had a milder course of illness with no acute sequelae associated with primary VZV infection such as pneumonia or encephalitis. However, all four women developed symptomatic varicella in the first or second trimester of pregnancy, rather than in the peripartum period as in this case.

The main differential to varicella re-infection would be disseminated shingles. Disseminated shingles in immunocompetent people is a rare occurrence.[10,12] It typically presents with a vesicular rash in a dermatomal pattern followed by extra-dermatomal lesions days later; but a generalized distribution has been reported.[12] Serological investigations will not assist in distinguishing between VZV re-infection and disseminated shingles as they will be serologically similar with rising IgG titres and absent IgM.[4,12] Although shingles is common in pregnancy, fetal complications are extremely rare,[17] with only one reported case of infection in utero.[18] There have been no case reports in the literature of peripartum disseminated shingles causing neonatal varicella post-delivery.

It is highly likely that this case represents a clinical re-infection by VZV in pregnancy rather than disseminated herpes zoster for several reasons:

1) the generalized onset of the rash with no dermatomal distribution,
2) the development of neonatal varicella in the newborn,
3) the presence of varicella zoster IgG, and
4) the mild course of illness in both the mother and the newborn.

This case suggests that a clinical re-infection by varicella in the peripartum period can cause neonatal varicella, however more case reports of this rare phenomenon will be required to confirm this. Moreover, this case demonstrates that the presence of varicella IgG does not necessarily exclude a diagnosis of varicella or guarantee immunity. Clinicians need to remain alert for the possibility of varicella re-infection. Pregnant women are a group of the population at higher risk of morbidity and mortality from varicella, although the evidence suggests that the course of illness may be milder, the diagnosis of varicella re-infection should still be considered if the clinical picture is consistent; isolation protocols should be enacted swiftly and specialist advice sought.

**REFERENCES**


