Neonatal Varicella : A Report of 26 Cases

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Abstract

Varicella infection usually occurs in childhood and is uncommon in neonates.We reported 26 cases of neonatal varicella seen at the Queen Sirikit National Institute of Child Health, Bangkok, from 1988 to 1995. The sex ratio of male to female was equal. The age of onset was between 6 to 27 days. Twelve cases contracted varicella from mothers who were infected between 6 days before delivery to 2 days after delivery (perinatal varicella) and fourteen cases contracted varicella from mothers or siblings in the postnatal period (postnatal varicella). All babies developed vesicular rash. Intravenous acyclovir was given in high risk and severe cases (nine perinatal and three postnatal varicella patients). Complications of neonatal varicella included clinical sepsis 8 cases (30%), pneumonia 7 cases (26%), pyoderma 9 cases (35%) and hepatitis 1 case (4%). There was no statistical difference between the complications of perinatal and postnatal group ($p > 0.05$). No death was observed during this study. Clinical manifestations of neonatal varicella varied from mild to severe, depending on the onset of rash in the mother and baby and mode of transmission of the disease. Although we have no varicella - zoster immunoglobulin (VZIG), acyclovir therapy is beneficial in the treatment of neonatal varicella.

Key word : Varicella, Infection, Neonates

Varicella infection usually occcurs in childhood and is uncommon in neonates and pregnant women(1). However, when varicella develops in pregnant women, the effect to the fetus and neonate varies. If the mother contracts varicella during the first trimester, it can cause congenital varicella syndrome which is characterized by limb atrophy, cicatricial skin lesions, eye defects and central nervous system anomalies. The risk of the anomalies vary from about 3 to 5 per cent(2-6). If the mother had varicella during the last 3 weeks of pregnancy, 25 per cent of neonates will develop varicella and the mortality rate of untreated babies is high, about 20-30 per cent(7-8).

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We describe 26 cases of neonatal varicella seen at the Queen Sirikit National Institute of Child Health during an eight year study period.

MATERIAL AND METHOD

A retrospectively study was carried out on cases of neonatal varicella admitted to the Neonatal Unit, Queen Sirikit National Institute of Child Health from 1988 to 1995. The diagnosis of neonatal varicella was made from the history of maternal varicella or contact from siblings who had varicella and the clinical manifestation of generalised vesicular rash. Tzanck's smears were performed in all cases and were positive for multinucleated giant cells.

We divided the patients into two groups : perinatal and postnatal groups.

1) Perinatal group : infants who were born from mothers who had varicella within 21 days before delivery to 2 days after delivery (transplacental route).

2) Postnatal group : infants who were born from mothers who had varicella more than 2 days after delivery or infants who contracted varicella from other sources beside the mothers (non- transplacental : skin, respiratory route).

STATISTICAL ANALYSIS

We used Student's *t* test and Fisher's exact test for comparision between the two groups.

RESULTS

Demographic data (Table 1)

There were 26 cases of neonatal varicella, 12 cases in the perinatal group and 14 cases in the postnatal group. The sex ratio of male to female was equal. The ages of the mother were between 18 years to 33 years. Most of the babies were term babies. Mean birthweight of the babies were 3020 ± 370 grams. The sex ratio and mean birth weight of the two groups were not statistically different.

Table 1. Sex, birthweight and age of onset, birthweight between perinatal group & postnatal group.

	Perinatal	Postnatal	Total	p-value
Number of cases	12	14	26	
Sex ratio	0.6 : 1	1.8 : 1	1.1 : 1	0.2
Mean BW (g)	3095 ± 270	2956 ± 439	3020 ± 370	0.50
Mean age of onset (days)	10.9 ± 2.5	20.7 ± 5.1	16.5 ± 6.5	0.002

Table 2. Clinical manifestations, treatments and complications of perinatal varicella.

Cases	Onset of rash (days)		Clinical		Treatment		Complications
	Mother	Baby	Fever	Pneumonia	Acyclovir	Antibiotic	
*1	-6	7	+	+	+	IV	Sepsis, pneumonia
*2	-4	6	+	-	+	IV	Sepsis, pyoderma
3	-2	12	+	-	+	-	Pyoderma
*4	-2	10	+	++	+	IV	Pneumonia with respiratory failure
*5	-2	15	+	-	+	IV	Sepsis, pyoderma
6	-2	11	-	-	+	-	-
7	-1	11	-	-	-	-	-
8	0	9	+	-	-	PO	Pyoderma
*9	+1	13	+	+	+	-	Pneumonia
10	+1	12	-	-	-	-	-
*11	+2	12	+	+	+	IV	Sepsis, pneumonia
*12	+2	13	+	-	+	IV	Sepsis

NB * severe cases; IV = intravenous route; PO = per oral

Cinical manifestations (Table 1, 2, 3)

For the perinatal group, the mothers had the onset of rash from 6 days before delivery to 2 days after delivery, the babies had onset of rash between 6 days to 15 days after birth. (mean age of onset = 10.9±2.5 days)

All the babies had generalised vesicular rashes which varied from mild with only a few vesicles, to numerous and widespread monomorphous vesicular rash (Fig. 1-3). In this group, four cases developed pneumonia shown by clinical symptoms and film chest. One case (the 4th case) developed pneumonia with respiratory failure. Five cases developed clinical sepsis and five cases developed pyoderma.

Table 3. Clinical manifestations, treatments and complications of postnatal varicella.

Cases	Onset of rash (days)		Clinical		Treatment		Complications
	Mother	Baby	Fever	Pneumonia	Acyclovir	Antibiotics	
1	+3	13	-	-	-	-	-
2	+3	13	-	-	-	-	-
3	+3	17	-	-	-	IV	Pyoderma
*4	+4	14	+	+	+	IV	Sepsis, pneumonia
*5	+10	25	+	+	+	IV	Sepsis, pneumonia
*6	+11	18	+	+	+	IV	Sepsis, pneumonia
7	+10	20	-	-	-	-	-
8	+20	27	-	-	-	-	-
9	-	20	-	-	-	PO	Pyoderma
10	-	21	+	-	-	PO	Pyoderma
11	-	25	-	-	-	IV	Pyoderma (Cellulitis)
12	-	25	-	-	-	-	-
13	-	25	-	-	-	-	Hepatitis
14	-	27	-	-	-	IV	Pyoderma

NB. * severe cases IV = intravenous PO = per oral

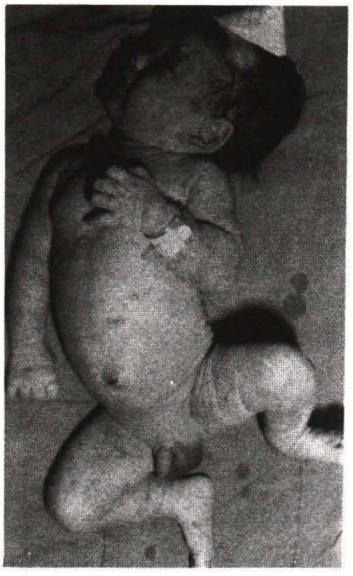

Fig. 1. Generalised vesicular rash in neonatal varicella.

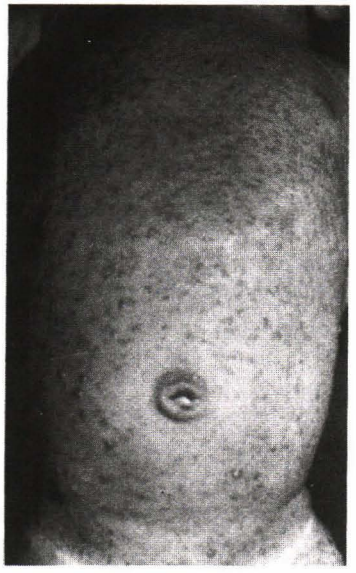

Fig. 2. Extensive monomorphous vesicular rash on the abdomen.

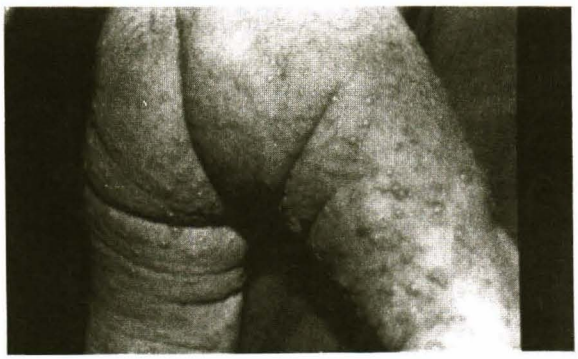

Fig. 3. Widespread monomorphous vesicular rash on the buttock.

Table 4. Complications of neonatal varicella.

	Perinatal (N=12)	Postnatal (N=14)	p-value
Pneumonia	4 (33%)	3 (21%)	0.4
Sepsis	5 (41%)	3 (21%)	0.24
Pyoderma	4 (33%)	5 (35%)	0.6
Hepatitis	0 (0%)	1 (7%)	0.5

N = Number of cases

In the postnatal group, eight cases (case No.1-8) contracted varicella from mothers who had varicella more than 2 days after delivery and six cases (case No. 9-14) contracted varicella from siblings. Mean age of the onset of rash in this group was 20.7±5.1 days which was longer than the perinatal group. All cases developed mild vesicular rash which was the same as in older children. In this group the clinical manifestations were mild, only with skin lesions except the 4th, 5th and 6th cases who had pneumonia and the 13th case who developed hepatitis.

Treatment (Tables 2, 3)

In the perinatal group, intravenous acyclovir in the dose of 30 mg/kg/day for 7 to 10 days was given in 9 cases due to clinical sepsis and pneumonia and for prophylaxis in the high risk group. Intravenous cloxacillin and gentamicin were given in seven cases of perinatal varicella due to sepsis and pyoderma. Another three cases were healthy without antiviral or antibiotics treatment.

In the postnatal group, most of the babies (11 cases) were healthy without clinical sepsis except the 4th, 5th and 6th cases. Acyclovir was given in these three cases because of clinical sepsis and pneumonia. Systemic oral antibiotics were given due to pyoderma (5 cases).

Complications

The complications of neonatal varicella were pneumonia (7 cases), clinical sepsis (8 cases), pyoderma (9 cases) and hepatitis (1 cases). No death was observed during this study.

There was no statistically significant difference between the complications of perinatal and postnatal group ($p>0.05$). (Table 4)

DISCUSSION

Varicella rarely occurs in the neonatal period as 98 per cent of the population acquire the disease during childhood and pregnant women transfer passive immunity to the fetus[4]. Varicella in the neonates are acquired by transplacental route during the stage of viremia in the mother or by direct contact from the varicella lesions on the mother's skin or siblings during postpartum[8,9]. The clinical manifestation of neonatal varicella is more severe than in older children because of the immature immune system and the route of infection is from transplacental rather than respiratory route or skin[9].

Diagnosis of neonatal varicella is usually made by history of either recent maternal varicella or postnatal exposure and the generalised vesicular exanthem. In some cases without the definite history, the differential diagnosis of vesicular eruption in neonates includes neonatal herpes simplex, impetigo and contact dermatitis.In neonatal herpes, the vesicles tend to occur in clusters rather than in the more generalised distribution seen in varicella. Fever, marked toxicity and encephalitis are more common in neonatal herpes infection. In impetigo, large blebs are present instead of small vesicles of varicella. For contact dermatitis, papules and vesicles may appear on exposed body surfaces after exposure to specific chemical irritants[10]. In this study all the patients had a history of varicella either from the mother or the family.

The clinical course of neonatal varicella varies from mild to severe depending on the onset of rash in the mother and baby, and on the mode of transmission.

Onset of rash in the mother and in the baby

If the mother had varicella within 4 days before delivery to 2 days after delivery, it is considered to be high risk and the clinical manifestation is severe because of viremia in the mother and absence of transplacental antibody. If the mother had varicella for more than 5 days before delivery to 2 days after delivery, the mother would have had protective antibody to protect the baby, so the clinical manifestation is mild.

It was hypothesised that in the neonates with early onset (5 to 10 days), maternal illness had occurred long enough before parturition to allow antibodies from the mothers to cross the placenta.

Meyers found four deaths among 13 neonates (31%) whose mothers' rash developed within 4 days before birth, but no deaths were observed among 23 neonates with congenital varicella whose mothers developed rash five or more days before birth. Meyers also found that no deaths occurred among 22 infants whose onset of rash was between birth to 4 days of age. In contrast 4 of 19 (21%) of neonates in whom the rash began 5 to 10 days after birth died(11).

Mode of transmission

If the baby contracts varicella during the perinatal period, the clinical manifestation is more severe than from the postnatal period(7,8).

The clinical manifestations of neonatal varicella may vary in its progression as well as in the severity. Infants who had only mild illness developed few macules, papules and vesicles over a period of 3 to 5 days without fever or other systemic illness. Some infants had extensive cutaneous eruptions and visceral involvement like other immunocompromised hosts.The mortality rate of neonatal varicella is as high as 30 per cent. In fatal cases, postmortem examinations revealed generalised involvement of the lung, liver, spleen, heart, adrenal, pancreas, kidneys, gastrointestinal tract and skin(8,910).

Management of neonatal varicella includes isolation of the baby in the first instance. Infants whose mothers had onset of rash within 5 days before delivery or within 2 days after delivery, varicella-zoster immunoglobulin (VZIG) should be given as soon as possible after delivery. In normal fullterm infants whose mothers' rash developed more than 48 hours after delivery, VZIG is not indicated because they are not known to be at any greater risk of complications of varicella than older children. However, hospitalised premature infants (<28 weeks gestation or < 1000 grams) who are exposed to varicella should receive VZIG because of poor transfer of varicella antibody across placenta to the baby(13-19).

In this study, we had no VZIG therapy, so intravenous antiviral therapy was the drug of choice for treatment of severe neonatal varicella. Acyclovir was given in 9 cases in the perinatal group as the complications of pneumonia and in the high risk patients. For the postnatal group, acyclovir was not indicated in all cases but in this study, three cases in the postnatal group were severe, so acyclovir was given.

In conclusion, management of neonatal varicella depends on the onset of rash in the mother and in the baby, but the most important things are the clinical manifestations of the baby. If the patient has fever and signs of visceral involvement, antiviral therapy should be given as soon as possible.

(Received for publication on November 14, 1997)

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อีสุกอีใสในทารกแรกเกิด : รายงานผู้ป่วย 26 ราย

ศรีศุภลักษณ์ สิงคาลวณิช, พ.บ., วนิดา ลิ้มพงศานุรักษ์, พ.บ.*, สุนทร ฮ้อเผ่าพันธ์, พ.บ.**, วิไล ราตรีสวัสดิ์, พ.บ.***

ผู้รายงานได้ทำการศึกษาโรคอีสุกอีใสในทารกแรกเกิด จำนวน 26 รายซึ่งรับไว้ในสถาบันสุขภาพเด็กแห่งชาติมหาราชินี ตั้งแต่ปีพ.ศ. 2531-2538 ผลการศึกษาพบว่าเพศชายเท่ากับเพศหญิง แบ่งผู้ป่วยเป็น 2 กลุ่ม กลุ่มที่ 1 ทารกได้รับเชื้อจากมารดาที่เป็นอีสุกอีใสภายใน 6 วันก่อนคลอดถึง 2 วันหลังคลอด (perinatal group) จำนวน 12 ราย กลุ่มที่ 2 ทารกได้รับเชื้อจากมารดาที่เป็นอีสุกอีใสมากกว่า 2 วันหลังคลอดหรือได้รับเชื้อจากญาติพี่น้องที่เป็นอีสุกอีใส จำนวน 14 ราย ผู้ป่วยทุกรายมีตุ่มใสกระจายทั่วร่างกาย การรักษา กลุ่มที่ 1 ได้รับยาต้านไวรัสทางเส้นเลือดดำ 9 ราย กลุ่มที่ 2 ได้รับยาต้านไวรัสทางเส้นเลือดดำเพียง 3 ราย ผลการรักษา ผู้ป่วยทุกรายหายเป็นปกติ โรคแทรกซ้อนที่พบทั้งหมดได้แก่ ซึม 8 ราย (30%) ปอดอักเสบ 7 ราย (26%) การติดเชื้อแบคทีเรียที่ผิวหนัง 9 ราย (36%) และตับอักเสบ 1 ราย (4%) โดยพบว่าโรคแทรกซ้อนทั้ง 2 กลุ่ม ไม่แตกต่างกันอย่างมีนัยสำคัญทางสถิติ อาการและอาการแสดงของอีสุกอีใสในทารกแรกเกิดอาจแตกต่างกันตั้งแต่ไม่รุนแรงจนถึงรุนแรงขึ้นกับระยะเวลาที่ทารกได้รับเชื้อจากมารดา อายุทารกและอาการแสดงของทารกในรายที่มีอาการรุนแรงจำเป็นต้องได้รับการรักษาด้วยยาต้านไวรัสอย่างทันท่วงที

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