

Original Article

Clinical characteristics and prognosis of collodion babies

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Abstract: Objective: This study aimed to investigate the clinical characteristics of collodion babies. Methods: Clinical information of 16 collodion babies that received treatment in the Neonatal Intensive Care Unit, between 2009 and 2018, was retrospectively reviewed. Perinatal factors, clinical manifestations, therapeutic response, and findings from follow ups were analyzed. Results: There were 11 full-term babies and 5 premature babies. Caesarean section was noted in 13 cases (82%) and the first delivery in 12 (71%). Of these, the disease was cured in 16 cases and improved in 7 cases. One collodion baby refused to receive treatment and one died. Two babies developed skin sclerosis and decrustation, twice, due to concomitant pneumonia or sepsis. New skin slowly formed and complete formation of new skin was observed for up to 30 days in babies with sepsis. Infections (pneumonia and sepsis) often affect disease progression or cause recurrence, but they had no influence on prognosis. Prevention and infection control are crucial for treatment of collodion babies. Conclusion: Collodion babies usually have a good prognosis. Extra-hospital rational skin care is key for protection and maintenance of skin appearance and function and for improved quality of life.

Keywords: Collodion baby, ichthyosis

Introduction

Collodion baby (CB), as a disease, was first reported in 1884 by Hallopean. It is a rare skin disease with an incidence of 1:50,000-1:100,000 [1, 2]. The term CB refers to a newborn whose entire body is covered with an adherent, supple, and parchment-like membrane at birth. Skin lacks elasticity and is systemically bright. Limb motion is usually limited by the skin and ectropion of lids and lips. Auricular deformity may also be present [3]. The parchment-like membrane generally falls off about 3-4 weeks after birth and normal skin forms, but the skin may develop different types of ichthyosis later [3, 4]. Diagnosis of CB is easy but there are some complications at initial stages of CB that are difficult to treat. Moreover, most parents have no confidence regarding treatment and prognosis of CB. Currently, there

are no studies on CB with large sample sizes. The present study retrospectively reviewed clinical information of 16 babies with CB, receiving treatment in the past 9 years. Clinical characteristics and prognoses were reported.

Materials and methods

Patients

A total of 16 babies with CB were retrospectively analyzed. Babies with an adherent, supple, and parchment-like membrane at birth were diagnosed with CB.

Clinical characteristics

General characteristics: Of the 16 babies diagnosed with CB, there were 8 males and 8 females. There were 11 full-term babies and 5 premature babies. Cesarean section was noted

Collodion baby

Table 1. Perinatal characteristics

Case	Gender	No of delivery	Pregnancy term (weeks)	Type of delivery	Age of mother	Reasons for cesarean section	Apgar score	Placenta	Amniotic fluid	Umbilical cord	Birth weight (g)	Gestational complications
1	F	1	38+2	Cesarean section	27	Oligohydramnios	10/10/10	Normal	Less	Normal	3400	No
2	F	2	39+6	Eutocia	20	No	9/9/9	Normal	Normal	Normal	2200	No
3	F	1	38+	Cesarean section	25	Breech presentation	9/10/10	Calcification	Normal	Umbilical cord around the neck	2900	No
4	F	1	37+5	Cesarean section	30	Premature rupture of membranes	10/10/10	Normal	Normal	Normal	3100	No
5	M	1	40+6	Cesarean section	28	Oligohydramnios	9/9/9	Normal	Less	Normal	3300	No
6	M	1	37+2	Cesarean section	28	Premature rupture of membranes	10/10/10	Normal	Bloody amniotic fluid	Normal	3040	No
7	M	1	35	Cesarean section	34	No	10/10/10	Normal	Normal	Normal	2510	No
8	F	1	40+6	Cesarean section	30	Fetal heart rate acceleration	10/10/10	Normal	Amniotic fluid pollution	Normal	3300	No
9	F	1	36	Cesarean section	25	Pre-eclampsia	10/10/10	U/A	Normal	Normal	2000	No
10	F	2	39	Cesarean section	33	Scar uterus	10/10/10	Normal	Normal	Normal	2930	No
11	F	1	39	Cesarean section	28	Breech position	10/10/10	Normal	Normal	Normal	3160	No
12	M	1	35	Cesarean section	28	Placental abruption	10/10/10	Placental abruption	Normal	Normal	2980	No
13	M	1	39+2	Cesarean section	30	Difficult delivery	10/10/10	Normal	Normal	Normal	3900	Gestational diabetes
14	M	2	36+3	Cesarean section	32	Premature rupture of membranes	10/10/10	Normal	Normal	Torsion of the umbilical cord	3100	Gestational diabetes
15	M	2	36	Eutocia	35	Amniotic fluid pollution	9/9/9	Normal	Amniotic fluid pollution	Knot of the umbilical cord	3030	No
16	F	1	40	Eutocia	29	Normal	10/10/10	Normal	Normal	Normal	3000	No

Collodion baby



Figure 1. A: At 4 hours after birth, the whole-body skin became red and light, and was collodion or parchment like. B: At 1 day after birth, ectropion of lids and lips, “O” type mouth and auricular deformity were observed. C: At 4 days after birth, parchment like skin became shedding; fresh and red skin was exposed at the chapped site and became erythema-like; the fresh skin had light-yellow exudate and was uneven. D: At 10 days after birth, fresh skin formed, ectropion of lids and lips disappeared, and cracks were observed at skin folds. Photos were used with approval from the guardians of these patients.

in 13 cases and eutocia in 3 cases. Placental abruption was found in 1 case, premature rupture of membranes in 3 cases, and placental calcification in 1 case. Amniotic fluid pollution was observed in 2 cases, bloody amniotic fluid in 1 case, and oligohydramnios in 1 case. Pre-eclampsia was found in 1 case and scarred uterus in 1 case. Breech delivery was noted in 2 cases, knot of umbilical cord in 1 case, and umbilical cord around the neck in 1 case. Apgar scoring showed that scores of these babies were ≥ 8 at 1, 5, and 10 minutes after birth. Birth weights ranged from 2000 g to 3900 g, while one baby was small for gestational age.

Characteristics of mothers: All mothers received regular prenatal examinations. Mean age of the mothers was 28.9 ± 3.7 years (20-28 years: $n=8$; 29-35 years: $n=8$). All mothers had singleton pregnancies. First delivery was noted in 12 mothers (71%) and second delivery in 4 mothers. Moreover, CB was found in both deliv-

eries of two mothers. Gestational diabetes mellitus was also found in 2 mothers (**Table 1**).

Clinical characteristics: CB occurred at 3-16 hours after birth. All babies developed skin cracks or shedding within 16 hours after birth. This was more evident at the perioral area, joints of the limbs, and abdominal or chest areas, with intense activities and skin wrinkles. Chapped skins exposed red fresh skin which was erythema-like, had light-yellow exudate, and was uneven. Skin shedding initiated at the chapped sites and, thereafter, involved the whole body. Skin shedding of the head, hands, and feet occurred later. Skin stripping occurred at 1-2 weeks after birth in most babies. Fresh skin became keratotic, the whole-body fresh skin formed at about 2-3 weeks, and the ectropion of lids and lips disappeared. Two babies had concomitant sepsis and pneumonia, thus their course of CB was longer. Skin sclerosis and shedding occurred twice and skin keratini-

Collodion baby

Table 2. Case details

Case	Time of disease onset (h)	Fresh skin formation	Ectropion of lids and lips/auricular deformity	Complications	Time of treatment (d)	Therapeutic response
1	4	-	-/-	No	4	Improvement
2	2	15	+/-	Pneumonia	17	Improvement
3	3	-	+/+	Pulmonary hemorrhage, septicemia, hypokalemia, hyperglycemia, acute renal failure	2	Death
4	4	30 (occurring twice)	+/+	Sepsis	59	Recovery
5	12	21 (occurring twice)	+/+	Sepsis, pneumonia, hyperbilirubinemia	25	Recovery
6	16	9	-/-	Pneumonia, hypernatremia	11	Recovery
7	4	20	+/+	Pneumonia	34	Improvement
8	7	9	+/-	Pneumonia, hyperbilirubinemia	9	Recovery
9	12	14	+/-	Pneumonia	17	Improvement
10	2	15	+/+	Pneumonia	25	Improvement
11	3	20	+/-	Pneumonia	33	Improvement
12	3	13	+/+	Pneumonia, myocardial injury, hypoproteinemia, hyperbilirubinemia	17	Improvement
13	4	16	+/-	Pneumonia, myocardial injury, hypokalemia, IDM syndrome	22	Recovery
14	3	10	+/+	IDM syndrome	15	Recovery
15	3	-	+/+	Pneumonia, sepsis, myocardial injury, patent ductus arteriosus, pulmonary hypertension, etc	7	Refuse to receive treatment
16	8	10	+/+	No	15	Recovery

Collodion baby

Table 3. Case details

Case	Age (yr)	Gender	Itching	Anhidrosis	Skin allergy	Desquamation	Hair loss	Palmoplantar skin keratosis, cracking	Facial features	Character, psychology	Development	Factors related to deterioration	Seasonal change	Phenotype	Treatment
1	9	F	+	-	-	Whole-body White scaly exuvium	-	+	Red face	-	-	-	Deterioration in spring and winter	1	Silicone oil
2	9	F	-	-	-	White exuvium at armpits, and groin	-	-	-	-	-	-	-	1	Emollient
3	/		/	/	/	/	/	/	/	/	/	/	/	/	/
4	8	F	+	+	-	Grey white scaly exuvium at chest and femoribus internus	-	-	-	-	-	-	Deterioration in spring and winter	2	Silicone oil
5	7	M	+	+	-	Whole-body dry skin; White scaly exuvium	-	+	-	-	-	-	Deterioration in spring and winter	2	Emollient
6	7	M	+	-	-	Whole-body dry skin; White scaly exuvium	-	-	-	-	-	-	Deterioration in spring and winter	1	
7	5	M	-	-	-	Gray ichthyosis around the belly button	-	-	-	-	-	-	Deterioration in spring and winter	2	Silicone oil
8	5	F	+	+	-	Dry skin at chest and back; whole body and head exuvium	-	+	-	-	-	-	-	2	-
9	5	M	+	-	-	Grey scaly exuvium at chest and back	-	-	-	-	Thin	-	Deterioration in spring and winter	2	Emollient
10	5	F	-	-	-	Whole-body dry skin; White scaly exuvium	-	+	-	-	-	-	Deterioration in spring and winter	2	Silicone oil
11	5	F	+	+	-	Whole-body dry skin; White scaly exuvium	+ oligotrichosis	+	-	Mild influence	-	Sensitivity to temperature and wind	Deterioration in spring and winter	2	Emollient
12	4	M	+	+	-	Whole-body dry skin; White scaly exuvium	-	+	-	-	-	-	Deterioration in winter	2	Emollient
13	4	M	-	+	-	Whole-body dry skin; grey scales at abdomen and groin	-	+	-	-	-	-	Deterioration in winter	2	Emollient
14	0.7	M	-	-	-	White scaly exuvium at chest and back	-	-	-	-	-	-	-	1	Silicone oil
15	/	M	/	/	/	/	/	/	/	/	/	/	/	/	/
16	0.6	F	-	-	-	Dry skin	-	-	-	-	-	-	-	Normal	Emollient

Notes: 1. congenital ichthyosiform erythroderma; 2. Lamellar ichthyosis.

zation stopped at about 1 month after birth (**Figure 1**). Neonatal pneumonia was found in 10 cases, pulmonary hemorrhage in 1 case, myocardial injury in 3 cases, septicemia in 4 cases, hyperbilirubinemia in 2 cases, infant of diabetic mother (IDM) syndrome in 2 cases, hypokalemia in 2 cases, hypoglycemia in 1 case, hypoproteinemia in 1 case, and hypernatremia in 1 case. Echocardiography showed patent ductus arteriosus and pulmonary hypertension in 1 case (**Table 2**).

Treatment

After admission, the babies were placed in an incubator with a humidity of 60-70%. Procedures were reduced, aiming to decrease skin friction, and sterilized gloves were used for each procedure. Nitrofurazone solution was used for bathing every day and retinoic acid ointment was used on the whole skin to improve dry skin. For babies with ectropion of lids, their eyes were covered with vaseline gauze to protect the cornea and conjunctiva. Tobramycin eye drops were used for prevention of eye infections. Ectropion of the lips may cause difficulty in food intake. Thus, most babies received nasal feeding soon after admission, then oral feeding. For babies with infections, antibiotics were actively used. Nutritional support was administered, intravenous fluid infusions were performed to prevent dehydration, and measures were taken to prevent complications.

Prognosis

Of the 16 babies, 2 were siblings but there was no family history in other patients. In these patients, 14 babies were discharged after recovery (n=7) or improvement (n=7), the parents of one baby refused to receive treatment, and one baby died. In addition, 2 babies had concomitant pneumonia or sepsis. Skin sclerosis and shedding occurred twice. Fresh skin slowly formed and complete fresh skin formation was noted for up to 1 month. The parents of one baby refused to receive further treatment due to serious disease (this was the second delivery of the mother, the first baby was also diagnosed with CB and died of secondary infection 2 months after birth). One baby had concomitant pulmonary hemorrhaging, acidosis, hyperglycemia, and hypokalemia, and died. Thus, follow up was performed via telephone for 14 babies, with ages ranging from 6 months to 8 years. Whole-body dry skin was noted in all

babies, with this condition varying over seasons (**Table 3**). A total of 9 babies developed typical lamellar ichthyosis, ranging from gray, lamellar, and armor-like scales at local sites (such as the abdomen, groin, chest, back, and head) in mild cases to whole-body gray scales with itching in serious cases. Once the disease deteriorated in a specific season, ectropion of lids and chapped palmoplantar skin were present. A total of 4 babies developed mild congenital non-bullous type ichthyosis-like erythema, characterized by whole-body reddish skin with white scales. One baby showed red skin on the face. One baby had dry skin without scaly exuvium (**Figure 2**). Six patients had anhidrosis and their skin was sensitive to temperature. Eight patients displayed palmoplantar skin sclerosis and cracks. In one baby, severe lamellar ichthyosis mildly affected character and psychology (irritability and introversion), but abnormalities in character, psychology, hearing, vision, intelligence, and behavior were not observed in the remaining babies. For treatment, emollients were used in most babies (such as silicone oil cream).

Discussion

CB is an autosomal recessive disease found to be associated with mutations of TGM1, ALOX12B, and ALOXE3 [3]. CB is a phenotype diagnosis, sharing clinical manifestation of different types of ichthyosis at early stages [5]. It has the potential to progress into different types of ichthyosis, of which lamellar ichthyosis and congenital ichthyosiform erythroderma are the most common [6]. About 10-20% of babies with CB will develop mild ichthyosis, also known as self-healing ichthyosis [7]. With development of medical and nursing techniques, the mortality of CB babies has reduced from 80% in 1960 to 11% in 1986. It is 5% presently [1, 3]. There are no specific measures for prevention and treatment of CB. Babies with CB may have multiple complications, including hypernatremia, hypoproteinemia, hypothermia, dehydration, infections, conjunctivitis, and corneal injury in the neonatal period [8]. Prevention of dehydration, nutritional support, management of complications, and skin care are critical in the treatment of this disease [1].

In the present study, premature babies accounted for 31%. Of these, 1 was small for gestational age. Cesarean section was noted in 13 cases due to premature rupture of membranes, amni-

Collodion baby



Figure 2. A: Oligotrichosis with massive scales shedding. B: Lamellar scales on the face and bilateral mild ectropion of lids. C: Lamellar scales on the neck. D: Finger skin sclerosis, cracking, and peeling with restricted motion. E: Mild desquamation at lower abdomen. F: mild dry skin at abdomen. G: Dry skin at palm. H: Lamellar scales in lower limbs. I: Dry skin at back with white scaly exuvium. J: Brown scaly exuvium at back. Photos were used with approval from the parents.

otic fluid contamination, fetal malposition, and placental abruption, according to the order of incidence. However, there was no significant correlation between cesarean section and CB. There is evidence showing that CB is more likely found in male babies [3, 9], but this was not observed in present cases (male: n=7; female: n=9). One baby had serious complications (such as pulmonary hemorrhage, sepsis, and acute renal failure), causing death, but ichthy-

sis was not the direct cause of death. The parents of one baby were concerned with the prognosis and refused to receive treatment due to serious complications. CB in the remaining babies recovered or improved and patients were discharged. Ten babies had concomitant pneumonia. The high incidence of pneumonia might be ascribed to the aspiration of shedding scales in the amniotic fluid [10]. Four babies had concomitant sepsis. Of these, premature

rupture of membranes was noted in 2 cases, oligohydramnios in 1 case, and amniotic fluid pollution in 1 case. Sepsis was caused by staphylococcus epidermidis in one baby and by urine enterococci another baby. Two babies with sepsis had recurrent skin peeling. Fresh skin grew slowly, possibly related to the intra-uterine infection after premature rupture of membranes and impaired skin barrier function. IDM syndrome was found in 2 babies but the control of blood glucose did not affect formation of new skin. One baby had hypernatremia, likely caused by skin-related dehydration. One baby had hypoproteinemia, likely related to protein exudation after placental abruption and skin chapping. Although it has been reported that the use of emollient will increase the risk for skin infection [3], use of retinoic acid ointment in present cases achieved good skin protection, consistent with previous reports [11]. Beverley et al. found the plasma uric acid and lactic acid increased after use of urea and lactic acid ointment, respectively, in 2 babies [12]. Yamamura et al. reported that external use of cuticle exfoliants could cause salicylic acid poisoning in babies [13]. Therefore, some clinicians have speculated that the skin of these babies may absorb drugs, causing subsequent poisoning. In the present study, nitrofurazone solution after dilution was used for bathing. This did not cause liver and kidney dysfunction or other manifestations of poisoning. Moreover, this management achieved good prevention of skin infections (only 1 baby developed staphylococcus epidermidis infection).

Regarding humidity of the incubator, 60% has been recommended by most investigators [1, 8]. It has been suggested that humidity should be maintained at 60-70% and adjusted according to fluid intake and urination. The time to transfer babies from the incubator to bed has not been specified [14], while gradual accommodation to extra-incubator environment and reduction in incubator humidity may achieve good efficacy [8]. Perez-Lopez et al. recommended that the early use of N-acetylcysteine was helpful for prevention of corneal injuries due to ectropion of lids [15]. In the present cases, vaseline gauze was used to cover the eyes and tobramycin eye drops were employed for protection of the cornea and prevention against conjunctivitis. Follow ups were completed via telephone in 14 cases (2 were lost to follow up, 1 died, and 1 refused to receive treatment). Ages of these patients ranged from 6

months to 9 years, with CB mainly progressing into lamellar ichthyosis and congenital ichthyosiform erythroderma. Dry skin and systemic or focal scaly scaling deteriorated over seasons. This may have been related to poor moisturizing of the skin, along with dry air and low temperatures in the spring and winter of Northern China. Six babies had anhidrosis. Their skin was sensitive to temperature and palmoplantar skin cracking was noted in most cases. This might be ascribed to the damage to hair follicles and appendages in neonatal period. Of babies receiving follow ups, one had serious lamellar ichthyosis, which deteriorated over seasons. Itching, anhidrosis, hair loss, and palmoplantar skin cracking were also observed (**Figure 2**). Character and psychology were affected by this disease as well. In the remaining babies receiving follow ups, development of intelligence, hearing, language, and behavior was normal, except for mild or serious ichthyosis (**Table 2**). Taieb et al. speculated that the times of formation and shedding of parchment-like membranes were closely related to prognosis of CB [16].

In the present analysis of clinical characteristics and prognosis, results failed to identify factors related to the prognosis of CB, consistent with previous reports [4]. In the present cases, mild CB babies had mild dry skin, but no scales. Skin was normal in one baby diagnosed with self-healing CB. However, skin pathological examinations and gene examinations were not performed in this study. Therefore, diagnosis of self-healing CB should be further confirmed by more examinations. Anders Vahlquist et al. performed gene analysis in babies with self-healing CB. They proposed replacing self-healing CB with the term "self-improving collodion ichthyosis" (SICI), as it is better to summarize and supplement this type of ichthyosis due to its genetic diversity and clinical overlap [17]. In these cases, infections (pneumonia and sepsis) were found to deteriorate the disease condition and delay fresh skin formation, causing recurrence.

Prophylactic use of antibiotics is not recommended for CB babies, but infections should be dynamically monitored. Once infection was noted, effective antibiotics should be promptly used to prevent against deterioration due to complications [1]. Based on findings from follow up, CB in most babies progressed to different types of ichthyosis, suggesting a good prognosis. Clinicians should deepen their under-

standing of this disease and communicate with patient families, relieving their nervousness, anxiety, and fear about this disease. When the disease condition becomes stable, clinicians should encourage the mothers to perform breast-feeding [8]. During extra-hospital treatment, skin care (especially in the winter or spring with disease deterioration) is a key for maintenance of skin appearance and function. In addition, serious ichthyosis mildly affects the character and psychology of a baby, suggesting the necessity of psychological intervention.

Taken together, CB is a disease with impaired skin barrier function. Development of neonatal care significantly reduces the mortality of CB babies. Prevention and control of infections are crucial for treatment of CB in the neonatal period. After discharge, rational skin care is key for protection and maintenance of normal skin function, as well as improved quality of life.

There were limitations to this study. Skin pathological examinations and gene examinations were not performed. Therefore, this study failed to evaluate prognosis according to phenotype. This will be done in future clinical work.

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Disclosure of conflict of interest

None.

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